

Universidade Federal do Rio de Janeiro
Instituto de Psiquiatria
Programa de Pós-Graduação em Psiquiatria e Saúde Mental

ANÁLISE DAS TENTATIVAS DE SUICÍDIO, QUALIDADE DE VIDA E DE
POLIMORFISMOS NOS GENES 5-HTT, IL 10 E TNF ALFA EM PACIENTES DO
SERVIÇO PÚBLICO DE SAÚDE DE ARAPIRACA - ALAGOAS

Verônica de Medeiros Alves



UFRJ

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Tese de doutorado apresentada ao
Programa de Pós-graduação em
Psiquiatria e Saúde Mental, da
Universidade Federal do Rio de Janeiro,
como parte dos requisitos necessários à
obtenção do título de Doutora em Saúde
Mental.

Orientador: Antonio Egidio Nardi

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“Por vezes sentimos que aquilo que fazemos não é senão uma gota de água no mar. Mas o mar seria menor se lhe faltasse uma gota”.
(Madre Teresa de Calcutá)

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RESUMO

ANÁLISE DAS TENTATIVAS DE SUICÍDIO, QUALIDADE DE VIDA E DE POLIMORFISMOS NOS GENES 5-HTT, IL 10 E TNF ALFA EM PACIENTES DO SERVIÇO PÚBLICO DE SAÚDE DE ARAPIRACA – ALAGOAS

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Resumo da Tese de Doutorado submetida ao Programa de Pós-graduação em Psiquiatria e Saúde Mental, da Universidade Federal do Rio de Janeiro - UFRJ, como parte dos requisitos necessários à obtenção do título de Doutora em Saúde Mental.

Introdução: Os transtornos mentais e as tentativas de suicídio exercem impacto significativo sobre a vida do paciente e de sua família. Encargos econômicos e psicossociais, familiares e individuais, rupturas e desorganização das rotinas cotidianas e de trabalho, perdas de produtividade, gastos específicos ligados ao tratamento, estigma e oportunidades perdidas são exemplos de fatores que interferem na Qualidade de Vida (QV) de pacientes com transtornos mentais. Os transtornos mentais e o suicídio sofrem interferência de fatores ambientais e genéticos. Diversos estudos mostram sua associação com polimorfismos genéticos, mas estes ainda são inconclusivos. **Objetivo:** Analisar as tentativas de suicídio, qualidade de vida e polimorfismos nos genes 5-HTT, IL 10 e TNF alfa em pacientes do serviço público de saúde de Arapiraca/Alagoas. **Metodologia:** Esta tese engloba dados epidemiológicos e genéticos e será dividida em dois capítulos. 1) Os dados epidemiológicos estão em 06 artigos, sendo 5 originais e um de revisão sistemática. 2) Os dados genéticos estão em 03 artigos, sendo uma revisão sistemática, uma metanálise e um artigo original. **Resultado:** Os artigos com perfil epidemiológico identificaram que o hospital em estudo apresentou um grande número de atendimento por tentativa de suicídio, sendo mais frequente em mulheres. O adulto jovem tentou suicídio com mais frequência, mas os idosos apresentaram resultado significativo em relação ao número de tentativas. O meio mais utilizado foi o envenenamento por medicamento ou por veneno, produto químico e raticida.

Avaliando os enfermeiros que trabalham no hospital em estudo e os policiais do batalhão militar da cidade de Arapiraca/Alagoas percebemos que alguns apresentaram nível de ansiedade elevado; risco para depressão e ideação suicida ao longo da vida; e cronotipo indiferente. Identificamos que a maioria das pessoas entrevistadas com transtorno mental e tentativa de suicídio atendidas pelo serviço de saúde da cidade de Arapiraca eram solteiras, com baixa escolaridade, ganhavam menos de um salário mínimo, não trabalhavam, tinham risco para tentativa de suicídio à época do exame e baixa QV. Os transtornos mentais mais significantes entre os que tentaram suicídio foram: transtorno obsessivo-compulsivo, transtorno do estresse pós-traumático, transtorno depressivo, episódio maníaco, transtorno do pânico, fobia social, transtorno de ansiedade generalizada e dependência/abuso de álcool. Os artigos com características genéticas identificaram a participação de diversos genes relacionados ao transtorno bipolar. O gene transportador de serotonina (5-HTT) apresenta um polimorfismo (5-HTTLPR) como preditor de transtorno mental e suicídio. O alelo C do polimorfismo rs1800871 (IL10) está associado a presença de transtorno mental sem tentativa de suicídio em mulheres. O genótipo A/T do polimorfismo rs2020933 (5-HTT) foi identificado como fator de proteção para o número de tentativas de suicídio (2-3 vezes). A ausência do alelo T do polimorfismo rs2020933 apresentou correlação com histórico familiar de transtorno mental. TNF- α (rs1800629) não apresentou associação com transtorno mental e tentativa de suicídio. **Discussão:** Não existem registros de dados psiquiátricos nos prontuários dos pacientes atendidos nesse hospital, o que dificulta fazer relações entre tentativa de suicídio e presença de transtorno mental ou acompanhamento psiquiátrico e psicoterápico. Existem poucas publicações sobre suicídio em idosos e as que existem não trazem dados completos sobre as condições de saúde do mesmo. Os enfermeiros e policiais que não apresentaram cronotipo indiferente tem mais dificuldade de concentração e menos disposição em trabalhar em turnos que não coincidem com seu cronotipo, o que pode trazer complicações futuras a sua saúde. A baixa QV dos pacientes com transtorno mental e tentativa de suicídio pode ser reflexo da baixa escolaridade e renda mensal, desemprego e precárias condições de saúde. A análise dos polimorfismos estudados permitiu identificar a participação do gene IL10 no transtorno mental sem tentativa de suicídio em mulheres e do gene 5-HTT no histórico familiar de transtorno mental e no número de tentativas de suicídio. **Conclusão:** A identificação

do perfil das tentativas de suicídio contribui para o planejamento de cuidados de prevenção e reabilitação mais objetivos. O controle e dispensação de medicamentos, agrotóxicos e raticidas devem ser mais rigorosos, evitando seu fácil acesso. Quanto a participação de polimorfismos nos genes 5-HTT, IL10 e TNF- α , outros estudos precisam ser realizados em populações variadas para identificar a participação desses polimorfismos nos transtornos mentais e nas tentativas de suicídio. Esse tipo de pesquisa apresenta forte potencial de contribuição para etiologia e tratamento de alguns transtornos mentais.

Palavras-chave: Transtorno mental, tentativa de suicídio, qualidade de vida, estudo de associação, polimorfismo, IL10, TNF alfa, 5-HTT.

ABSTRACT

ANÁLISE DAS TENTATIVAS DE SUICÍDIO, QUALIDADE DE VIDA E DE POLIMORFISMOS NOS GENES 5-HTT, IL 10 E TNF ALFA EM PACIENTES DO SERVIÇO PÚBLICO DE SAÚDE DE ARAPIRACA – ALAGOAS

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Antonio Egidio Nardi

Abstract da Tese de Doutorado submetida ao Programa de Pós-graduação em Psiquiatria e Saúde Mental, da Universidade Federal do Rio de Janeiro - UFRJ, como parte dos requisitos necessários à obtenção do título de Doutora em Saúde Mental.

Introduction: Mental disorders and suicide attempts suffer interference from environmental and genetic factors, causing a significant impact on the life of the patients and their families. Economic and psychosocial, disruption, disorganization of every day routines and work, productivity losses, specific expenses related to treatment, stigma and missed opportunities are examples of factors that interfere in the quality of life (QoL) of patients with mental disorders. Several studies show their association with genetic polymorphisms, but these are still inconclusive. **Objective:** To analyze suicide attempts, quality of life and polymorphisms in the 5-HTT, IL 10 and TNF alfa genes in patients of public health service of Arapiraca/Alagoas. **Methodology:** This thesis includes epidemiological and genetic data and was divided into two parts. 1) Epidemiological data are in six articles, being five originals and one systematic review. 2) Genetic data are in three articles, being one systematic review, one meta-analysis and one original article. **Result:** Articles with epidemiological profile identified that there were a large number of attendance for attempted suicide in hospitals, which are more frequent in women. Young adult attempted suicide more often, but elderly showed significant results when were compared to the number of attempts and death. The most used was the medicinal poisoning or by poison, chemical and rat poison. Comparing nurses who were working in hospital and police officers of Arapiraca/Alagoas, we realized that some studies showed high level of anxiety; risk for depression and suicidal ideation over the life; and chronotype indifferent. We have identified that most of people

interviewed with mental disorder and suicide attempt who were assisted by health service of Arapiraca were single, with low education level, earned less than minimum wage and did not work, had risk for suicide attempt at the time of the exam and low QoL. The most significant mental disorders among those who committed suicide attempt were: obsessive-compulsive disorder, post-traumatic stress disorder, depressive disorder, manic episode, panic disorder, social phobia, generalized anxiety disorder and alcohol dependence/abuse. Articles with genetic traits identified that there were participation of several genes related to bipolar disorder. The serotonin transporter gene (5-HTT) presents a polymorphism (5-HTTLPR) as a predictor of mental disorder and suicide. The C allele polymorphism rs1800871 (IL10) was associated with the presence of mental disorder without attempted suicide in women. The A/T genotype of rs2020933 polymorphism (5-HTT) has been identified as a protection factor for the number of suicide attempts (2-3 times). The absence of the T allele of rs2020933 polymorphism showed correlation with family history of mental disorder. TNF- α (rs1800629) showed no association with mental disorder and suicide attempt. **Discussion:** There were no psychiatric data records on patients' medical charts in this hospital, which complicates making relations between suicide attempt and presence of mental disorders. There were few publications on suicide in elderly, which did not provide complete data on health conditions of the patient. Nurses and police officers who were not indifference chronotype and they had more trouble concentrating and less willingness to work in shifts that didn't match their chronotypes, which might get future disturbance in their health. The low QoL in patients with mental disorders and suicide attempts might be a reflection of low education and income, unemployment and poor health conditions. Polymorphisms studies have identified the IL10 gene involvement in mental disorder without attempted suicide in women and the 5-HTT gene in family history of mental disorder and in number of suicide attempts. **Conclusion:** The identification of the profile of the suicide attempts contributes to the planning of prevention and rehabilitation care more objectives. Providers must have to control of medicines, pesticides and rodenticides as necessary so prevent its easy access. Presence of polymorphisms in the 5-HTT, IL10 and TNF alpha genes, other studies need to be conducted in several population to identify the participation of these polymorphisms in mental disorders and suicide attempts. This type of research presents strong potential to contribute to the etiology and treatment of some mental disorders.

Keywords: Mental disorder, suicide attempt, quality of life, study of association, polymorphism, IL10, TNF alpha, 5-HTT.

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LISTA DE ABREVIATURAS, SÍMBOLOS E SIGLA

IDH	Índice de Desenvolvimento Humano
IL10	Interleucina 10
QV	Qualidade de Vida
QoL	Quality of Life
TNF alfa	Fator de Necrose Tumoral alfa
UFRJ	Universidade Federal do Rio de Janeiro
5-HTT	Transportador de serotonina
5-HTTLPR	Polimorfismo na região promotora do gene transportador de serotonina

1 INTRODUÇÃO

O transtorno mental é um dos principais precedentes para o comportamento suicida. Cerca de 90% a 98% das pessoas que se suicidam têm um transtorno mental¹. Transtornos afetivos, esquizofrenia, dependência de drogas e transtorno de personalidade são os transtornos mentais mais comuns².

O comportamento suicida é uma expressão relacionada a uma série de fenômenos ligados ao suicídio e engloba: suicídio, tentativa de suicídio e ideação suicida³.

O suicídio é entendido como o ato suicida propriamente dito, quando o desfecho é sempre o óbito do indivíduo. A palavra suicídio deriva do latim e significa Sui - de si mesmo e Caedes - ação de matar. Caracteriza-se por um desejo da própria pessoa em pôr fim a sua vida, a fim de escapar de uma dor ou um sofrimento insuportável⁴.

A tentativa de suicídio tem as mesmas características fenomenológicas do suicídio, diferindo deste apenas quanto ao desfecho, que não é fatal³. Já a ideação suicida é caracterizada por pensamentos suicidas e/ou pela verbalização do desejo de suicidar-se expresso pelo indivíduo⁵.

A Organização Mundial de Saúde estima que a causa das mortes por suicídio é de 1 milhão de pessoas por ano. O risco maior é entre 15 e 44 anos de idade. Para cada morte por suicídio estima-se que existam 20 vezes mais casos de tentativa de suicídio⁶.

Entre os anos de 1998 e 2008, o total de suicídios no Brasil representou um aumento de 33,5%, enquanto o crescimento da população do país foi de 17,8%, no mesmo período⁷. O Brasil está entre os dez países com maiores números absolutos de suicídio⁸. Apresenta ainda, representativa diferença entre as taxas de suicídio nas diversas regiões geográficas^{1,9}. Arapiraca é uma das cidades do Estado de Alagoas que apresenta um elevado número de suicídios¹⁰. Foram sete óbitos em 2009 (3,32/100.00 hab.). Entre os anos 2000 e 2009, foram registrados 110 óbitos, com uma média de 11 óbitos por ano (0,9 óbitos/mês)¹⁰.

Inexistem registros sistemáticos das tentativas de suicídio no Brasil. A falta desse registro dificulta um melhor conhecimento da situação e das características dos sujeitos, bem como o planejamento de serviços¹. Para cada suicídio, existem

pelo menos dez tentativas que exigem atenção médica e para cada tentativa de suicídio registrada, existem quatro não conhecidas¹¹. Isto nos mostra que, os poucos dados que dispomos sobre as tentativas de suicídio estão subnotificados e não representam a nossa realidade.

Existem vários fatores interferindo no desencadeamento do suicídio. São fatores psicológicos, sociais, ambientais, familiares, culturais e genéticos. Dentre esses fatores destaca-se o abuso físico ou sexual, morte de um amigo ou familiar, desemprego, vergonha ou desonra, decepções amorosas, a presença de transtorno mental e de tentativa de suicídio na família, histórico de transtorno mental e de tentativa de suicídio pelo indivíduo³. Fatores sociais, tais como viver sozinho ou não viver com a família, também têm sido associados com um risco aumentado de suicídio¹².

Existem ainda vários fatores de proteção para transtornos mentais que podem contribuir como fatores protetores para o suicídio, como alojamento seguro, segurança em geral, boa alimentação e períodos adequados de repouso³, viver com a família, receber suporte social, uso de medicamento adequado e a adesão ao tratamento eficaz¹²⁻¹⁴.

Pessoas com transtorno mental e trabalhadores que lidam com situações de estresse estão mais sujeitas a alterações emocionais que influenciam no comportamento suicida. Enfermeiros e policiais militares são profissões que se enquadram nesse risco.

O trabalho da polícia, mesmo pacífica e em países desenvolvidos, é um trabalho difícil e estressante, com altos níveis de risco as exposições, a violência e aos horários de trabalho exaustivo. Esses trabalhadores têm um maior risco para transtornos mentais, como depressão, ansiedade, transtorno de estresse pós-traumático e suicídio, com maior prevalência que a população em geral¹⁵.

Miquelin e colaboradores¹⁶ referem que o ritmo intenso de atividade do profissional de Enfermagem desrespeita o seu ritmo biológico. Além disso, a ausência de um programa de trabalho, as longas distâncias percorridas durante as jornadas laborais, a dimensão e disposição inadequada dos mobiliários, somados à grande quantidade de informações relativas ao trabalho e a atitude de vigília podem ocasionar não só o desgaste físico como também a fadiga mental e o estresse.

Mediante as particularidades de trabalho dos enfermeiros e policiais militares, o estudo dos cronotipos mostra-se relevante. Nas últimas décadas, houve um

crescente interesse pela cronobiologia do comportamento mental, psicológico e social, sendo avaliada sob o aspecto do ritmo biológico, certamente devido à periodicidade de seus sintomas¹⁷.

A cronobiologia pode ser descrita como a ciência que estuda a organização temporal dos fenômenos biológicos, fisiológicos e/ou psicológicos, que permite a compreensão de que o organismo é fisiologicamente diferente a cada momento do dia, com capacidade diferente de reagir aos estímulos ambientais, sejam eles físicos, químicos, biológicos ou sociais¹⁸.

Cronotipos são diferentes padrões de atividade comportamental relacionada aos denominados perfis cronobiológicos, que se classificam como matutinos, vespertinos e indiferentes¹⁹. Os matutinos são indivíduos que se sentem ativos pela manhã, prefere deitar e acordar cedo. Os vespertinos são aqueles que conseguem deitar tarde porque sentem-se mais ativos à tarde e início da noite e podendo, dormem pela manhã, e os indiferentes são aqueles indivíduos que têm maior flexibilidade, escolhendo horários intermediários de acordo com as necessidades de sua rotina^{19,20}.

O suicídio é um fenômeno complexo de causas diversas, sendo importante indicador da qualidade de vida das populações²¹. A própria insatisfação do paciente interfere na maneira como ele interpreta a sua Qualidade de Vida (QV), influenciando o mesmo a tentar o suicídio. A QV deve ser entendida como algo que vai além do crescimento econômico de um país. Ela está envolvida com fatores como: relacionamentos sociais, realização pessoal, percepção de bem-estar, possibilidades de acesso a eventos culturais, oportunidades de lazer, educação, saúde, satisfação e liberdade^{22,23}. Os fatores ambientais, físicos, psicológicos e relações sociais da QV identificam as condições de vida em que vivem as pessoas com transtorno mental e história de tentativa de suicídio. Essa avaliação da QV pode contribuir com informações que minimizem suas angustias e insatisfações e promovam o bem-estar²⁴.

O comportamento suicida se manifesta devido a uma combinação de fatores biológicos, comportamentais e sociais. Embora estudos com gêmeos tenham relatado uma herdabilidade significativa em 30% a 50% dos casos²⁵, a etiologia do suicídio continua sendo desconhecida. Assim, fatores psicológicos, biológicos, econômicos e sociocultural fazem do suicídio, um fenômeno complexo²⁶.

Estudos realizados com genes candidatos à susceptibilidade ao suicídio vêm sendo realizados e vários genes candidatos ao desenvolvimento de transtornos mentais e tentativa de suicídio têm sido investigados em diferentes populações no mundo²⁷⁻³⁰. Para alguns genes, a associação com transtorno bipolar²⁷, esquizofrenia²⁸, depressão maior²⁹ e transtorno obsessivo compulsivo³⁰ vem mostrando dados consistentes. Em outro grupo de genes³¹⁻³³, os resultados são conflitantes, o que reforça a necessidade de se investigar pacientes com diferentes perfis genético e populacionais³⁴.

Um dos fatores que dificultam as pesquisas em transtornos mentais é a heterogeneidade genética, ou seja, o mesmo fenótipo resultar de diferentes genes comprometidos^{35,36}. Dados da literatura apontam a relação de diversos genes com transtornos mentais e tentativa de suicídio. Dentre eles, podem ser citados os genes: IL10 (Interleucina 10)^{32,37,38}, TNF- α (Fator de necrose tumoral alfa)³³ e 5-HTT (Transportador de serotonina)³⁹.

O gene IL10 e TNF- α são citocinas inflamatórias e podem causar inflamação no sistema nervoso central⁴⁰. Essa inflamação pode interferir na função da serotonina⁴¹, levando a entender que haja participação do gene transportador de serotonina na patofisiologia do transtorno do humor e comportamento suicida⁴².

Citocinas pró e anti-inflamatórias vem apresentando relação com transtornos mentais como a depressão³³ e esquizofrenia^{32,37,38}, mas seu mecanismo patofisiológico ainda necessita de investigação²⁷. O gene IL10 está relacionado a produção da interleucina 10, que é uma citocina anti-inflamatória. O gene TNF- α está relacionado a produção do fator de necrose tumoral alfa, que é uma citocina pró-inflamatória. O gene 5-HTT está relacionado com a presença de transtornos mentais e suicídio^{39,43-46}.

Estes genes necessitam de uma análise mais complexa sobre a sua possível contribuição na tentativa de suicídio e transtornos mentais. Estudos de associação correlacionam frequências alélicas e genotípicas entre indivíduos afetados não relacionados e o grupo controle. Os estudos de associação visam identificar os loci de susceptibilidade. A maioria dos estudos de associação se utiliza diretamente de genes hipoteticamente relacionados ao fenótipo (genes candidatos). Esta estratégia tem permitido a identificação de genes envolvidos com diferentes transtornos psiquiátricos, em diversas populações.

Pesquisas sobre polimorfismos genéticos disponíveis na literatura científica são insuficientes para serem aplicadas na prática clínica, mas a preocupação com esta investigação é uma tendência crescente e mundial.

A análise genética desse estudo possibilitou a correlação das variações genéticas individuais com parâmetros clínicos como o número de tentativas de suicídio, tipo de transtorno mental e histórico familiar de transtorno mental, contribuindo com dados de grande significância científica.

O levantamento do perfil das tentativas de suicídio, a análise da QV dos pacientes com transtornos mentais e tentativa de suicídio, em conjunto com a avaliação genética pode contribuir com informações relevantes para um melhor planejamento de cuidado à esse grupo. Isso permitirá um melhor acolhimento, acompanhamento e tratamento a esses pacientes. Portanto, a presente tese tem como objetivo: Analisar as tentativas de suicídio, qualidade de vida e polimorfismos nos genes 5-HTT, IL 10 e TNF- α em pacientes do serviço público de saúde de Arapiraca - Alagoas.

2 METODOLOGIA

O tema de estudo dessa tese surgiu mediante a vivência das aulas práticas da disciplina de Saúde Mental que ministrou no Curso de Enfermagem da Universidade Federal de Alagoas – Campus Arapiraca. Havia uma grande quantidade de pessoas atendidas no serviço de saúde mental de Arapiraca, por tentativa de suicídio. Surgiu então, minha curiosidade em saber o que poderia estar influenciando esse número elevado de casos.

a) Local de estudo: A pesquisa foi realizada nos Centros de Atenção Psicossocial (CAPS) e nas Unidades de Saúde da Família (USF) localizados em Arapiraca/Alagoas.

b) Sujeitos da pesquisa: A amostra foi composta por usuários com transtornos mentais e história de tentativa de suicídio. Usuários sem transtorno mental e sem história de tentativa de suicídio. Usuários sem transtorno mental e sem história de tentativa de suicídio, que foram considerados o grupo controle. Enfermeiros do hospital de urgência e emergência de Arapiraca/Alagoas. Policiais militares do batalhão de Arapiraca/Alagoas.

c) Aspectos éticos: Este projeto foi aprovado pelo Comitê de Ética e Pesquisa da Universidade Federal de Alagoas (UFAL) e os sujeitos estudados expressaram sua aquiescência através do Termo de Consentimento Livre e Esclarecido.

d) Instrumentos: Foram utilizados o Questionário de Identificação, Questionário de Avaliação da Qualidade de vida (WHOQOL)⁴⁷, Escala de Ideação Suicida de Beck⁴⁸, MINI (Mini International Neuropsychiatric Interview)⁴⁹, Questionário Horne-Ostberg (Tipos Matutinos – Vespertinos)⁵⁰, Escala de depressão do *Center for Epidemiologic Studies* – CES-D⁵¹ e Inventário de Ansiedade de Beck⁵².

e) Análise genética: A coleta de DNA ocorreu por meio de esfregaço bucal utilizando escova citológica estéril e descartável. O material coletado foi armazenado num microtubo (2 mL) contendo solução TES (10 mM Tris HCl, 1 mM EDTA e 0,6% SDS). O DNA foi extraído utilizando solução salina segundo protocolo modificado de Abrão et al.⁵³. A amostra de DNA foi armazenada num tubo contendo solução TE (10 mM Tris HCl, 1 mM EDTA), a -20°C no Laboratório de Genética Molecular e Expressão Gênica da Universidade Federal de Alagoas, localizado em Arapiraca. A integridade do DNA foi avaliada por eletroforese em gel de agarose a

1%. A genotipagem dos polimorfismos estudados foi realizada por meio do kit de reagentes e avaliação de discriminação de alelos TaqMan (Applied Biosystem, Foster City, CA, USA) no aparelho Steep One Plus (Applied Biosystems, USA).

Esta tese engloba dados epidemiológicos e genéticos e foi dividida em duas partes: Resultados epidemiológicos e Resultados genéticos.

A) Parte 1 - Resultados epidemiológicos: estão em 06 artigos, sendo 5 originais e uma revisão sistemática.

- 1) Alves VM, Silva AMS, Magalhães APN, Andrade TG, Faro ACM, Nardi AE. Suicide attempts in a emergency hospital. *Arquivos de Neuropsiquiatria* 2014; 72(2):1-6.
- 2) Magalhães APN, Alves VM, Comassetto I, Lima PC, Faro ACM, Nardi AE. Atendimento às tentativas de suicídio por serviço de atenção pré-hospitalar. *Jornal Brasileiro de Psiquiatria* 2014; 63(1):16-22.
- 3) Alves, VM, Maia ACCO, Nardi AE. Suicide among elderly: a systematic review. *MEDICALEXPRESS* 2014; 1(1):1-7.
- 4) Alves VM, Santos MBF, Nascimento LMS, Ferro GC, Silva LKB, Nardi AE. Suicidal ideation and chronotype assessment in nurses and police officers. *MEDICALEXPRESS* 2015; 2(3):1-6.
- 5) Alves VM, Francisco LCFL, Belo FMP, de-Melo-Neto VL, Barros VG, Nardi AE. Evaluation of the quality of life and risk of suicide. *Clinics*, in press.
- 6) Alves VM, Francisco LCFL, Melo AR, Novaes CRMN, Belo FMP, Nardi AE. Trends of suicide attempts in emergency service. Submetido para publicação.

B) Parte 2 - Resultados genéticos: estão em 03 artigos, sendo uma revisão sistemática, uma metanálise e um original.

- 1) Alves VM, Silva ACP, Neto VLM, Andrade TG, Nardi AE. Associations between genetic polymorphisms and bipolar disorder. *Revista de Psiquiatria Clínica* 2012; 39(1):34-9.
- 2) Alves VM, Bezerra DG, Andrade TG, de-Melo-Neto VL, Nardi AE. Genetic Polymorphisms Might Predict Suicide Attempts in Mental Disorder Patients: A Systematic Review And Meta-Analysis. *CNS & Neurological Disorders - Drug Targets* 2015; 14:820-827.

- 3) Alves VM, Silva ACP, Souza EVM, Francisco LCFL, Moura EL, Nardi, AE.
Suicide attempt in mental disorders: their association with 5-HTT, IL-10 and
TNF-alpha polymorphisms. Submetido para publicação.

3 RESULTADOS

Parte 1 - Resultados epidemiológicos

Suicide attempts in a emergency hospital

Perfil de tentativas de suicídio em um hospital de emergência

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Abstract

This study aimed to characterize the profiles of suicide attempts that were attended to in the Hospital of Alagoas in the year 2010. Four hundred sixty-one charts and service bulletins were analyzed. Patients attempting suicide were predominately female. There were significant difference for suicide attempts (SAs) among men and women in the age of 10 to 19 years and 60 to 69 years. Women have tried more suicide aged between 10 and 19 years and men between 60 and 69 years. The ingestion of drugs was the most frequent method for women; and poisoning, use of sharp objects and hanging for men. The results of this study may contribute to elaboration, planning and implementation of preventive measures to reduce cases of SAs.

Keywords: suicide, attempted, suicide, emergency service, hospital, epidemiology.

Resumo

Este estudo teve como objetivo caracterizar o perfil das tentativas de suicídio (TS) que foram atendidos num Hospital de Alagoas, no ano de 2010. Quatrocentos e sessenta e um boletins foram analisados. Houve diferença significativa para as tentativas de suicídio entre homens e mulheres nas faixas etárias de 10 a 19 anos e de 60 a 69 anos. As mulheres cometem mais suicídio na faixa etária entre 10 e 19 anos e os homens entre 60 e 69 anos. A ingestão de drogas foi o método mais frequente para as mulheres; o envenenamento, uso de objetos pontiagudos e enforcamento para homens. Os resultados deste estudo podem contribuir para a elaboração, planejamento e implementação de medidas preventivas em casos de TS.

Palavras-chave: tentativa de suicídio, suicídio, serviço hospitalar de emergência, epidemiologia.

The most important baseline predictors of suicide attempts (SAs) are baseline severity, the number of previous hospitalizations and the length of the current episode of depression¹. The probability of having two or more SAs over the past year increased with the severity of substance use and violent behavior across attempter subtypes. A previous study indicates that the treatment of depressive symptoms in teen attempters remains an important goal².

Suicidal and nonsuicidal self-harm are both significant risks for depressed adolescents treated in the clinic. The

presence of family dysfunction, high levels of suicidality and recent self-harm (suicidal or nonsuicidal) should alert us to a high risk for future SA. The presence of recent nonsuicidal self-injury is by far the strongest predictor of future nonsuicidal self-injury³.

A previous study has shown that, regardless of gender, the risk factors that are significantly associated with increased odds of SA include suicidal ideation, depressive symptoms, having a friend with a past history of attempted or completed suicide, and having a family member with a history of

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attempted suicide. Parental loss predicts the likelihood of SA after a year but not after 7 years, suggesting that the mental health consequences resulting from the death of a parent may not persist into young adulthood⁴.

A study of the death registration data for 83 countries identified only 20 countries that had high-quality death registration data that could be used to estimate injury mortality because the data were frequently classified using imprecise and partially specified categories. Analytical methods that can derive national estimates of injury mortality from alternative data sources are needed for countries without reliable death registration systems⁵.

Thus, suicide demands intersectorial actions of confrontation for damage reduction, that have multidisciplinary and transdisciplinary characteristics⁶. The planning and implementation of intersectorial actions is necessary to meet the profile of SA cases of the region. This objective of this study was to characterize the profile of SA cases that were attended to in the Hospital of Urgency and Emergency of interior Alagoas in the year 2010.

METHOD

This study employed a quantitative approach with descriptive and retrospective documental analysis. The study population was identified through input newsletters for patient care due to SA between January and December of 2010. All charts and service bulletins suicide attempts made in 2010

were analyzed. Newsletters that were erased, illegible or contained indefinite diagnoses of SA during the study period were excluded. Data collection was performed in the Emergency Unit by Dr. Daniel Houly, Brazil/Alagoas/Arapiraca from January to March of 2012. The Emergency Unit is a state public service that provides urgent inpatient treatment.

To extract information concerning the study sample, we used a form that included the following information: date and hour of treatment in hospital, age, sex, reason for treatment in hospital, municipality of origin, use of alcohol/drugs, use of prescriptions, presence of psychological assessments, presence of mental disorder (identified by the patient or relatives report) and methods used in the suicide attempts.

Data analysis was performed with the EPI INFO 2000 statistical program and is organized and presented in the form of a table and graphics to aid discussion of the results. The χ^2 statistical test was used. Data analysis employed odds ratios with 95% confidence intervals with confidence limits, and a significance level of $p < 0.05$ was used to determine significance.

This study was approved by the Ethics and Research Committee of the Federal University of Alagoas/Brazil under Protocol no. 014804/ 2011-06 in December 20, 2011.

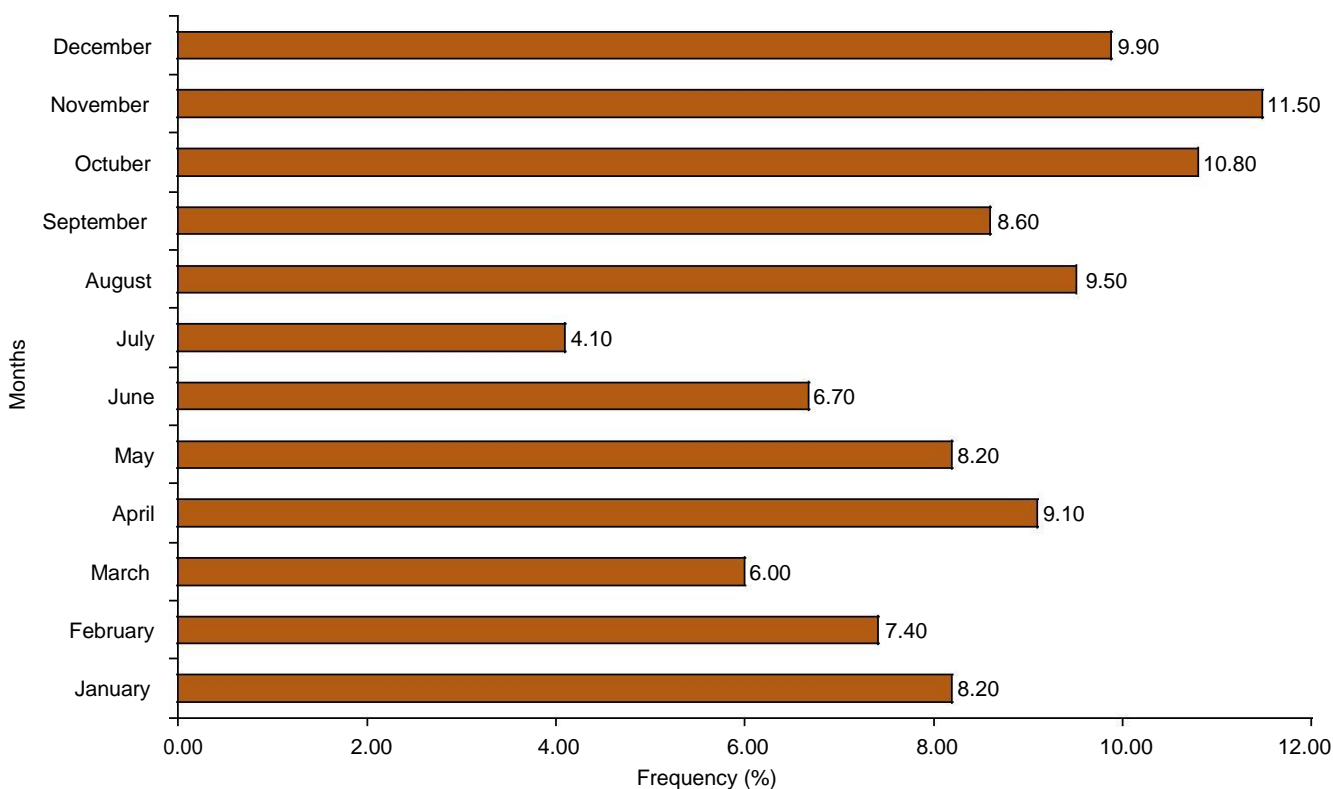


Figure. Percentage distribution by months of the year relative to cases of suicide attempt, attended in a hospital of urgency and emergency of Alagoas, Brazil, in 2010.

RESULTS

Four hundred sixty-one cases of SA were analyzed, and there were an average of 38,4 monthly hospital visits due to SA. November was the month of with the most occurrences (53–11,5%) hospital visits due to SA, and July had the lowest occurrence (19–4.1%) (Figure).

SAs occurred most frequently between 12h00 and 17h59 hours (177–38.4%). The interval with the least frequent occurrence of cases (46–9.9%) was between 00h00 and 05h59 hours. Eighty-five cases occurred between 6h00 and 11h59 (18.4%), and 153 (33.2%) cases occurred between 18h00 and 23h59.

We observed a predominance of SAs in females (307–66.6%) relative to males (154–33.4%). Comparison of the age ranges and the sexes revealed that the majority of women that tried suicide were younger than the men that did so. One hundred twenty (26%) of the cases of SA attended to were in the age range of 10–19 years old, 178 (38.6%) were between 20–29 years old, and 83 (18%) were between 30–39 years old (Table 1). We found a statistically significant difference ($p=0.00069$) between women and men in the age range of 10 to 19 years old; women in this age range had a 2.31 fold ($1.38<OR<3.90$) greater chance of SA than men in the same age range. The age range of 20 to 29 years old stands out as the age range with the highest occurrence of cases in both sexes (Table 1) ($p=0.3574$). No cases of SA were found

in individuals 75 years or older. In the age range of 60 to 69 years old, men had an 8.36 fold ($1.62<OR<57.69^*$) greater chance of SA than women in the same age range (*Fisher test, $p=0.0031$). There were two cases, one in each gender, of SA in 10-year-old children.

Among the 461 SA cases treated in Emergency Unit Dr. Daniel Houly, 220 (47.7%) cases were from Arapiraca. Arapiraca is the second most populous city in the State of Alagoas, Brazil and has a population of 214.006 inhabitants. The 241 (52.3%) remaining cases were referred to SA of resident people in several surrounding cities.

Women were observed to ingest medications with greater frequency (279–58.7%) (Table 2), and this was the method most frequently used by women (225–71.2%). A statistically significant difference ($p=0.0000$) was found in the ingestion of medications as an SA method; women had a 4.81 fold ($3.13<OR<7.39$) greater chance of using this method. The utilization of the intentional poisoning (124–26.1%) occurred with the greatest in men (63–39.6%) (Table 2). A statistically significant difference ($p=0.0000$) was found in the use of poisoning in SAs; men had a 2.74 fold ($1.76<OR<4.28$) greater chance of using this method.

The most violent means of SAs, such as biting objects (25–5.3%), hanging (7–1.5%) and firearms (3–0.6%), were methods that were employed preferentially by males

Table 1. Distribution of suicide attempts according to age range and gender, in the hospital of Alagoas, Brazil (urgent and emergency care), 2010.

Age (years)	Female		Male		p	Total	
	N°	%	N°	%		N°	%
10–19	95	30.9	25	16.2	0.00069	120	26
20–29	114	37.1	64	41.6	0.3574	178	38.6
30–39	50	16.3	33	21.4	0.1753	83	18
40–49	34	11.1	19	12.3	0.6885	53	11.5
50–59	11	3.6	5	3.3	0.8524	16	3.5
60–69	2	0.7	8	5.2	0.0031	10	2.2
Ignored	1	0.3	–	–	–	1	0.2
Total	307	100	154	100	–	461	100

Table 2. Distribution of methods used in suicide attempts, in the hospital of Alagoas, Brazil (urgent and emergency care), 2010.

Methods to Attempt	Female		Male		p	Total	
	N°	%	N°	%		N°	%
Ingestion of medication	225	71.2	54	34	0.0000	279	58.7
Poisoning	61	19.3	63	39.6	0.0000	124	26.1
Ingestion of cleaning products	14	4.4	12	7.5	0.1588	26	5.5
Ingestion of others chemical products	3	1	4	2.5	0.1812	7	1.5
Cutting objects	8	2.5	17	10.7	0.00017	25	5.3
Firearms	0	0.0	3	1.9	–	3	0.6
Hanging	2	0.6	5	3.1	0.03204	7	1.5
Precipitation from a great height	2	0.6	1	0.6	0.996	3	0.6
Others	1	0.3	0	0.0	–	1	0.2
Total	316	100	159	100	–	475	100

(Table 2). No woman made use of a firearm in a SA. A statistically significant difference ($p=0.00017$) in the use of bit-ing objects as a means of SA was found; men had a 4.61 fold ($1.83<OR<11.95$) greater chance of using this method. Regarding the use of hanging, men (5–3,1%) were more likely to use this method than women (2–0.6%) (Table 2).

Among the cases of SA, 423 (90.4%) people had a main natural lesion of intoxication. This type of lesion was followed by cuts (23–5%), perforating wounds (5–1.1%), asphyxia (4–0.9%), head trauma (3–0.6%), fractures (2–0.4%), polytraumas (2–0.4%), contusions (1–0.2%), other lesions (3–0.6%) and unreported lesions (2–0.4%).

Among the cases of SAs by poisoning (124–26.1%) in which the toxic agent was specified, 31 (24.2%) were intoxicated with aldicarb. The use of a poison that is used on tobacco plantations (12–9.3%) was also a means of SA in the population of this study.

Multiple organs (423–90%), the upper limbs (16–3.4%) and the neck (10–2.1%) were the regions of the body with the most damage resulting from SAs. Following these regions were the head/face (8–1.7%), lower limbs (8–1.7%), abdo-men/hip (2–0.4%), thorax/dorsum (1–0.2%) and unreported lesions (2–0.4%).

Among the women, 17 (5.5%) were identified as expect-ant mothers. Of these, seven (41.2%) were in the first trimes-ter of gestation, one (5.9%) was in the second, and one (5.9%) was in the third. This information was not available in eight (47%) cases.

Forty-three (9.3%) cases of SA occurred under the influence of alcohol. The frequency of the use of alcohol was higher among men (24–55.8%) than women (19–44.2%). A statistically signif-icant difference ($p=0.00107$) between SA and consumption of alcohol was found; men had a 2.8 fold ($1.42<OR<5.54$) greater chance of consuming alcohol and attempting suicide.

Among the 461 newsletters analyzed, only 15 (3.3%) registers reported previous SAs, and only 42 (9.1%) registers reported the presence of related mental disorders. The type of disorder was reported in only eight cases, and records of the use of psychoac-tive medications were present for only 26 (5.6%) cases.

Regarding developments of cases, 326 (70.7%) obtained medical discharge, 73 (15.8%) were routed to other servic-es, and followed after discharge to until they failed to appear (7–1.5%), obtained a waiver (1–0.2%), were ignored (37–8%)

or died (17–3.7%). The routed services included Psychosocial Care Centers (53–72.6%), ambulatory hospitals (3–4.1%), psy-chiatric hospitals (3–4.1%) and others (14–19.1%). Only 112 (24.3%) patients were submitted to a psychological evaluation, and 340 (73.7%) did not receive this type of evaluation.

Death was more frequent in males (13–76.5%) than females (4–23.5%) ($p=0.00012$). Men had a 6.98 fold ($20.7<OR<25.86$) greater chance of death during an attempt-ed suicide than women (Table 3). Poisoning was the main cause of death in both sexes (11–64.7%), followed by hanging (3–17.6%) and firearms (2–11.8%) (Table 3). The highest incidence of death occurred in the age range of 20 to 39 years old (9–52.8%; seven males and two females). The number of cases diminished among males at 40 years old and grew between ages of 60 to 69 years old (3–17.6%).

DISCUSSION

Suicide attempts are violent self-inflicted events that bring serious repercussions to both the attempter and the family and friends. Discussions related to this theme are still considered taboo due to the fear that discussion may stimu-late the act. It is known that speaking about suicide is one of the best methods of preventing it. Thus, research in this area is of extreme relevance to eliminate this stigma.

Epidemiological studies of suicide attempts are not com-mon in Brazil; thus little is known about the prevalence and profiles of suicide. A study that traced the profile of 160 cases of SA that were attended to in a general hospital of Rio de Janeiro identified September as the month with the highest occurrence of the SA (20 cases), while March had the lowest occurrence (7 cases)⁷. The present study found the months of November and July to have the highest and lowest frequen-cies of suicide attempts, respectively.

Studies of cases of SA that were attended to in urgency and emergency units of Brazilian municipalities have shown prevalences in females (300–58%) that are higher than those of males (214–41%)^{8,9}. This is similar to the current study by presenting similar sample and predominance of suicide attempts in females.

This study examined the records of three cases of SA in children. National data suggest that suicide is practically

Table 3. Distribution of deaths following suicide attempts, in the hospital of Alagoas, Brazil (urgent and emergency care), 2010.

Mode of death	Female		Male		p	Total	
	Nº	%	Nº	%		Nº	%
Poisoning	3	27.3	8	72.7	0.555	11	64.7
Hanging	1	33.3	2	66.7	0.579	3	17.6
Firearm	0	0.0	2	100	-	2	11.8
Other substance	0	0.0	1	100	-	1	5.9
Total	4	23.5	13	76.5	0.00012	17	100

non-existent until the age of 10 years old. However, starting at this age the SA rate strongly increases and reaches its maximum between 20 and 27 years old⁸. In Brazil in 2008, the number of deaths by suicide among 15 to 19 year old people was nearly double that of 10 to 14 year old people¹⁰.

The identification of the profile of the SA could contribute to strategic planning that would make possible the prevention of the use of certain SA methods or help to design plans of care for subjects who have used methods. Several studies have reported which are the more commonly used means of SA¹¹⁻¹³. The ingestion of medication, hanging and the use of cutting objects in SAs must be taken into consideration in the planning of care for the studied population.

Despite the studies that show the relation of agrotoxins and suicide attempts, it is not yet known why this relationship exists^{14,15}. In the actual study, the authors perceive the necessity of investigating the influence of agrotoxins on SAs in view of the relevance of the use of this substance in SAs. Exposure to pesticides has been linked to increases in SAs in Brazilian workers¹⁵.

SAs of pregnant women raise the suspicion of the presence of a mental disorder. Hormonal changes may also be factors affecting the predisposing to SAs in the pregnant. Maternal suicide is associated with an increased risk of suicide-attempt hospitalization in the offspring that goes beyond the risk associated with maternal accidental death¹⁶.

A study showed a relation of alcohol consumption and a greater frequency of SAs that is consonant with results of this research. A study that interviewed 4,352 individuals identified 423 (9.7%) people that did use alcoholic drinks. Among those who used alcohol drinks, 34 (8%) had histories of SAs, and SAs were most common in males (26–76.5%) in the age range of 18 to 35 years old (18–53%)¹⁷.

Several motives can lead a subject to attempt suicide, but the presence of a mental disorder is one of the predictive factors^{18,19}. The record in relation the presence of a mental disorder and the use and type of psychotropic medications used can underestimate the reality of the intents; indeed the literature indicates that

the presence of a mental disorder is one of the main risk factors for suicidal behavior²⁰.

The main limitation of this study was the sub-enrollment of presence of mental disorders. It was impossible for the realization of the association of mental disorders with suicide attempts.

Another limitation was the difficulty to identify suicide attempts, because many of hospital's outpatient clinic attendances studied may have been suicide attempts (e.g. accidents).

In this study, the most frequently used method of SA among those who died was poisoning, followed by hanging and the use of a firearm. This finding differs from that of a study performed in Amurel (southern Santa Catarina) that indicated hanging was the most-used method to commit the suicide (67–68.4%), followed by use of a firearm (12–12.2%), exogenous intoxication (8–8.2%) and drowning (6–6.1%)²¹.

In contrast to this study, which found a higher frequency of deaths between the ages of 20 to 39 years old, another study that was performed between 1980 and 2005 and examined cases of death by suicide in the extreme West of Santa Catarina found that the majority of the deaths occurred in the age range of 20 to 49 years old. This study found that the number of deaths was lowest (4/100,000) in the age range between 10 to 19 years old and highest (60/100,000) in individuals over 60 years old²².

The results of this study support those reported in the literature. The prevalence of SA was higher in females, especially in the younger population (10 to 29 years old). Intoxication was the main method used, and medications were predominantly used by women, followed by intentional poisoning by men. Cutting objects, hanging and firearms were used by men.

The present study served as a subsidy in the planning and elaboration of new instruments and strategies of prevention. The necessity of intervention in the area of promoting health to detect and prevent new suicide behaviors both local and regional was noticed. We also emphasized the need for improvement in the quality of records available.

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ARTIGO ORIGINAL

Atendimento a tentativas de suicídio por serviço de atenção pré-hospitalar

Pre-hospital attendance to suicide attempts

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RESUMO

Objetivo: Investigar as características das vítimas de tentativa de suicídio atendidas em serviço pré-hospitalar e os intervalos de tempo consumidos nessa fase de atendimento. **Métodos:** Estudo transversal utilizando dados da fase pré-hospitalar de atendimento às vítimas de tentativa de suicídio no município de Arapiraca, no ano de 2011. Para análise dos dados, foram realizados teste exato de Fisher, teste t de Student e regressão logística múltipla.

Resultados: Foram atendidas 80 vítimas de tentativa de suicídio pelo serviço de atenção pré-hospitalar. As mulheres, com idade superior a dos homens, foram as que mais tentaram suicídio (n = 44, 55%), e a intoxicação por medicamentos foi o método mais utilizado (n = 44, 55%). As tentativas de suicídio ocorreram com maior frequência no outono (n = 29, 36,25%), no dia de domingo (n = 18, 22,5%), principalmente no período vespertino (n = 33, 41,25%). O tempo gasto para o atendimento pré-hospitalar variou entre 34,4 e 40,5 minutos. As variáveis que estiveram associadas às tentativas de suicídio por sexo foram idade (p = 0,03) e tempo de transporte (p = 0,01). **Conclusão:** Foram encontradas diferenças entre os sexos das vítimas de tentativa de suicídio atendidas pelo serviço de atenção pré-hospitalar. As mulheres apresentaram maior idade que os homens e o tempo de transporte foi maior em vítimas do sexo masculino, sugerindo maior gravidade nas tentativas de suicídio cometidas por esse grupo.

ABSTRACT

Objective: To investigate the characteristics of the victims of suicide attempts treated in pre-hospital services and the time intervals consumed in this phase of care. **Methods:** Cross-sectional study, which used data from pre-hospital care to victims of suicide attempts occurred in the town of Arapiraca, in 2011. For data analysis, Fisher's exact test, Student's t test and multiple logistic regression were performed. **Results:** A total of 80 victims of suicide attempts were treated by pre-hospital care service. Women over the age of men were the most attempted suicide victims (n = 44, 55%) and drug intoxication was the most used method

Palavras-chave

Tentativa de suicídio,
suicídio, serviços
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Keywords

Suicide attempted, suicide, emergency medical services, epidemiology.

(n = 44, 55%). Suicide attempts occurred more frequently in autumn (n = 29, 36.25%), on Sunday (n = 18, 22.5%), mainly in the afternoon (n = 33, 41.25%). The time spent in the pre-hospital care varied between 34.4 and 40.5 minutes. The variables that were associated with suicide attempts by sex were: age (p = 0.03) and the transportation time (p = 0.01). **Conclusion:** It was found that there were differences between the sexes of the victims of suicide attempts treated by pre-hospital attendance. Women were older than men and the transportation time was higher in male victims, suggesting greater severity in suicide attempts committed by this particular group.

INTRODUÇÃO

O comportamento suicida é um fenômeno complexo, universal e representa um grande problema de saúde pública em todo o mundo¹. Segundo a Organização Mundial da Saúde (OMS), as taxas de suicídio aumentaram 60% nas últimas décadas, tornando-se a terceira causa de morte entre indivíduos com idade entre 15 e 44 anos².

No Brasil, cerca de quatro habitantes por 100 mil, em média, suicidam-se, e um número difícil de calcular tenta se autoinfligir³. Embora as taxas de suicídio sejam consideradas baixas quando comparadas às de outros países², entre 1998 e 2008 o total de suicídios no Brasil representou um aumento de 33,5%, enquanto o crescimento da população do país foi de 17,8%, no mesmo período⁴.

A tentativa de suicídio tem as mesmas características fenomenológicas do suicídio, diferindo deste apenas quanto ao desfecho, que não é fatal⁵. Alguns fatores têm sido associados ao comportamento suicida, como presença de um transtorno mental, antecedentes familiares, uso de álcool, sexo, idade, ausência de um companheiro, estar desempregado ou aposentado, isolamento social e história de abuso sexual na infância⁵. O risco de suicídio aumenta de acordo com o número de tentativas e também está associado a intervalos de tempo menores entre essas tentativas. Entre os pacientes atendidos em setores de emergência por tentativa de autoextermínio, estima-se que de 30% a 60% tiveram tentativas prévias e que de 10% a 25% tentarão novamente no prazo de um ano¹.

Dentre os cuidados iniciais oferecidos às vítimas de tentativa de suicídio, destaca-se o atendimento realizado pelo serviço de atenção pré-hospitalar. Este é definido como o atendimento que procura chegar precocemente à vítima, após ter ocorrido um agravo à sua saúde que possa levar a sofrimento ou mesmo à morte, garantindo atendimento e/ou transporte adequado a um serviço de saúde integrado ao Sistema Único de Saúde (SUS)⁶.

O atendimento adequado e o tempo decorrido entre a tentativa de suicídio e a admissão hospitalar são fatores extremamente relevantes para reduzir a mortalidade das vítimas⁷.

A primeira hora (*golden hour*) após a ocorrência de uma lesão traumática é considerada o tempo crítico para a

instituição do tratamento que modificará o prognóstico, uma vez que até 40% dos óbitos ocorrem antes da assistência hospitalar⁸.

No Brasil não existem registros sistemáticos das tentativas de suicídio⁵. A utilização de dados advindos dos serviços de atendimento pré-hospitalar pode contribuir para o conhecimento das características sociodemográficas e clínicas dos indivíduos que tentam suicídio, fornecendo informações para o planejamento das ações em saúde e o desenvolvimento de medidas de prevenção mais eficazes.

O presente estudo tem por objetivo investigar as características das vítimas de tentativa de suicídio atendidas em serviço pré-hospitalar e os intervalos de tempo consumidos nessa fase de atendimento.

Métodos

Trata-se de um estudo transversal que utilizou dados da fase pré-hospitalar de atendimento a vítimas de tentativa de suicídio, no ano de 2011, no município de Arapiraca, localizado na região central de Alagoas, distante 136 km da capital Maceió, com uma população de 214.067 habitantes⁹. Em termos populacionais e econômicos, é a segunda maior cidade do estado, concentrando mais de 400 mil habitantes em seu entorno imediato.

Os dados foram coletados por meio das fichas de atendimento pré-hospitalar do Serviço de Atendimento Móvel de Urgência (Samu). Foi utilizado um formulário validado por teste piloto contendo as seguintes variáveis: sexo, idade, método utilizado, uso de bebida alcoólica, estação do ano, dia da semana, horário de ocorrência, local do evento, encaminhamento da vítima e óbito.

Os intervalos de tempo considerados no atendimento pré-hospitalar (em minutos) também foram analisados: tempo de resposta (entre o acionamento da equipe e a chegada à cena), tempo de cena (entre a chegada da equipe na cena e a partida para o hospital de destino), tempo de transporte (entre a saída da cena e a chegada ao hospital de destino) e tempo total (entre o acionamento e o hospital).

Para verificar associação, foram utilizados o teste exato de Fisher e o teste t de Student. A análise dos fatores associados às tentativas de suicídio segundo sexo foi realizada por meio de regressão logística múltipla. Foram consideradas candidatas ao modelo multivariado todas as variáveis significativas no nível de 0,20. Em seguida, as variáveis

menos significativas foram retiradas, uma de cada vez, até permanecerem no modelo somente as variáveis significativas no nível de 0,05. A adequação do modelo foi avaliada pelo teste de Hosmer-Lemeshow. Para a análise dos dados, utilizou-se o pacote estatístico SPSS versão 17.0 (SPSS Inc., Chicago, USA).

Este estudo derivou de uma investigação sobre causas externas em adultos no município de Arapiraca. Por isso, foram excluídos dados referentes a indivíduos menores de 18 anos, não residentes no município em estudo, e fichas de atendimento pré-hospitalar ilegíveis. Em virtude do pequeno número de registros, os métodos de enforcamento e au-tolesão por objetos cortantes foram agrupados na categoria outros métodos.

Este estudo foi aprovado pelo Comitê de Ética em Pesquisa da Escola de Enfermagem da Universidade de São Paulo (EEUSP), sob parecer nº 5.953/2012.

RESULTADOS

Foram realizados 80 atendimentos por tentativas de suicídio no ano de 2011 pelo serviço de atenção pré-hospitalar, o que corresponde a uma média de um atendimento por tentativa a cada 4,6 dias.

Entre as vítimas atendidas, 44 (55%) eram do sexo fêmea e 36 (45%), do masculino. A média geral de idade foi de 29,1 anos (desvio-padrão – dp = 9,9), apresentando os homens a média de 26,5 (dp = 8,1) anos e as mulheres, de 31,3 (dp = 10,6) anos. Ao comparar a idade entre o sexo das vítimas que tentaram suicídio, observou-se que as mulheres possuíam idade superior a dos homens.

Em relação aos meios utilizados nas tentativas de suicídio, verificou-se que a intoxicação por medicamentos (n = 44, 55%) e a intoxicação por veneno (n = 18, 22,5%) foram os meios mais comuns (Tabela 1). A intoxicação voluntária por

Tabela 1. Características das tentativas de suicídio atendidas pelo serviço pré-hospitalar segundo sexo (Arapiraca, Alagoas, Brasil, 2011)

Características	Sexo				Total		p
	Masculino		Feminino				
	N	%	N	%	N	%	
Método utilizado							0,053
Intoxicação por medicamentos	14	31,8	30	68,2	44	100	
Intoxicação por produtos químicos	4	50,0	4	50,0	8	100	
Intoxicação por veneno	12	66,7	6	33,3	18	100	
Outros métodos	5	62,5	3	37,5	8	100	
Uso de bebida alcoólica							0,225
Sim	9	60,0	6	40,0	15	100	
Não	5	38,5	8	61,5	13	100	
Estação do ano							0,162
Verão	10	55,6	8	44,4	18	100	
Outono	10	34,5	19	65,5	29	100	
Inverno	10	62,5	6	37,5	16	100	
Primavera	5	31,3	11	68,8	16	100	
Dia da semana							0,653
Domingo	9	50,0	9	50,0	18	100	
Segunda	7	43,8	9	53,6	16	100	
Terça	2	25,0	6	75,0	8	100	
Quarta	2	22,2	7	77,8	9	100	
Quinta	6	50,0	6	50,0	12	100	
Sexta	3	60,0	2	40,0	5	100	
Sábado	6	54,5	5	45,5	11	100	
Faixa horária							0,665
6h às 11h59	8	61,5	5	38,5	13	100	
12h às 17h59	14	42,4	19	57,6	33	100	
18h às 23h59	11	42,3	15	57,7	26	100	
0h às 5h59	3	37,5	5	62,5	8	100	

medicamentos foi duas vezes mais utilizada pelas mulheres que pelos homens. Entretanto, não houve diferença estatística entre sexo e os diferentes métodos.

Entre as vítimas atendidas, identificou-se que 15 (18,7%) pessoas fizeram uso de álcool. Na maioria dos casos ($n = 52$, 65%) essa informação foi ignorada. Não foi encontrada significância estatística entre o consumo de álcool por sexo (Tabela 1).

Na tabela 1, observa-se que as tentativas de suicídio ocorreram com maior frequência no outono ($n = 29$, 36,25%) e no verão ($n = 18$, 22,5%). O domingo foi o dia da semana com maior número de atendimentos por tentativas de suicídio ($n = 18$, 22,5%), seguido pela segunda-feira ($n = 16$, 20,0%). Nesses dias, o horário predominante para as tentativas de suicídio foi entre 12h e 17h59 ($n = 33$, 41,25%).

Em relação aos locais de ocorrência, 54 (67,5%) tentativas de suicídio ocorreram no domicílio, duas (2,5%) em uma delegacia e em 24 (30%) fichas de atendimento pré-hospitalar não constava essa informação.

Quatro (5%) indivíduos tentaram suicídio mais de uma vez. Os homens em idade jovem (18 a 21 anos) foram os que mais repetiram a tentativa ($n = 3$, 75%), e o método mais utilizado por eles foi a intoxicação por medicamentos ($n = 3$, 75%). Verificaram-se quatro (5%) tentativas de suicídio com desfecho letal, sendo dois óbitos em mulheres e dois em homens.

Quanto à média dos tempos consumidos nas fases do atendimento pré-hospitalar (em minutos), observou-se diferença entre sexo e os tempos de transporte e total (Tabela 2). Constatou-se que o tempo de transporte foi significativamente maior nos atendimentos aos homens.

Verificou-se, por meio da análise de regressão logística (Tabela 3), que as variáveis que permaneceram no modelo final com maior associação com o sexo foram tempo de transporte e idade. Quanto maior for o tempo de transporte, maior a chance de a vítima ser do sexo masculino. Em relação à idade, quanto mais velha for a vítima, maior a chance de ela ser do sexo feminino. O teste de adequação de Hosmer-Lemeshow apontou para um bom ajustamento do modelo final ($p = 0,250$).

Tabela 2. Distribuição da média de tempo consumido (em minutos), em cada fase de atendimento às vítimas de tentativa de suicídio, segundo sexo (Arapiraca, Alagoas, Brasil, 2011)

Tempos nas fases de atendimento	Sexo		p
	Masculino	Feminino	
Tempo de resposta	15,76	15,21	0,751
Tempo de cena	11,35	11,03	0,823
Tempo de transporte	10,50	7,03	0,018
Tempo total	40,59	34,40	0,045

Tabela 3. Modelo de regressão logística para vítimas de tentativa de suicídio atendidas em serviço pré-hospitalar, segundo sexo (Arapiraca, Alagoas, Brasil, 2011)

Variável	Razão de chance	Intervalo de confiança (95%)	p
Tempo de transporte	1,22	1,04-1,43	0,01
Idade	0,92	0,85-0,99	0,03

A maior parte das vítimas foi encaminhada para unidade de emergência de referência para o atendimento por tentativa de suicídio ($n = 64$, 80%); seis (7,5%) tiveram alta no próprio local de atendimento; quatro (5%) recusaram-se a ser encaminhadas para a unidade hospitalar e uma (1,2%) foi encaminhada para um hospital psiquiátrico. Uma (1,2%) ficha de atendimento apresentou registro indeterminado para essa informação.

DISCUSSÃO

O presente estudo identificou que uma pessoa foi atendida por tentativa de suicídio a cada 4,6 dias, no serviço pré-hospitalar. Ao levar em consideração que uma em cada três pessoas que tentam o suicídio chega a ser atendida em um serviço médico de urgência¹⁰, é provável que a quantidade de tentativas seja bem maior.

Muitas tentativas de suicídio podem não chegar ao atendimento hospitalar por serem de baixa complexidade. Isso porque a maioria dos meios suicidas empregados nessa circunstância é pouco violenta, como a ingestão de medicamentos e outras substâncias químicas¹¹. Além do grau de gravidade, outros fatores também podem influenciar a procura por um serviço médico após a tentativa de suicídio. Dentre eles, destacam-se: o acesso e a confiança no sistema de saúde, o estigma da população em relação ao comportamento suicida e o medo da criminalização do ato¹⁰.

As mulheres, adultas jovens, cometeram mais tentativas de suicídio que os homens. Esses achados são consistentes com os da literatura^{1,10,12,13}. Na faixa etária entre 31 e 35 anos, estudos relacionam o comportamento suicida ao grupo de mulheres que não trabalham fora de casa, indicando que a realização de atividades laborais fora do ambiente doméstico promove benefícios à saúde mental desse grupo^{1,12}.

Mulheres apresentam comportamento suicida mais frequente e realizam mais tentativas, sendo o método mais utilizado a ingestão de medicamentos e de outras substâncias tóxicas¹. Esse meio é o eleito por ser menos invasivo e, conseqüentemente, não afetar a estética^{14,15}.

Os homens cometem mais suicídios e preferem métodos que evidenciem sua virilidade, utilizando meios mais letais como enforcamento, arma de fogo e precipitação de lugares elevados^{1,14-16}.

O predomínio de tentativas de suicídio por autointoxicação é reiterado por pesquisas sobre o tema^{1,17}. Geralmente, mais de um tipo de substância química, medicamentosa ou não, é utilizado quando o método é a intoxicação vo-luntária¹².

Em estudo retrospectivo com 206 casos de tentativas de suicídio por intoxicação medicamentosa, os grupos farma-cológicos que mais se destacaram foram os tranquilizantes (25,5%), antidepressivos (17%) e anticonvulsivos (15%)¹². Como a sobredose intencional de medicamentos é considerada o método mais utilizado para a tentativa de suicídio, são necessários uma avaliação cautelosa do estado psíquico e emocional do paciente antes de prescrever tais substâncias¹² e um acompanhamento contínuo.

Dados obtidos no atual estudo destacam a intoxicação voluntária por veneno, sobretudo por agrotóxicos. A utilização dessas substâncias tem crescido mundialmente e se tornado um grande problema em alguns países asiáticos, latino-americanos e em Portugal¹⁵.

No município de Arapiraca, os óbitos por ingestão de pesticidas e outros produtos químicos utilizados na agricultura têm chamado a atenção¹⁸. A disponibilidade dos agrotóxicos pode favorecer atos suicidas não planejados, ocorrendo muitas vezes de maneira impulsiva¹⁵.

A ingestão de álcool esteve relacionada a 18,7% das tentativas de suicídio. Entretanto, 65% das fichas de atendimento pré-hospitalar não apresentaram registros referentes a essa informação. Acredita-se que o uso abusivo do álcool seja maior do que o constatado neste estudo e que a não associação encontrada entre essa variável e a tentativa de suicídio pode estar relacionada à falta de informação. Daí a necessidade de conscientização dos profissionais da saúde quanto ao registro do uso nocivo de álcool para o planejamento de estratégias de cuidado e prevenção.

Em relação à sazonalidade, estudos sugerem que há diferenças entre as variações climáticas e o comportamento suicida^{19,20}. Neste estudo, houve maior proporção de tentativas de suicídio no outono, achado semelhante ao de um estudo epidemiológico realizado no interior da Bahia²¹.

Nos Estados Unidos, um estudo sobre tentativas de suicídio associadas ao uso de álcool e outras drogas, com vítimas atendidas em serviços de emergência, constatou que o percentual de tentativas no outono foi maior do que no inverno e na primavera¹⁹. Possivelmente, flutuações no clima e na luz solar causadas pelas estações do ano influenciam o aparecimento de sintomas depressivos¹⁹.

Quanto aos dias da semana, o domingo, principalmente no período vespertino, foi o dia mais frequente para as tentativas de suicídio. Isso pode ter acontecido pelo fato de as pessoas estarem mais sozinhas, ou ainda pelo fato de as pessoas em tratamento psicológico não terem disponível, de forma adequada, o atendimento especializado nos serviços de saúde. Além disso, no fim de semana, as pessoas estão mais predispostas ao uso de bebida

alcoólica, o que pode favorecer a tentativa de suicídio.

Entre os casos de atendimento pré-hospitalar deste estudo, 5% dos indivíduos tentaram suicídio e repetiram a tentativa em menos de uma semana. Esse achado merece destaque, pois, tanto para aqueles que tentam pela primeira vez quanto para os repetidores, o primeiro ano constitui o período de maior risco¹. Essa afirmativa é reforçada pelos resultados obtidos em estudo de coorte retrospectivo com 807 indivíduos, no qual 60% das mortes por suicídio ocorreram no primeiro ano depois da tentativa-índice¹.

A maioria das vítimas (80%) assistidas pelo serviço pré-hospitalar foi encaminhada para o hospital de referência da região. Durante a fase pré-hospitalar, foram realizados os primeiros cuidados para evitar complicações à saúde das vítimas.

A identificação do tempo de duração do atendimento pré-hospitalar é um fator relevante, pois, para pacientes gravemente feridos, os primeiros 60 minutos são cruciais para a manutenção da vida²². Neste estudo, o uso do serviço pré-hospitalar permitiu que todas as vítimas de tentativas de suicídio fossem assistidas dentro da referida *golden hour*.

O tempo consumido no atendimento pré-hospitalar é resultante de um conjunto de fatores que o influenciam, como experiência e capacitação profissional da equipe, condições de tráfego local, dia da semana e período do dia, tipo e número de veículos disponíveis e localização desses veículos²³.

O presente estudo mostra que o tempo de transporte foi maior em vítimas de tentativa de suicídio do sexo masculino. Possivelmente, esse fato está relacionado à maior gravidade das tentativas de suicídio cometidas pelos homens, pois, de acordo com os dados encontrados na tabela 2, as vítimas do sexo masculino utilizaram métodos considerados mais letais, o que pode ter acarretado a realização de procedimentos mais complexos durante o transporte deles, como a intubação endotraqueal, que necessitam que a viatura seja parada para serem realizados.

O comportamento suicida é um fenômeno complexo e influenciado por vários fatores. Por isso, sua dinâmica precisa ser mais bem compreendida para que sejam propostas estratégias para a prevenção desses agravos e, ao mesmo tempo, adequação das práticas de saúde para melhor assistir suas vítimas. Para isso, é preciso estabelecer um protocolo de intervenções, a ponto de ter impacto sobre a sobrevivência da vítima sem consumir tempo desnecessário²⁴.

Os profissionais da atenção pré-hospitalar precisam estar capacitados para lidar com as peculiaridades do comportamento suicida, garantindo abordagem e encaminhamento adequados às vítimas de tentativas de suicídio. É necessário, ainda, que os serviços de saúde estejam articulados, para que haja garantia de acolhimento e continuidade de tratamento, mesmo nos casos menos graves¹.

A quantidade de informações faltantes nas fichas de atendimento pré-hospitalar merece destaque, pois o regis-

tro insuficiente prejudica o conhecimento mais detalhado sobre a distribuição e a magnitude das tentativas de suicídio. Conforme Malvestio²⁵, as razões para o mau preenchimento das fichas de atendimento pré-hospitalar podem ser decorrentes da condição de saúde das vítimas encontradas no momento da cena, principalmente quando há casos mais graves, ou podem ser explicadas pela falta de compreensão da importância desse ato pelas equipes de atendimento.

Dessa forma, é fundamental estimular os profissionais de saúde para o preenchimento adequado das fichas de atendimento pré-hospitalar. A obtenção dessas informações pode fornecer subsídios para o planejamento e a avaliação das ações realizadas, permitindo a continuidade da assistência à vítima de tentativa de suicídio no ambiente hospitalar.

As principais limitações deste estudo referem-se à exclusão de indivíduos menores de 18 anos e à utilização de dados secundários incompletos. O estudo apresentado revela-se importante, por contribuir para a avaliação das características das tentativas de suicídio e suas vítimas, bem como para a identificação da qualidade do serviço de urgência prestado pelas equipes de atenção pré-hospitalar.

CONCLUSÃO

Os dados apresentados no presente estudo evidenciam diferenças entre as tentativas de suicídio cometidas por homens e mulheres, fato esse que corrobora a literatura e ressalta a importância de se proporem diferentes estratégias de prevenção para cada grupo específico.

Outra questão a ser destacada é o uso frequente de medicamentos e de agrotóxicos para a tentativa de suicídio, o que leva à necessidade de um rigoroso controle sobre a prescrição e a distribuição de medicamentos (principalmente psicofármacos) e sobre a utilização de agrotóxicos (com a utilização de agrotóxicos de menor toxicidade), pois essas são medidas fundamentais para a diminuição das taxas de autoenvenenamento¹⁷.

Diante disso, é importante destacar que as capacitações nos serviços de atendimento pré-hospitalar devem priorizar, além das habilidades para o atendimento precoce e a manutenção da vida das vítimas, o reconhecimento dos casos de tentativa de suicídio, as principais formas de atuação e o preenchimento adequado das fichas de atendimento pré-hospitalar, pois o conhecimento sobre o comportamento suicida e seus fatores de risco pode contribuir para a qualificação da assistência e para a realização de ações de prevenção, em qualquer nível.

CONTRIBUIÇÕES INDIVIDUAIS

Ana Paula Nogueira de Magalhães – Contribuiu na concepção e elaboração do estudo, análise e interpretação dos

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Os autores declaram não haver conflitos de interesse nem financeiros a serem declarados.

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Suicide among elderly: a systematic review

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This article aimed to perform a systematic review of suicide among the elderly. The literature review was conducted using three databases (SCOPUS, Medline/Pubmed and ISI Web of Science) using the terms *suicide and elderly*, *suicide and older adult* and *suicide attempt*. The publication dates were restricted between 2008 and 2013. Review or theoretical articles were excluded; only epidemiologic studies were selected. A total of 1613 references were found, but only seven met the inclusion criteria, namely articles that assessed the prevalence of suicide in elderly through retrospective cohort studies. The average study period was 7.9 years. The following average annual suicide rates were calculated: Italy (173/cases-year), New York (118.1/cases-year and 51 cases/ year – two studies), Ireland (92/cases-year), Finland (12.9/cases-year), Turkey (3.5/cases-year) and England (3/cases-year). All of the studies reported that elderly males had a higher rate of death by suicide compared to elderly females. Hanging, shooting by firearms, drowning and jumping from high places were prevalent suicide methods. Three articles reported that death by suicide was associated with the presence of psychiatric disorders, psychoactive substance use, and physical illnesses, as well as economic and emotional reasons. This review determined that the topic of suicide among the elderly is rarely discussed and that little is known about influences, causes, or prevalence of suicide among the elderly. Moreover, neither the type of health monitoring nor the medications that are used as interventions for eventual suicide victims are commonly reported in elderly populations.

KEYWORDS: Suicide; Elderly; Primary Care.

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■ INTRODUCTION

Despite the global increase in the elderly population, little is known about how suicide presents itself among this group. Epidemiological studies on suicide in the elderly are scarce, but show an increase in incidence. Knowledge regarding the profile of suicide attempts may help in the development of strategies for the prevention of attempts and of suicidal acts themselves. Studies have shown that the presence of depression among the elderly is one factor that is associated with suicidal ideation and suicide attempt, and consequently, with the act of suicide.^{1,2}

Studies profiling elderly individuals who have attempted suicide are necessary for developing preventive care plans for this vulnerable group. In addition, the education of primary care providers in diagnosing and treating depression is an evidence-based suicide prevention practice.³

When undiagnosed and untreated, depression — a common psychiatric disease among the elderly⁴ — can cause physical, social and functional impairment, thereby contributing to decreased quality of life and, at more severe degrees, to suicide.¹

Suicide among the elderly is a global public health problem that is expected to worsen as society ages.⁵ Consequently, health professionals must be attentive to the signs and symptoms of depression and the risk factors that can trigger depression.

Suicide assessment and prevention is one component of optimal care for patients who present with depression. Primary care professionals must be competently prepared and trained in the procedures of suicide assessment and prevention and must be familiar with the patient and provider factors that can influence this process.⁶ Primary care is likely to be the most suitable setting in which to implement a strategy for suicide prevention for the elderly, especially because more people visit primary care clinics than secondary care clinics prior to committing suicide.⁷

Thus, due to the need for primary care planning aimed at suicide prevention among the elderly, this article sought to perform a systematic review of suicide among the elderly.

■ MATERIALS AND METHODS

The literature review was conducted in three databases (SCOPUS, Medline/Pubmed and ISI Web of Science) using terms *suicide and elderly*, *suicide and older adult* and *suicide attempt*.

The publication dates were restricted to the period between January 1, 2008 and December 31, 2013. Review

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or theoretical articles were excluded; only epidemiological studies were selected for this review. Repeated references were excluded.

RESULTS

A total of 1613 references were found (viz., 110 in SCOPUS, 1083 in Medline/Pubmed, and 420 in ISI Web of Knowledge). Of these, 498 were duplicate references. The remaining 704 references underwent abstract analysis, and 349 were excluded. Sixty-three articles were short-listed for full-text reading. Following this process, only seven articles met the inclusion criteria of articles that assessed the prevalence of suicide in elderly or older adults. These articles included retrospective cohort studies. Figure 1 illustrates the selection process. The data from the seven studies found on this subject are shown in Table 1. Four studies were conducted with people over 65 years of age, whereas two studies were conducted with individuals over 60 years and one with individuals over 55 years.

All of the studies observed that elderly males had a

higher rate of death by suicide compared to elderly females (above 70%), as shown in Table 1. Hanging^{5,8-12} shooting by firearms^{5,8-12} drowning^{5,8,10,11} and jumping from high places^{5,9-11} were the prevalent suicide methods among the elderly as shown in Table 2.

Three articles did not address the issue of psychiatric disorders associated with suicide. The remaining articles reported that deaths by suicide were related to the presence of a psychiatric disorder (e.g., depression, schizophrenia, mood disorder), psychoactive substance use, or a physical illnesses (e.g., cancer, systemic disease), as well as economic or emotional reasons. Only one study¹¹ presented data about the presence of psychiatric treatment among the elderly. None of the studies cited psychological accompaniment (Table 3).

The study populations described in the articles evaluating suicide among the elderly varied between localities: Ireland,¹¹ Turkey,¹² Finland,⁸ New York,^{9,10} England¹³ and Italy,⁵ as shown in Table 1.

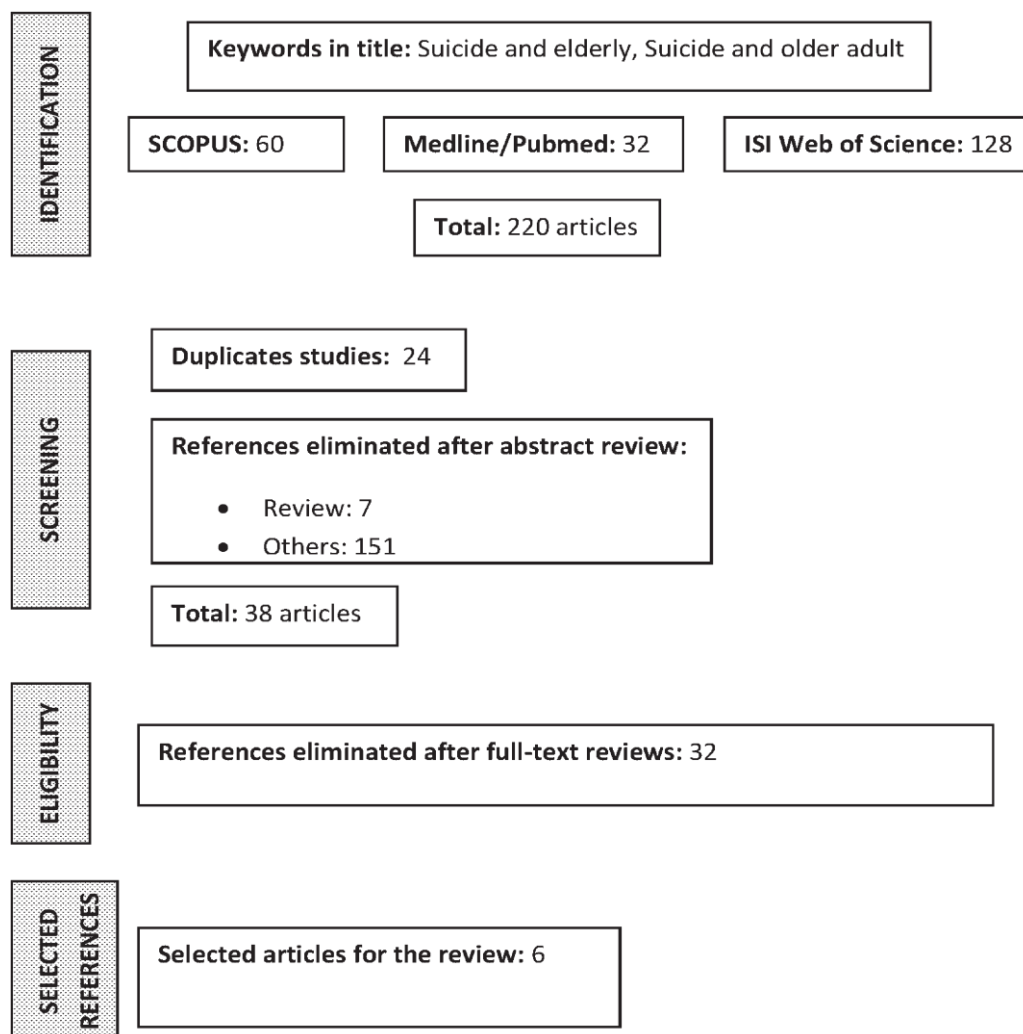


Figure 1 - Results of the systematic review.

Table 1 - Local description, average age, analysis time and frequency of suicide in elderly

AUTHORS	LOCATION	AVERAGE AGE	STUDIED PERIOD	ANNUAL AVERAGE	TOTAL	SUICIDE		
						TOTAL	MALE	FEMALE
Karvonen et al, 2008	Finland	>65	1988–2003	12,9	1877	194 (10%)	146 (75%)	48 (25%)
Mezuk et al 2008	New York	>60	1990 to 2005	118,1		1,771	1231 (69,5%)	493 (30,5%)
Abrams et al, 2009	New York	>65	2000 - 2004	51		255	183 (71,8%)	72 (28,2%)
Corcoran et al,2010	Ireland	>55	1997–2006	92		921	691 (75%)	230 (25%)
Erel et al, 2011	Turkey	>65	2003 - 2007	3,5	148 autopsies	17 (11,5%)	14 (82%)	3 (18%)
Terranova et al, 2012	Italy	>65	2005 – 2010	173		1,038	812 (78%)	226 (22%)
Murphy et al, 2012	England	>60	2000 - 2007	3	1,177	24	14 (58,3%)	10 (41,7%)

* autopsies performed.

The studies reporting deaths by suicide considered the period of time from 1988 to 2010. The average study period was 7.9 years. After accounting for differences in the study periods between localities, the following average annual suicide rates were calculated: Italy (173/cases-year), New York (118.1/cases-year), Ireland (92/cases-year), New York (51/cases-year), Finland (12.9/cases-year), Turkey (3.5/ cases-year) and England (3/cases-year) (Table 1).

DISCUSSION

This review shows that few epidemiological studies have focused on suicide among the elderly. Most extant articles consider the psychosocial aspects of suicide in the family of the elderly individual; these articles were excluded from this study. Only seven articles retrospectively presented cohort results.^{5,8-12}

Half of the identified studies did not cite the presence of a disease related to suicide. Among the articles that did cite the influence of disease, psychiatric disorders were most commonly identified. Only one study directly associated depression with suicide.¹² Other studies identified depressive symptoms¹⁴ and major depression¹⁵ as being related to suicidal ideation. Studies on suicide attempts among the elderly showed correlations with major, unipolar, bipolar and minor depression.¹⁶⁻¹⁹ With respect to the psychiatric diseases related to suicide, research on drug and psychological treatments would be interesting when evaluating the importance of treatment in the prevention of suicide among the elderly.

A large proportion of suicides among elderly males was found. In the literature, this phenomenon has been observed in all age groups.²⁰ Several factors may influence such high rates, including loss, loneliness and physical disease. These factors should be considered warning signs of suicidal behavior.¹² The standard patriarchal features that still prevail among men are reflected in suicidal behavior. It is essential to give special attention to men during the transition from working life to retirement, in the loss of status, in situations of familial losses, upon diagnoses of chronic degenerative diseases that cause disabilities, in the loss of autonomy or upon the onset of sexual impotence.²¹

Suicidal ideation is present in a significant proportion of depressed primary care patients but is rarely discussed. Men, who carry the highest risk for suicide, are unlikely to be asked about or disclose such. The existence of patient-centered communications and a positive healthcare climate do not appear to increase the likelihood of suicide-related discussions. Health professionals should be encouraged to ask about suicidal ideation in their depressed patients and, when

disclosure occurs, facilitate discussion and develop targeted treatment plans.²²

Men over 65 years are more affected by illness, the death of spouse, and loneliness, because they have not prepared for it due to differing socialization roles.⁴ One study in Japan showed that administering programs in the prevention of suicide and impulsivity would be effective for older men.²³

Depression is more prevalent among women across the lifespan, but these differences diminish above the age of 65 years. It is important to diagnose depression in this age group to aid suicide prevention,⁴ as was demonstrated by a Japanese study that showed that implementation of suicide prevention programs may be effective for older women.²³

Prevention measures for the elderly — and, specifically, elderly males — should be implemented through primary health care. Such measures can include health education programs aimed at sensitizing the elderly to the importance of healthy living habits, including physical and leisure activities. Accordingly, strategic locations already existing in the community (e.g., the spaces to be used for these activities) should be leveraged to favor social interactions and expand support networks among the elderly.¹

Hanging, shooting by firearms, drowning and jumping from high places are considered to be violent methods of suicide. Primary health care strategies for limiting access to these methods should be implemented.^{24,25} Moreover, families should be aware of the risks of suicide commission among the elderly, and they should become allies in the prevention of suicide attempts and, consequently, of suicide completion.

One of the problems faced when attending to the elderly is that some signals and symptoms of depression are common at this stage of life. In some cases, elderly individuals cease to express their wishes, fears and thoughts because they do not have anyone with whom to talk. Consequently, these elderly individuals may become lonely. This phenomenon, among other factors, may contribute to the emergence of depression. Primary care may help to reduce suffering and dependency; social programs that assist elderly people in establishing social interactions in their communities and achieving dignity at the end of life should be encouraged.² Motivating the elderly to fulfill activities that go beyond distraction, and instead promote social interactions, provides the highest level of wellbeing, keeps them active, and improves quality of life while also reducing depressive symptoms.¹

The articles reviewed, and corrected for the period of time analyzed, suggest that Italy and New York present the highest annual rates of suicide among the studied locations

Table 2 - Description of the means used in suicide in the elderly

AUTHORS	Karvonen et al, 2008			Mezuk et al 2008	Abrams et al, 2009	Corcoran et al, 2010			Erel et al, 2011	Terranova et al, 2012		
MEANS USED	Male	Female	Total	Total	Male	Female	Male	MEANS USED	Male	Female	Total	
Hanging		72 (49,3%)	16 (33,3%)	503 (28.4)	64 (25,1%)	280 (40,6%)		6 (42,9%)	2 (66,7%)	327 (40,3%)	46 (20,3%)	
Firearms		36 (24,7%)	0 (0%)	286 (16.1)	38 (14,9%)	62 (9%)	1 (0,3%)	3 (21,4%)		152 (18,7%)	1 (0,4%)	
Drowning		18 (12,3%)	15 (31,3%)		5 (2%)	198 (28,7%)	90 (39%)			40 (4,9%)	25 (11,1%)	
Jumping				533 (30.1)	98 (38,4%)		2 (14,3%)			189 (23,3%)	98 (43,4%)	
Drug overdose				224 (7.0)	18 (7,1%)	52 (7,6%)	57 (25%)					
Poisoning							2 (14,3%)	1 (33,3%)		8 (1%)	16 (7,1%)	
Cutting				81 (4.6)						23 (2,8%)	7 (3,1%)	
Killed by motor vehicle or train					10 (3,9%)					12 (1,5%)	1 (0,4%)	
Burning							1 (7,1%)					
Other		20 (13,7%)	17 (35,4%)	143 (8.1)	22 (8,6%)							

Table 3 - Description of mental and physical illnesses related to suicide in the elderly

MENTAL AND PHYSICAL ILLNESSES	Corcoran et al, 2010	Erel et al, 2011	Terranova et al, 2012
Psychiatric treatment	7 (41.2%)		
Systemic disease treatment	5 (29.4%)		
Cancer treatment	1 (5.9%)		
Schizophrenia and other psychoses		11 (5.7%)	
Depression and other mood disorders		43 (22.2%)	
Substance related disorders		17 (8.8%)	
Other psychiatric disorders		12 (6.2%)	
Other disease		111 (57.2%)	
Mental illness			357 (34.4%)
Physical illness			216 (20.8%)
Economic reasons			21 (2%)
Emotional alterations			56 (5.4%)
Other			378 (36.4%)
Not described			10 (1%)

six-year cohort study, which was conducted in Italy,⁵ identified 1,038 deaths by suicide among the elderly (males: n=812; females: n=226). Another 15-year cohort study, which was conducted in New York,⁹ found 1,171 deaths by suicide among the elderly (males: n=1,231; females: n=493).

Among the studied locations, the lowest annual rate of suicide among the elderly was observed for Turkey and England (Oxford, Manchester and Derby). We have discussed a five-year cohort study,¹² reporting 17 deaths by suicide among an elderly population of 148 autopsies (males: n=14; females: n=3) in Turkey. Twenty four deaths by suicide were detected in England in an eight year study.

The populations studied were limited to countries in North America (specifically, New York City), Europe (Ireland, Italy, England and Finland) and Eurasia (Turkey). These locations present varied social structures, economics and geographies. No cohort study was drawn from Latin America. Among the locations identified in the study, Turkey was the single developing country, which demands

reflection on the low rates of suicide reported in that study. This value may be accurate or underestimated; alternatively, it may be that cities in the developing world are not so strongly influenced by the increases in suicide rates linked to the developed world. One study performed in Brazil offers evidence that violence itself occurs in micro-regions with low levels of poverty,²⁶ which supports the idea that developing countries should experience high rates of suicide.

Many elderly individuals who die by suicide have had recent contact with a primary care physician. Because risk-assessment and referral processes for suicide are not readily comparable to procedures for other high-risk behaviors, it is important to identify areas of care that require quality improvement.²⁷

Primary care professionals must be competently prepared and trained in the suicide assessment and prevention process, and they must be familiar with age-related factors that may influence this process and the presenting symptomatology.⁶ An approach to aging that is both comprehensive and systemic must focus on personal welfare and must recognize the importance of vigilant and effective services that promote life-saving behaviors and counteract suicide.²⁸ Therefore, a decrease in suicide cases would be expected to accompany greater attention taken by managers and health professionals toward the support offered to the elderly through health services. The management of suicide risk includes: A) understanding the difference between risk factors and warning signs, B) developing a suicide risk assessment, C) and managing suicidal crises in a practical manner.²⁸

CONCLUSION

This review exposes that little is known about the causes, influences, and prevalence of suicide among the elderly. Moreover, neither the type of health monitoring that eventual suicide victims receive nor the medications that are used as interventions are commonly reported. Finally, no health care focus on the prevention of suicide, particularly for elderly males, was identified.

Family participation in suicide prevention is of paramount importance to the elderly, who often live alone or feel abandoned by family and society. Health centers that focus on primary care should pay special attention to this group and act as a link between families and the elderly. It is necessary to regard the elderly as individuals who are vulnerable not only to physical illness but also to mental illness.

RESUMO

Este artigo teve como objetivo realizar uma revisão sistemática sobre suicídio entre os idosos. A revisão da literatura foi feita utilizando três bancos de dados (Medline/Pubmed, SCOPUS e ISI Web of Science) usando os termos *suicide and elderly*, *suicide and older adult* and *suicide attempt*. A publicação se restringe entre 2008 e 2013. Revisão ou artigos teóricos foram excluídos; apenas estudos epidemiológicos foram selecionados para esta revisão. Um total de 1613 referências foram encontradas e apenas sete preencheram os critérios de inclusão de artigos que avaliou a prevalência de suicídio em idosos. Estes artigos incluíam estudos de coorte retrospectivo. O período médio de estudo foi de 7.9 anos. Calculou-se as seguintes taxas de suicídio anual média: Itália (173 casos/ano), Nova Iorque (118 casos/ano e 51 casos por ano, dois estudos), Irlanda (92 casos/ano), Nova Iorque (51 casos/ano), Finlândia (12.9 casos/ano), Turquia (3.5 casos/ano) e Inglaterra (3 casos/ano). Todos os estudos observaram que homens idosos tinham uma maior taxa de morte por suicídio, em comparação com mulheres idosas. Enforcamento, arma de fogo, afogamento e saltar de lugares altos foram os métodos de suicídio prevalentes entre os idosos. Três artigos relataram que a morte por suicídio estava associada com a presença de transtornos psiquiátricos, uso de substâncias psicoativas e doenças físicas, bem como com causas econômicas e emocionais. Esta revisão determinou que o tema do suicídio entre os idosos é raramente discutido e que pouco se sabe sobre as influências, causas ou prevalência entre os idosos. Além disso, o tipo de acompanhamento recebido, bem como os medicamentos são usados para suicidas eventuais são comumente relatados

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ORIGINAL RESEARCH

Suicidal ideation and chronotype assessment in nurses and police officers

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BACKGROUND: Nurses and police officers are professionals that work in shifts and have jobs that require attention and responsibility. They work under conditions that can cause stress, anxiety and changes in sleep patterns. **OBJECTIVE:** This study aims to identify symptoms of anxiety and depression, chronotype and the presence of suicidal ideations in nurses and police officers in the city of Arapiraca/Alagoas, Brazil.

METHODS: This is a descriptive and quantitative study. The interviews were conducted using (i) identification records and general data, (ii) the Beck Anxiety Inventory, (iii) the Center for Epidemiologic Studies Depression Scale and (iv) the Horne-Östberg Questionnaire.

RESULTS: Fifty-three nurses and 111 police officers participated in the research. Nurses and police officers exhibited indifferent to moderate matutinal chronotypes. Most of the nurses and police officers reported minimal to light levels of anxiety. Nurses and police officers presented elevated risk for depression. Five nurses and six police officers had considered attempting suicide at the time of the research. There were no significant differences between the study groups with respect to anxiety and depression symptoms, chronotype and suicidal ideations.

CONCLUSION: The nurses and police officers examined presented high risk for symptoms of anxiety and depression; a considerable number of nurses and officers had lifetime suicidal ideations. Implementation of preventive measures is necessary for the early diagnosis of anxiety and depressive disorders in order to prevent complications, including possible suicide.

KEYWORDS: Nursing, Police, Anxiety, Depression, Suicidal ideation, Chronobiology phenomena.

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■INTRODUCTION

Conditions in the workplace influence workers' health; these changes may generate a conflict in the relationship between the bodily functions and work requirements, resulting in alterations in health.¹

One of the ways of organizing work is through the introduction of night shift work; this organization is performed in order to meet the demands of the population and establish uninterrupted services to the community.¹

Work performed in shifts, mainly at night, may harm the health of workers from the perspective of chronobiology, because damage can be caused by

temporary changes in organic function.² Fast-paced work, excessive journeys and work shifts are factors that can induce occupational stress.³

Chronotype relates to the adaptability and performance of daily activities when changes in sleeping habits cause deprivation or deficit of this important functional state.⁴ The human population can be divided into three basic chronotypes: matutinal, vespertine (both of which can be extreme or moderate) and indifferent.⁵

Work performed in shifts relates not only to the emergence of sleep disorders, but also to increased daytime drowsiness and decreased alertness. The effects of these changes in the sleep- wake cycle can cause an increased risk for negative outcomes such as accidents at work and impairment of the quality of life.^{6,7}

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Police personnel are subject to specific challenges. In Brazil, public safety suffers from a continuous growth of various forms of violence and crime.⁸ Intensification of violence requires more effective public security policies, resulting in a physical and emotional overload for police officers. In addition, to dealing with the pressure of society to provide efficient policing, the often precarious working conditions in Brazil interferes with the performance of these professionals, affecting their health and generating dissatisfaction, which in turn results in symptoms of stress and psychological suffering.⁹⁻¹¹

Nursing personnel are likewise subject to specific challenges. Hospital environments are unhealthy places that can be painful and dangerous and may subject workers to an increased risk of illness. Hospital work is often characterized by long commuting, contact with stressful situations, and high levels of tension; these factors can lead to physical and mental health problems such as repetitive strain injury, anxiety, anguish and stress, to name a few.¹²

The intense pace of activity in the nursing profession infringes upon the human biological rhythm. In addition, absenteeism, long distances covered during workdays, inadequate provisioning of security, large amounts of work information and vigilant attitudes can cause physical wear as well as mental fatigue and stress. These factors predispose nursing professionals to physical and mental illnesses.¹³

The importance of studies examining psychiatric comorbidities in these two populations lies in the need to generate contributions which may alert authorities, society, health professionals and public safety experts about the occupational risks and in the need for mental health care in these two professions.

Because the professional routines of nurses and police officers involve an overload of activities and inadequate work shifts, this study aims to identify symptoms of anxiety and depression, chronotype and the presence of suicidal ideations in nurses in a hospital emergency service and in police officers in the city of Arapiraca (population: 214 thousand), in the state of Alagoas, Brazil.

■ METHODS

This study was conducted at the Hospital of Urgency and Emergency and at the Police Battalion, in Arapiraca.

The hospital staff included 70 nurses, 53 of which participated in this study. The inclusion criterion was: nurses that worked at the emergency hospital unit. Exclusion criterion: nurses that were on vacation or on license from the hospital service for any reason.

The Battalion included 280 officers, 111 of which participated in the study. We included police officers that currently or previously carried out combat activities outside of the headquarters. Officers on license from service or that

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were not active in external police activities were excluded from the study.

The Committee of Ethics in Research at the Federal University of Alagoas approved this study.

Instruments used in the data collection of this study were Identification Records and General Data, Beck Anxiety Inventory, CES-D (Center for Epidemiologic Studies Depression Scale) and the Horne-Östberg Questionnaire (Matutinal types - Vespertine).

Data collection in the hospital occurred from January to August 2013. Data collection in the battalion occurred from October 2012 to February 2013. Data analysis was performed using the Epi Info 2000 program (Atlanta, Georgia, USA). The chi-squared test was used to evaluate the differences between the groups. The level of significance for this study was $p < 0.05$.

■ RESULTS

Fifty-three nurses participated in the study, 51 (96%) of them were female and two (4%) were male. Most of nurses were between 21 and 30 years of age ($n = 22$; 41%), as shown in Table 1.

One hundred and eleven police officers were interviewed from different ranks; 93 (84%) were male and 16 (14%) were female. Most of police officers were between 21 and 30 years of age ($n = 46$; 41%), as shown in Table 1.

When evaluated on the predictive signs and symptoms of anxiety, it was found that most of the nurses presented minimal levels of anxiety ($n = 27$; 51%), followed by light ($n = 16$; 30%), moderate ($n = 7$; 13%) and severe ($n = 3$; 6%), as shown in Table 2. Most of the police officers ($n = 61$; 55%) presented minimal level of anxiety, followed by light ($n = 25$; 22%), moderate ($n = 13$; 12%) and severe ($n = 10$; 9%) as shown in Table 2. The evaluation of anxiety between the groups was conducted using the chi-squared test. There were no significant differences ($p > 0.05$) between the groups.

Among the nurses in our study, 17 (32%) presented elevated risk for depression (Table 2). Among police officers, 30 (27.0%) presented elevated risk for depression (Table 2). The evaluation between the groups was conducted using the chi-squared test. There were no significant differences ($p > 0.05$) between the groups.

With regard to the chronotype of study participants, most of the nurses interviewed presented indifferent chronotype ($n = 25$; 47%), followed by the moderate matutinal chronotype ($n = 20$; 38%) as shown in Table 2. Among the police officers, 51 (46%) presented indifferent chronotype, followed by the moderate matutinal chronotype ($n = 48$; 43%), moderate vespertine chronotype ($n = 7$; 6%) and extreme vespertine chronotype ($n = 5$; 4%), as shown in Table 2. The evaluation between the groups was conducted using the chi-squared test. There were no significant differences ($p > 0.05$) between the groups.

Table 1 - Age of the included police officers and nurses

Age (Years)	Police Officers		Nurse		p
	N	%	N	%	
21 - 30	46	42	22	41	0,872
31 - 40	26	23	17	32	0,323
41 - 50	37	33	10	19	0,083
+ 50	2	2	2	4	0,595
Indeterminate	-	-	2	4	-
Total	111	100	53	100	-

Table 2 - Evaluation of anxiety and depression, chronotype and suicidal ideations in included police officers and nurses

Anxiety	Nurse		Police Officers		x ²	p
	N	%	N	%		
Minimum	27	51	61	55	0.10	0.753
Light	16	30	25	22	0.75	0.386
Moderate	7	13	13	12	0.00	0.985
Severe	3	6	10	9	0.19	0.551
Not responded	-	-	2	2	-	-
Total	53	100	111	100	-	-
Depressão	N	%	N	%	x ²	p
Without risk of depression	35	66	76	69	0.02	0.894
With risk of depression	17	32	30	27	0.23	0.628
Not responded	1	2	5	4	0.15	0.665
Total	53	100	111	100	-	-
Chronotype	N	%	N	%	x ²	p
Indifferent	25	47	51	46	0.00	0.984
Moderate matutinal	20	37	48	43	0.25	0.617
Extreme matutinal	3	6	5	4	0.00	0.714
Moderate vespertine	3	6	-	-	-	-
Extreme vespertine	1	2	7	6	0.71	0.439
Not responded	1	2	-	-	-	-
Total	53	100	111	100	-	-
Suicidal Ideation	N	%	N	%	x ²	p
Yes	5	9	6	5	0.40	0.336
No	48	91	102	92	0.00	0.771
Not responded	-	-	3	3	-	-
Total	53	100	111	100	-	-

Among the nurses, five (9%) reported suicidal ideation by the time of the interview (Table 2), reporting reasons such as relationship problems or losses. When asked about the time at which the suicidal ideations occurred, four (80%) mentioned that the ideations occurred more than 3 years ago. Psychotherapy (n = 2; 40%) was the solution that was most cited as the reason for resolution of the suicidal ideations.

Among the police officers, six (5%) reported suicidal ideation by the time the interview (Table 2). The police officers cited the following reasons for suicidal ideations: problems with stress, anxiety, and/or depression (n = 1; 17%), finances (n = 1; 17%), as well as other reasons. Among the officers that reported suicidal ideations at least once in their lives, three (50%) indicated that the ideations occurred more than three years ago, two

(33%) reported that it occurred less than one year ago and one (17%) reported that occurred between one and two years ago. Regarding the reason for the resolution of their suicidal ideations, two (33%) reported that they had taken no action, one (17%) reported having had medical follow-up, one (17%) reported that he sought religious assistance and with a professional psychologist, one (17%) sought religious assistance and one (17%) simply tried to stop thinking about it. Evaluation between the groups was conducted using the chi-squared test. There were no significant differences ($p > 0.05$) between the groups.

■ DISCUSSION

Most nurses in this study were females (96%); this result is consistent with the predominance of this gender in the nursing profession. In Brazil, in spite of the admission of men into the nursing labor market, nursing is still a predominantly female profession (87%).¹⁴ A study has shown that, among women, the risk for mental health problems was relatively high when they were exposed to continuously occurring stressors at work.¹⁵

The police officers participating in our study reflects the fact that police duty is typically a male profession in Brazil. We find that 84% of officers are male; this finding may be related to the traditional philosophy of the police force, which are influenced by the National Army. The same study cited above has shown that, among men, a recent episode of stress at work is associated with a high risk of developing mental health problems such as anxiety and depression.¹⁵

A study examining the chronobiology, sleep-wake cycle and anxiety level of nurses working in different shifts showed that 47% had between 31 and 40 years of age.² Another study evaluating the correlation between everyday stress levels and chronotype in nurses found that 87% of nursing professionals had between 20 and 39 years of age,¹⁶ similar to the data found in the current study. The age of the majority of police officers in our study is between 21 and 30 years of age (41%). A study described in a military report shows an average age of 33.5 years.⁸ Depression is more evident in the younger than in the older age groups.¹⁷ This finding may have influenced the higher frequency of depressive symptoms seen among police officers.

Nurses are the professionals that most interact with people in need of help.¹⁸ Studies of nurses and nursing assistants in a public hospital in São Paulo show the increased mental health demands of nurses, reporting that the diseases most referred to by workers, without a medical diagnosis, were emotional disorders including depression, anxiety and insomnia.¹⁹

A study of nursing professionals showed that situations within the work environment could cause anxiety.²⁰ These situations include instability or deterioration of the state of health of patients; lack of materials, equipment and/or personnel; relationships with the patient's family;

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difficulties with the systematization of nursing care and high-complexity procedures.²⁰

A Study of nurses involved in perioperative care showed that these professionals require greater attention to mental health care because of the intensity of physical and mental work, professional liability, complexity of care, shift work and urgent/emergency situations that can create anguish and anxiety.²¹

A study used the Beck Anxiety Inventory to evaluate anxiety in nursing professionals and found 49% of nurses with moderate to severe anxiety symptoms.²²

A study conducted in Rio de Janeiro²³ examined the impact of professional activities on the physical and mental health of uniformed and civilian police and noted that 34% of police in the study reported psychological suffering (psychosomatic symptoms, depression and anxiety) compared to a rate of 20% among other civilians.

When referring to the association between psychopathology and sleep disorders, some have reported that this relationship is bidirectional.²⁴ Mental disorders affect the occurrence of sleep disorders, as disruptions in sleep patterns are related to the occurrence of mental disorders. It is widely recognized that night shift work alters the circadian rhythm of individuals, causing an increase in stress, which in turn changes sleep patterns, promoting a feedback loop of the situation.¹⁶ Daytime sleep does not have the same restorative quality as nighttime sleep, causing night shift workers to develop a cumulative sleep debt, which results in decreased productive capacity.¹⁶ Thus, the schedule of daily activities should focus on the schedule that is most compatible with the degree of alertness for each chronotype, with the aim of improving performance and quality of life.¹

A study about chronotype and sleep deprivation status of nurses on the night hospital service showed that most presented an indifferent chronotype (64%), followed by moderately vespertine (24%) and moderately matutinal (12%) chronotypes. Extremes of matutinal and vespertine chronotypes were not seen.²⁵ In the current study, 25 (48%) nurses presented indifferent chronotype, 20 (38%) moderate matutinal chronotype.

A similar study was conducted in the city of Oporto, Portugal.²⁶ Gender differences are significantly related to the chronotype, with afternoon chronotypes being more prevalent in men compared with women.⁴ This information may explain the fact that nurses are predominantly of the moderate matutinal chronotype because most of the sample was composed of women.

Chronotype classifications in the police officers of this study revealed that 46% police had indifferent chronotype and 43% police had moderate matutinal chronotype. No previous studies were found that examined chronotypes in military. Study of North American police officers showed that sleep disturbances were common and significantly associated with an increased risk for problems related to health, performance and security.²⁷

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In this study, five nurses reported they had had suicidal ideations at the time of the study; the majority related that these ideations had occurred more than three years before. Depression sometimes represents the link between frames of anxiety and the risk of suicide.²⁸ A report on depressive symptoms and suicidal ideations among hospital nurses and doctors revealed that 4% attempted suicide.¹⁸ A study conducted with 24 tactical force police officers found that 92% always or sometimes felt stressed and that 21% reported having thought about suicide at some point.⁸ Current study differs from these results, because only 5% admitted to having suicidal ideations.

Summary

Nurses and military have high risk of anxiety and depression. Presence of suicidal ideation in their lives was relatively low. Indifferent and moderate matutinal chronotypes showed the highest prevalence in nursing and police.

Implementation of preventive measures is necessary for the early diagnosis of anxiety and depressive disorders in order to prevent complications, including suicide.

The limitation of this study is related to the fact that the measurement instruments were applied during the routine of work. This may have compromised the answers. To partially alleviate this situation, the interviews were made in a reserved place.

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IDEAÇÃO SUICIDA E AVALIAÇÃO DE CRONOTIPO ENFERMEIRAS E POLICIAIS MILITARES

INTRODUÇÃO: Enfermeiros e policiais militares são profissionais que trabalham em turnos e têm empregos que exigem atenção e responsabilidade. Eles trabalham sob condições que podem causar estresse, ansiedade e mudanças nos padrões de sono.

OBJETIVO: Este estudo visa identificar sintomas de ansiedade e depressão, cronotipo e a presença de ideação suicida em enfermeiros e policiais militares de Arapiraca/ Alagoas, Brasil.

MÉTODO: Este é um estudo descritivo e quantitativo. As entrevistas foram realizadas usando registros de Identificação e Dados Gerais, o Inventário de Ansiedade de Beck, a Escala de Depressão do Centro de Estudos Epidemiológicos e o questionário cronotipo de Horne-Ostberg

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RESULTADOS: Cinquenta e três enfermeiras e 111 policiais militares participaram do estudo. Militares e enfermeiras apresentaram cronotipo matutino indiferente e moderado. A maioria das enfermeiras e militares relatou níveis mínimos e leve de ansiedade. As enfermeiras e os policiais militares apresentaram um risco elevado para depressão. Cinco enfermeiras e seis policiais militares pensaram em tanto suicídio até o momento da pesquisa. Não houve diferenças significativas ($p > 0,05$) entre os grupos de estudo com relação aos sintomas de ansiedade e depressão, cronotipo e ideação suicida.

CONCLUSÃO: As enfermeiras e policiais militares estudados apresentaram um alto risco de sintomas de ansiedade e depressão. Um número considerável de enfermeiras e policiais militares tiveram ideação suicida ao longo da vida. A implementação de medidas de prevenção é necessária para o diagnóstico precoce de ansiedade e transtornos depressivos para evitar complicações, dentre estas, o suicídio.

UNITERMOS: Enfermagem. Polícia. Ansiedade. Depressão. Ideação suicida. Fenômenos de Cronobiologia.

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Evaluation of the quality of life and risk of suicide

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OBJECTIVE: To identify the socio-demographic profiles, suicidal ideation, the presence of mental disorders and the quality of life of patients using mental health services in Arapiraca, Alagoas, Brazil.

METHOD: Interviews were conducted in family health units and the Psychosocial Attention Center. The sample included 202 mental disorder patients with a risk of suicide attempts, 207 mental disorder patients without a risk of suicide attempts and 196 controls. This study used an identification questionnaire, the abbreviated World Health Organization Quality of Life questionnaire, Beck's Suicidal Ideation Scale and the Mini International Neuropsychiatric Interview.

RESULTS: Patients who had a mental disorder and a risk of suicide attempts tended to be single, had less education and lower family income, were not working and showed lower scores in quality of life domains; 73 of these patients had suicidal ideation in the previous week. Depressive disorders, manic episodes, hypomanic episodes, social phobias, obsessive compulsive disorder, post-traumatic stress disorder, psychotic syndromes and generalized anxiety disorder were more frequent and statistically significant for patients at risk for suicide attempts.

CONCLUSION: The management of patients with a risk of suicide attempts must focus on individual patients because this risk is directly linked to changes in quality of life and the improvement of these patients' prognosis.

KEYWORDS: Mental Disorders; Suicide Attempts; Suicidal Ideation; Quality of Life.

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Introduction

In 2014, the World Health Organization (WHO) (1) reported that almost 804,000 people commit suicide every year. According to the United Nations, 75% of these cases involve people from low- and middle-income countries. Brazil ranks eighth in the world for the number of suicides. In 2012, 11,821 deaths were recorded—9,198 men and 2,623 women. Between 2000 and 2012, the number of suicides has increased by 10.4% (1).

Suicidal behavior encompasses a number of phenomena linked to suicide, of which the most relevant are the suicide itself (death) and suicide attempts (2). Suicide attempts have the same phenomenological characteristics of suicides, differing only in terms of the outcome, which is not fatal in the case of suicide attempts (2).

It is believed that suicide attempts occur at least ten times more often than suicides, but official records regarding suicide attempts are scarcer and less reliable than those regarding suicide (3). There are no worldwide records on suicide attempts. It may be impossible to accurately obtain these data, as most of these attempts are never recorded in medical or legal contexts. It is estimated that the rates of suicide attempts may be 10 to 40 times higher than suicide rates (4). In addition, there may be at least ten times as many suicide attempts for each suicide, and there may be four unrecorded suicide attempts for each attempt recorded (5).

Mental disorder patients often complain of suicide attempts and/or suicidal ideation. The risk factors for suicide are social isolation, depression, schizophrenia, bipolar disorder, alcoholism, unemployment, extreme economic situations, difficult family relationships, a parental loss in childhood, a recent loss of a close friend or family member, organic diseases causing disability, chronic pain, malignant neoplasms, and AIDS (3). In addition, a family history of suicide is considered an aggravating factor (6).

Due to the consequences that suicide attempts generally introduce in the lives of the patient and his family, this study aims to identify the socio-demographic profiles, the suicidal ideation, the presence of mental disorders and the quality of life of patients who are receiving mental health services and who are at risk for suicide in Arapiraca, Alagoas, Brazil.

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Materials and methods

This quantitative research was conducted at the Psychosocial Attention Center (PAC) Nise da Silveira and in family health units (FHU) located in Arapiraca, Alagoas, Brazil.

The sample consisted of 605 people: 202 mental disorder patients and risk of suicide attempts (the MDRS Group); 207 mental disorder patients without a risk of suicide attempts (the MDWS Group); and 196 patients without mental disorder and without a risk of suicide attempt, who were the study's control group (the CO Group).

The exclusion criteria were patients with mental retardation and people who were younger than 18 years of age. The Research Ethics Committee of the Federal University of Alagoas approved this study, and the subjects studied expressed their acquiescence through informed consent.

The following scales and questionnaires were used: an identification questionnaire, the abbreviated WHO Quality of Life questionnaire (WHOQOL), Beck's Suicidal Ideation Scale and the Mini International Neuropsychiatric Interview (MINI 5.0) (7).

The identification questionnaire provided an economic profile and the social and health conditions of the patients studied. The WHOQOL allowed for an evaluation of the patient's quality of life in four domains: the physical, the psychological, social relations and the environment (8). The Suicidal Ideation Scale was used to identify the people who had had suicidal ideation in the last week (9). MINI 5.0 was used as a diagnostic interview. The control group consisted of patients who showed no mental disorder or suicide risk during the MINI. The analysis was conducted using the statistical programmer SPSS 20. Pearson correlation, χ^2 tests, and Student's *t* tests were used, with a significance value of $p \leq 0.05$.

Results

The MDWS group's average age was greater than those of the other groups ($p < 0.05$). Most of the patients interviewed were female (Table 1).

Most patients in the MDRS group were single or divorced, while most of the patients in the MDWS Group ($p < 0.05$) and the control group were married ($p > 0.05$) (Table 1). The level of education of the MDRS patients was lower than that the MDWS group ($p < 0.05$) and that of the control group ($p < 0.05$). A high level of education was found in the control group ($p < 0.05$), followed by the MDWS group ($p < 0.05$) (Table 1).

All patients claim to be religious. Most of the patients in the MDRS group have a family income of less than or equal to the minimum wage ($p < 0.05$), whereas most of the patients in the other groups have a family income exceeding the minimum wage (Table 1). Most of the patients in the MDRS group and the MDWS group do not work ($p < 0.05$), while most of those in the control group work ($p < 0.05$) (Table 1).

When health conditions are evaluated, it is clear that the most of the sample did not report the number of hospitalizations (Table 2). When compared with the other groups (Table 2), the MDRS group had the highest number of patients reporting that they had relatives with mental disorders ($p < 0.05$).

The MDWS group reported being more physically active ($p > 0.05$) (Table 2). The MDRS group reported more diseases (diabetes, hypertension and heart problems) ($p > 0.05$) (Table 2).

Among the 202 patients in the MDRS group, 168 had already attempted suicide, but only 73 showed suicidal ideation in the last week. In this group, the risk of suicide attempts was mild, followed by severe and moderate risks. Among the 207 patients in the MDWS group, 42 had already attempted suicide, but only four showed suicidal ideation in the last week. None of the patients from the control group presented suicide risks during the MINI 5.0 (Table 2).

In the general sample, it is clear that the 'environment' domain was the lowest. In the MDRS group, the lowest domains were the 'environment', the 'physical' and the 'psychological'. In the MDWS and CO groups, the lowest domain was the 'environment'. Statistical correlation has been found between these two groups ($p < 0.05$). Notably, the patients in the MDRS group presented lowest quality of life when compared with the other groups (Table 3).

The MINI 5.0 revealed that depressive disorders, psychotic syndromes, manic and hypomanic episodes, generalized anxiety disorder, social phobias, post-traumatic stress disorder and obsessive compulsive disorder are more common and statistically significant in the MDRS group ($p < 0.05$) (Table 4).

Discussion

The average age in the three groups studied were 36.4 (MDRS), 39.2 (MDWS) and 37.0 years (CO). Some studies show that these averages are within the age range of patients who reported more suicide attempts in the southern region of Brazil (30 to 39 years of age) (10) and in Ceará (30 to 59 years of age) (11). A study conducted in Alagoas showed that the average age was younger (20.1 years) (12), which conflicts with our study's findings.

Most patients interviewed were female, perhaps because the greatest demand for health services in Arapiraca comes from women. This gender ratio may present a bias in this study; however, as suicide attempts are more frequent among women (10-13), this ratio does not disqualify the findings of the study. Women attempt suicide more often than men, but men choose more lethal means to achieve that purpose (10).

One study shows that a higher risk of suicide exists among single and divorced/widowed people compared with married people (14). Our data corroborates this finding. However, a study conducted in southern Brazil shows that married women attempted suicide more often (10).

We have identified that the patients in the MDRS group had a lower level of schooling than patients in the other groups. A low educational level is common among those who attempt suicide (10, 11, 13). In this case, researchers should consider whether this low level of education is related to some previous mental disorder that reduces the individual's likelihood of achieving a higher level of education (15).

A rarely studied area involves several possible mechanisms by which religion can be associated with a lower risk of suicide (15). We found no difference between the groups regarding religion. Isolation and permanent feelings of exclusion may cause people who experience difficulties that are rarely discussed to distance themselves from religion, which could provide them with a glimpse of possible solutions and relief from their suffering (16). A study conducted in Ceará shows that patients who had attempted suicide were religious (96.5%) (11).

**Table 1** - General characteristics of the sample (n=605).

General data	MDRS*	MDWS*	CO*	t
Age				0.001
Mean (SD)	36.4 (11.3)	39.2 (13.4)	37.0 (12.8)	
Sex				
Female/Male	164/38	173/34	171/25	
Marital status				
Married	99 (49.0%)	137 (66.2%)	114 (58.2%)	
Single/Divorced	103 (51.0%)	70 (33.8%)	82 (41.8%)	
Schooling				
Complete and incomplete higher education	5 (2.5%)	23 (11.1%)	46 (23.5%)	
Complete and incomplete high school	40 (19.8%)	56 (27.1%)	67 (34.2%)	
Complete and incomplete elementary school	157 (77.7%)	128 (61.8%)	83 (42.3%)	
Religion				
Religious	189 (93.6%)	193 (93.2%)	186 (94.9%)	
Not religious	13 (6.4%)	14 (6.8%)	10 (5.1%)	
Family income				
Up to 1 minimum wage earner	119 (58.9%)	91 (43.9%)	69 (35.2%)	
More than 1 minimum wage earner	83 (41.1%)	116 (56.1%)	127 (64.8%)	
Employment				
Yes	49 (24.2%)	81 (39.1%)	105 (53.6%)	
No	153 (75.8%)	126 (60.9%)	91 (46.4%)	

* MDRS: mental disorder patients and risk of suicide attempts; MDWS: mental disorder patients without risk of suicide attempts; CO: control.

Most of the patients in the MDRS group had lower family incomes than those of the patients in the other groups. According to the WHO (17), the risk factors for suicides are social extremes, including low and high incomes. Some studies show that those who have attempted suicide more frequently belong to a low economic class (5, 11), identifying the classes C, D and E (13).

Most of the patients in the MDRS and MDWS groups did not work, while most of those in the control group worked. Mental disorders might hinder patients in MDRS and MDWS

groups from entering into the labor market. Some studies shows that unemployment is a risk factor for suicide attempts (5, 11). However, studies have shown suicide attempts among some workers (10).

A study conducted in Ceará identified that 68% of patients who attempted suicide had a history of psychiatric hospitalization (11). In this study, it has not been possible to identify how many times the patients have been hospitalized to evaluate how the number of hospitalizations relates to the risk of suicide attempts.

Table 2 - Characteristics of the health conditions of the sample (n=605).

Health conditions	MDRS*	MDWS*	CO*
Number of hospitalizations			
Up to 2	21 (10.4%)	7 (3.4%)	3 (1.5%)
More than 2	29 (14.4%)	12 (5.8%)	2 (1.0%)
None	152 (75.2%)	188 (90.8%)	191 (97.5%)
Relatives with mental disorders			
Yes	120 (59.4%)	89 (43.0%)	66 (33.7%)
No	72 (35.6%)	107 (51.7%)	107 (54.6%)
Do not know	10 (5.0%)	11 (5.3%)	23 (11.7%)
Physical activity			
Yes	41 (20.3%)	60 (29.0%)	52 (26.5%)
Comorbidity			
Diabetes	20 (9.9%)	15 (7.2%)	9 (4.6%)
Hypertension	37 (18.3%)	32 (15.5%)	25 (12.8%)
Heart problems	10 (5.0%)	6 (2.9%)	6 (3.1%)
Other	22 (10.9%)	30 (14.5%)	20 (10.2%)
Number of suicide attempts	168 (83.2%)	42 (20.3%)	0
1 time	67 (39.9%)	26 (61.9%)	0
2 to 3 times	28 (16.7%)	7 (16.7%)	0
More than 4 times	62 (36.9%)	5 (11.9%)	0
Not reported	11 (6.5%)	4 (9.5%)	0
Current suicidal ideation			
Yes	73 (36.1%)	4 (1.9%)	0
Risk of suicide (MINI)			
Mild	101 (50.0%)	0	0
Moderate	12 (5.9%)	0	0
Severe	89 (44.1%)	0	0

* MDRS: mental disorder patients and risk of suicide attempts; MDWS: mental disorder patients without risk of suicide attempts; CO: control.

**Table 3 - Average and standard deviation of domains in relation to the presence of mental disorders and the risk of suicide attempts.**

Mean (SD)	Physical	Psychological	Social relations	Environment	General quality of life	p
General	62.3 (17.8)	63.7 (17.4)	66.0 (17.6)	53.5 (14.4)	64.1 (20.7)	0.000
MDRS*	50.5 (17.4)	51.2 (18.3)	57.4 (18.3)	46.9 (14.7)	52.9 (22.4)	0.000
MDWS*	64.0 (15.4)	65.6 (13.3)	66.6 (15.9)	53.6 (12.4)	66.3 (17.8)	0.000
CO*	72.6 (12.6)	74.4 (11.2)	74.2 (12.4)	60.0 (12.9)	72.9 (16.2)	0.000

* MDRS: mental disorder patients with risk of suicide attempts; MDWS: mental disorder patients without risk of suicide attempts; CO: control.

Significant difference between the MDRS, MDWS and CO groups ($p=0.000$) (two-way ANOVA).

Presented correlation between the MDWS and CO groups ($p=0.001$) (Pearson correlation coefficient).

A family history of mental disorders increases the risk of suicidal behavior (2). In this study, we have shown that most patients in the MDRS group have relatives with mental disorders. Having a relative with a mental disorder was more common in the MDRS group.

Some studies have shown that degenerative diseases contribute to suicidal behavior (18). Study on Republic of Korea identified that heart problems and diabetes mellitus are risk factors for suicide (19). Study in Australia did not identify diabetes mellitus as a risk factor for suicide (20). Our study showed that patients in the MDRS group showed the highest frequency of chronic degenerative diseases, including diabetes, hypertension and heart problems.

In all three groups, we realized that the 'environment' domain performed worse than the other domains. The patients in the MDRS group showed lower quality of life when compared to other groups. In individual terms, emotional resiliency, the ability to solve problems and certain social skills can reduce the impact of adverse environmental factors or intrapsychic factors and can counterbalance the weight of some risk factors (2). Suicide is a complex phenomenon with various causes, and it is an important indicator of a population's quality of life (21).

The presence of a mental disorder is one of the most important risk factors for suicide. In general, it is believed that

90% to 98% of those who commit suicide have a mental disorder (2, 22, 23). Our study showed that depressive disorders, manic episodes, hypomanic episodes, social phobias, obsessive compulsive disorder, post-traumatic stress disorder, psychotic syndromes and generalized anxiety disorder are more common in patients in the MDRS group.

Mood disorders, in particular depressive disorders, represent the most frequent diagnoses among patients with mental disorders who committed suicide (2, 24, 25). In addition, studies show the presence of depression (13, 26) and anxiety disorders (13, 27) increases the risk of suicide.

Depression was the most common mental disorder in the MDRS group. Despite the severity of depression and the availability of effective treatments, only 30% of the cases worldwide receive the necessary care (28). Estimates show that, by 2020, depression will be the second most common disease and will be more prevalent in all age groups of both sexes worldwide (28).

This study shows that urgent mental health care measures should be implemented for mental disorder patients who present a higher risk of suicide attempts. Otherwise, there will be a considerable increase in the number of suicide attempts and, in turn, the number of suicides.

Table 4 - Frequency of mental disorders in patients with and without risk of suicide attempts.

Mental disorder	General*		MDRS*		MDWS*		OR	p
	n	%	n	%	n	%		
Current major depressive episode	209	34.5	139	68.8	70	33.8	4.3	0.000
Recurrent major depressive episode	148	25.3	89	44.1	59	28.5	2.0	0.001
MDE with melancholic features	139	23.0	98	48.5	41	19.8	3.8	0.000
Dysthymic disorder	30	5.0	22	10.9	8	2.9	3.3	0.006
Manic episode	133	22.0	84	41.6	49	23.7	2.6	0.000
Hypomanic episode	27	4.5	19	9.4	8	3.9	2.6	0.041
Panic disorder	53	8.8	31	15.3	22	10.6	1.7	0.123
Agoraphobia	184	30.4	93	46.0	91	44.0	1.1	0.747
Social phobia	69	11.4	50	24.8	19	9.2	3.2	0.000
Obsessive compulsive disorder	48	7.9	39	19.3	9	4.3	5.3	0.000
Post-traumatic stress disorder	52	8.6	40	19.8	12	5.8	4.0	0.000
Alcohol abuse/dependency	37	6.1	21	10.4	16	7.7	1.5	0.325
Substance abuse/dependency	12	2.0	7	3.5	5	2.4	1.5	0.650
Psychotic syndrome	162	26.8	106	52.5	56	27.0	3.6	0.000
Mood disorder with psychotic features	74	12.2	60	29.7	14	6.8	5.8	0.000
Anorexia nervosa	0	0	0	0	0	0	-	-
Bulimia nervosa	5	0.8	3	1.5	2	1.0	1.5	0.978
Generalized anxiety disorder	147	24.3	94	46.5	53	25.6	2.5	0.000
Antisocial personality disorder	6	1.0	4	2.0	2	1.0	2.1	0.659
Total	605	100.0	202	100.0	207	100.0		

* General: all patients studied; MDRS: mental disorder patients with risk of suicide attempts; MDWS: mental disorder patients without risk of suicide attempts. Chi-square tests were used to compare the MDRS, TMRS and MDWS groups.



This study has shown that the mental disorder patients with a risk of suicide attempt were mostly single, had a lower level of education, had a lower family income and were not working. They also had had suicidal ideation in the last week, had a lower quality of life, and suffered from depressive disorders, manic episodes, hypomanic episodes, social phobias, obsessive compulsive disorder, post-traumatic stress disorder, psychotic syndromes and/or generalized anxiety disorder.

The management of patients with a risk of suicide needs to be revised to enable changes in patients' quality of life and the care devoted to the mental disorders identified. A patient who does not receive the necessary care may be more likely to attempt suicide. Therefore, offering a mental health services network that facilitates patients' access to care may prevent and reduce the number of suicide attempts and contribute to the improvement of their quality of life.

The limitation of this study is related to the difficulty of interviewing men in the health service in Arapiraca's city. Have a more homogeneous sample about sex would make it possible to identify the profile of mental disorders, suicide attempts and quality of life in both sexes, but the men do not usually attend this type of service.

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AUTHOR CONTRIBUTIONS

Alves VM designed the study, wrote the protocol, managed the literature searches, analyzed the data, wrote the manuscript and performed the statistical analyses. Lima Francisco LC, Pereira Belo FM, de-Melo-Neto VL and Barros VG analyzed the data and wrote the manuscript. Nardi AE contributed to a critical review of the paper. This research is part of a doctoral thesis in Psychiatry and Mental Health by Veronica de Medeiros Alves, Institute of Psychiatry, Federal University of Rio de Janeiro. All authors contributed to and approved the final manuscript.

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Trends of Suicide attempts in emergency service.

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Abstract

Objective: The primary goal of this study was to characterize the profile of suicide attempts treated in the Emergency Unit of Arapiraca City, Alagoas, Brazil from 2009 to 2012.

Methods: We analyzed all forms of emergency bulletins with a diagnosis of suicide attempt. Data were evaluated using Student's t-test and Pearson's chi-squared. A value of $p < 0.05$ was used to determine significance. **Results:** We identified 2,142 cases. The suicide attempts were more frequent among women and young adults, but deaths were more frequent among men. Suicide attempts were more frequent among patients from ages 10 to 39 years old (81.1%). Exogenous poisoning were more frequent (95.1%). The month of April (10.6%) had the largest number of cases, and July had the smallest number (5.5%). Spring (28.3%), Sundays (18.4%) and Saturdays (16.8%), and from 12:00 pm to 5:59 pm all had more cases of suicide attempts. **Conclusion:** Suicide prevention measures in health services for young women, monitoring regarding the care provided, and the sale and use of medicines and poisons must be better monitored.

Key words: Suicide attempt, poisoning, emergency

Introduction

A mental health emergency refers to difficulties in thinking or in behaviors that requires immediate treatment. These challenges are associated with a risk of death, such as in suicide or in patients with violent behavior. Interventions to reduce complications are also required.¹

The number of patients in emergency hospitals is increasing due to a growing incidence of self-inflicted violence, altered mental status, and an alcohol dependence epidemic and other substance-related disorders.¹ The presence of a mental disorder is also one of the most important risk factors for suicide. In general, 90% to 98% of people who commit suicide have a mental disorder.^{2,3}

Although, there are fairly reliable national records for suicide deaths, there are not any systematic records of suicide attempts. This lack of information makes it difficult to understand and characterize the situations that lead to suicide attempts, as well as to plan

interventions for proper prevention and care after a suicide attempt.² It is estimated that the rate of suicide attempts may be 10 to 40 times higher than suicide deaths.^{4,5}

Although Brazil has lower rates of suicide among emerging countries, the problem is worsening,⁶ creating a public health crisis.⁷ Between 1998 and 2008, Brazil reported a 33.5% increase in the number of suicides.⁸ Today, Brazil is the eighth highest country in number of suicide attempts.⁹ From an economic perspective, suicide and suicide attempts represent an enormous cost to society. First, they use public resources that could be allocated differently. Second, they involve a loss significant of human capital⁶. Understanding suicide attempts can contribute to the planning of care directed to this specific population. Thus, this study aims to characterize suicide attempts treated in the Emergency Unit of Arapiraca City, Alagoas, Brazil between 2009 and 2012. Arapiraca is the main city of the state of Alagoas. It is located 123 km from the Maceió City and has a population of 214,000 inhabitants.

Materials and methods

It is quantitative, descriptive, retrospective, and a documentary study. The survey was conducted in the Urgent and Emergency Unit Dr. Daniel Houly located in Arapiraca City, Alagoas, Brazil. This hospital is a reference in the region for the treatment of trauma for several causes. We used a model form, following the service bulletin sheet used in this unit. How variables were studied: age, sex, the victim's vehicle, use of alcohol, if you're pregnant, presence of mental disorders, psychological follow-up, death by suicide, suicide method, city and neighborhood, month, day of week and season of suicide attempts.

Health professionals who serve in the hospital unit in this study, considered suicide attempts as exogenous poisoning, hanging, drowning, burning, use of weapons and firearms, and jumping from high places, as these are carried out with the purpose of ending one's life. This diagnosis was exclusively given by the medical service.

We analyzed all emergency bulletins with a diagnosis of suicide attempt from January 2009 to December 2012. Cases with erased bulletins, unreadable spellings, or no diagnoses of suicide attempts during the study period were excluded from the research. We used a standard form, similar to the emergency bulletin form used at the hospital, to acquire data. All healthcare professionals involved in the treatment of suicide attempt victims, recorded the data of patients who were treated in this hospital using this emergency bulletin.

The Research Ethics Committee of the Federal University of Alagoas approved the study. Data analysis was performed using the EPI INFO 7 program (Atlanta, Georgia, USA). Statistical analyses included Student's t-test and Pearson's chi-squared. A value of $p < 0.05$ was used to determine significance.

Results

We identified a total of 2,142 suicide attempts. There were 520 suicide attempts in 2009, 576 in 2010, 550 in 2011 and 496 in 2012. There are more women that attempted suicide than men. The frequency of cases of suicide attempts was statistically significant in the years 2009 and 2011 ($p < 0.05$) and in 2010 and 2011 ($p < 0.05$) (Table 1).

The average age of cases during the years studied was statistically significant [$t(3) = 62.2$; $p < 0.05$]. A similar result was found when comparing female [$t(3) = 104.7$, $p < 0.05$] and male patients [$t(3) = 32.7$; $p < 0.05$]. Women had a lower average age than men (Table 1). Suicide attempts were more frequent among patients between 10 and 39 years old (Table 1).

Only one half of the cases treated in the hospital were brought by an ambulance. The use of alcoholic beverages was more frequent in 2012 (25.2%). Underreporting in identifying the use of alcoholic beverage and mental disorders cases among patients treated for suicide attempt also occurred. Patients were discharged from the hospital based on a decision from the medical service and were referred to basic care services such as psychosocial attention

centers and psychiatric outpatient clinics. The years 2009 and 2010 showed a higher frequency of attempted suicide among pregnant women (Table 1). The death of patients was more frequent in males, except in 2012. The largest number of deaths was in 2010 (Table 1).

Exogenous poisoning was the main method used to attempt suicide. Medicine intoxication ($p < 0.05$) was the most frequent. Among the most aggressive methods, people who used a weapon were the most frequent, followed by hanging (Table 2).

In our analysis of the neighborhoods of Arapiraca that presented more suicide attempts, we identified that the countryside and the city center showed greater frequencies of attempted suicides (Table 3).

Arapiraca is one of the municipalities of Alagoas that has a large number of cases of suicide in people over 10 years of age (1.56/100.000 inhabitants in 2011). Despite this, we found a considerable number of cases among some neighboring towns: Taquarana (2.13/100.000 inhabitants in 2011), Lagoa da Canoa (1.61/100.000 inhabitants in 2010), Feira Grande (1.33/100.000 inhabitants in 2011), Craíbas (1.26/100.000 inhabitants in 2012), Girau do Ponciano (1.26/100.000 inhabitants in 2011), and Limoeiro de Anadia (1.18/100.000 inhabitants in 2012) (Table 3).

The months with the highest frequency of suicide attempts were from January to April, followed by a decline, but then a rise again from September to December. April had the highest number of cases and July had the lowest. Spring and autumn were the seasons of the year with the highest frequencies of suicide attempts. Saturday, Sunday, and Monday were the weekdays with the highest number of suicide attempts. The majority of occurrences of attempts were from 6:00 pm to 11:59 pm and from 12:00 pm to 5:59 pm ($p < 0.05$) (Table 4).

Discussion

From 2009 to 2012, there were a considerable number of cases of suicide attempts. This number remained similar over the years, suggesting that no preventive measures that were taken by the health services of the city. A similar study conducted in a mental health unit at the University Hospital Del Valle, Colombia, from 1994 to 2010 identified 2,012 cases of attempted suicide.¹⁰ Another study conducted in the micro region of Barbacena, Brazil composed of 15 municipalities and a population of approximately 230,000 residents identified 1,060 suicide attempts from 2003 to 2009.¹¹ Arapiraca has 214,000 inhabitants, which is less than the population of the study above. When compared to those studies, the amount of identified attempts in our study is alarming and deserves attention, as there were a greater number of cases over a shorter period of time.

Estimates show that for each suicide, there are at least ten attempts serious enough to require medical attention. Additionally, for each suicide attempt, four unknown attempts are made.⁶ Realistically, the consequences of the number of suicide attempts in this city are even greater. Thus, this study presents attempts to provide a profile of cases that can contribute to the identification of critical points in mental health care and care in urgent and emergency situations. Identification of sex that more often leads to suicide attempts and suicide and the media age are vital to care and prevention strategies. Finally, other variables that can be intervened include the use of alcoholic beverages, pregnancy, the season, month, day and hour.

A study conducted in the mental health unit at the University Hospital Del Valle, Colombia, from 1994 to 2010 identified that most patients who attempted suicide were women.¹⁰ Other studies show more cases of suicide attempts among women, corroborating what we found in our study.¹¹⁻¹⁵ Women attempt suicide more often than men, but men use more lethal methods when attempting suicide.^{3,13} A lower occurrence of suicide among women, in some studies, has been attributed to a low prevalence of alcohol dependence,

greater religiosity, social involvement, and influence of the roles of the mother, wife, and daughter. In addition, women are better at recognizing early signs of risk for depression, suicide, and mental illness; they are more likely to seek help in times of crisis and participate more in social support networks.¹⁶

A study in Korea identified that the average age of patients attempting suicide was 42.32 years.¹⁴ This result differs from our study, where the average age of the patients was a lower age. Studies show that the highest frequency of suicide attempts occurs among those ages 20 to 39 years,¹² from 30 to 40 years and from 20 to 25 years.¹³ In our study, the attempts occurred more frequently in younger people.

The fact that some of the patients in the hospital unit were not brought to the hospital by ambulance, leading to a rapid rescue by relatives or neighbors, suggests that individuals did not understand the gravity of the situation. This finding also suggests that there may be difficulties in accessing mobile relief services in this city.

Our study identified a small number of cases involving the use of alcohol. Consumption of alcohol in instances of suicide has been mentioned by some authors.^{17,18} In a deeper understanding of this relation is necessary to increase measures that can help prevent suicide attempts involving the abuse of alcohol.

Diagnosing the presence of mental disorders among patients treated for suicide attempts must also be encouraged, considering the fact that mental disorders are a risk factor for suicide attempts. Wider access to the identification and treatment of serious mental disorders are crucial to reducing suicidal behaviors. The current unsatisfactory situation of mental health care in Brazil may be contributing to the worsening of this problem.¹⁹ Not all cases of suicide can be prevented, but the ability to address suicide, makes a difference. Thousands of lives could be saved every year if all the people who attempted suicide were properly treated. A decrease in suicidal ideation and suicide attempts, must surely lead to decreased mortality.^{20,21} Despite of the patients being released from the hospital with a referral to a health service available in the city, it is not guaranteed that these individuals will obtain the health care they need. Not accessing timely assistance can worsen the patients' disease and consequently increase the risk of additional suicide attempts.

Cases of suicide attempts during pregnancy are not very common and should be considered a protective factor. The hormonal changes that occur in pregnancy leave pregnant women more sensitive, which may contribute to the emotional liability of pregnant women who already had a mood disorder prior to pregnancy. Our study identified that there was a higher frequency of cases of attempted suicide among pregnant women from 2009 to 2010. Studies on pregnant women have begun to identify the risk of suicide among this population.^{22,23} During pregnancy, women become vulnerable to the adverse consequences of depression, which are often exacerbated by the hormonal changes experienced during this period.²⁴ The prenatal period is an excellent opportunity to combine the efforts of different professionals to improve the psychosocial condition of pregnant women.²³

The largest number of deaths occurred among males. This finding is likely the result of the fact that men were more likely to use violent methods for their suicide attempts.

Our study identified an increased frequency of using medicines to attempt suicide. Studies indicate that this method is one of the most commonly used in suicide attempts.^{14,25-28} It is necessary to pay attention to the ease of access to medicines as a means for suicide attempt. Security measures must be taken to reverse this high number of cases.

A meta-analysis identified 62 methods of suicide in Japan. Poisoning was the most frequent.²⁹ This method was also identified as the most common in southern Brazil.¹³ In rural areas of China and Southeast Asia, the ingestion of pesticides has been linked to more than 60% of suicides.³⁰ In our study, most cases of suicide attempts occurred among those who resided in rural areas from Arapiraca.

Another poison used was rodenticide. Aldicarb is a rodenticide illegally sold in Brazilian cities. One study identified "aldicarb" as the most common method of suicide attempts by rat poison.^{28,31}

Restricting the use of toxic products combined with more rigorous actions by supervisory departments and companies responsible at points of sale should be the main strategies to minimize poisoning in Brazil.^{26,27}

A study in Rio Grande do Sul, Brazil, has identified a precarious balance between identifying people at risk of suicide and resistance from administrators of services to accommodate this demand in the emergency room.³² This problem is not just a feature of Rio Grande do Sul; Brazil's health system has difficulties in preventing suicide because of this factor.

Improving people's ability to value life and greater attention to mental disorders and psychological and psychiatric problems could alleviate the problem of some regions with higher suicide rates.⁶

It is important that those planning health practices consider universal access to health services. It is essential to properly train health professionals, emergency units, mental health services, and primary health care, which should be organized and articulate a protocol within health networks.¹¹ The strengthening of the network will allow early identification of crisis situations before they turn into suicide attempts.³¹

This research shows that young people have a higher risk of suicide attempts and that poisoning is the most frequently used method. People who use medicines to attempt suicide are the most common cases, which raises concerns about ease of access to these medications. Special attention must also be given to poisonings with actual poison, given that most of the suicide attempts of this type correspond to people residing in rural areas. This raises the concern of easing access to pesticides, as well as the use of chemicals and rodenticides.

The attendances for suicide attempts have increased in the hospital where the study was conducted. Despite this, there are a considerable number of cases from neighboring towns. A study in Sevilla, Spain, identified that most suicides occurred in rural areas.¹⁷ These results were similar to our study. However, a study conducted in southern Brazil identified that suicide attempts were more common among people who lived in an urban area.¹³

Studies are able to identify the frequency of suicide attempts according to the season, month, day of the week, and time of day. Suicidal behavior can be influenced by sunlight and follows a seasonal pattern. However, the seasons also bring changes in various other meteorological factors, and seasonal rhythms in social behavior can also contribute to fluctuations in suicide rates.³³

A study in Bahia, Brazil, has identified that autumn and spring presented a higher frequency of suicide attempts.¹² These results were important and corroborate with our study. Another study identified a greater frequency of suicide attempts in autumn.¹⁵

A study conducted at the University Hospital Del Valle (Colombia) found that the month of March had more suicide attempts and that the month of June had the lowest frequency of attempts.¹⁰ In our study, we found that April and July had the highest and the lowest occurrence of cases, respectively.

One study showed that Saturday and Tuesday were the days of the week with the most cases of suicide attempts.¹² Another study identified Sunday as having the highest number of cases.^{10,15} Our study identified Saturday, Sunday, and Monday as having the greatest number of suicide attempts. This could be due to several factors, including alcohol.

Studies have shown that suicide attempts occur in the morning and at night¹² or in the afternoon.¹⁵ In our study, we found that suicide attempts were most frequent during the afternoon and at night. It is not known what might be influencing the occurrence of these cases in the afternoon and at night.

The profile of cases identified in the Emergency Unit studied has identified that women and young adults were more likely to attempt suicide, but deaths were more frequent among men. The most commonly used method was drug poisoning. Arapiraca had the largest number of cases, as this is the city in which the hospital unit is located. Comparing the number of cases of suicide attempts with the number of inhabitants in the cities studied, identified that Taquarana had the highest rate of suicide per number of inhabitants, but this result cannot be taken into account, considering that other cases of suicide attempts in these cities may have been observed in other hospitals or medical clinics. The cases of suicide attempts were more frequent in April; in spring and autumn; on Saturday, Sunday and Monday; and during the morning and afternoon.

Earlier diagnosis of mental disorders is useful in preventing suicide attempts. To accomplish this, there needs to be an organized mental health network that encourages monitoring and treatment of patients who are at risk for suicide attempts. Restrictive measures regarding the use of toxic products and medicines must be carried out and emphasized. Guidance on the careful measuring, handling, and packaging of these products and the conscious use of medicines should be carried out by health services in cities with high rates of attempted suicide by poisoning. We know that we cannot prevent all cases of suicide attempts, but restrict access to medicines and treating patients with mental disorders are efficient ways to prevent them from happening as frequently.

The limitation of this study is that the authors cannot control variables of the patients studied in the Emergency Unit. For example, suicide attempts are more frequent among patients from 10 to 39 years old, but this is also precisely the age group more likely to be found seeking care in the Emergency Unit. Women (vs. men) and transportation to the emergency room from neighbors (vs. an ambulance) also represent a greater number of cases both in our study in the Emergency Unit in general. Another limitation is related to faults in the description of the conditions of psychiatric patients and failure to register some information from the hospital chart. This hindered the identification of other variables involved in suicide attempts. The relationship of suicide attempts with the use of alcoholic beverages presented in medical records, and registration failures prevented us from doing an analysis of association. The study cannot infer that the number of suicide attempts at this hospital represent the totality of cases from the city of Arapiraca. This is because some people may have been taken to smaller hospitals may not have needed medical attention provided in a hospital.

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Table 1 – General data of patients treated for suicide attempt in Urgency and Emergency Hospital Dr Daniel Houly between 2009 and 2012.

MEAN (SD) AGE	2009		2010		2011		2012		<i>t</i>
Total	26.83 (11.2)		27.8 (11.6)		26.98 (12.5)		28.76 (13.2)		<i>p</i> <0.05
Female	25.78 (10.86)		26.5 (11.1)		25.76 (11.37)		26.74 (11.2)		<i>p</i> <0.05
Male	28.8 (11.58)		30.3 (12.3)		30.21 (14.67)		33.26 (16.1)		<i>p</i> <0.05
AGE	2009		2010		2011		2012		
	N	%	N	%	N	%	N	%	
10 - 19 years	150	28.8	155	27.0	193	35.1	144	29.0	
20 – 29 years	201	38.6	210	36.4	176	32.0	165	33.3	
30 – 39 years	102	19.7	111	19.3	92	16.7	93	18.8	
40 – 49 years	43	8.3	66	11.4	54	9.8	63	12.7	
50 – 59 years	12	2.3	20	3.5	16	2.9	14	2.8	
60 – 69 years	10	1.9	12	2.1	13	2.4	9	1.8	
70 – 79 years	1	0.2	0	0	4	0.7	5	1.0	
80 – 89 years	0	0	0	0	0	0	3	0.6	
Without registration	1	0.2	2	0.3	2	0.4	0	0	
GENERAL DATA	N	%	N	%	N	%	N	%	
Female	338	65.0	379	65.8	400	72.7	342	69.0	
Male	182	35.0	197	34.2	150	27.3	154	31.0	
Came by ambulance	268	51.5	313	54.3	252	45.8	223	45.0	
Use of alcohol	47	9.0	60	10.4	32	5.8	125	25.2	
Mental disorder	45	8.6	53	9.2	33	6.0	26	5.2	
Pregnant	16	3.0	19	3.3	5	0.9	3	0.6	
Discharge	420	80.8	412	71.5	392	71.3	314	63.3	
Psychosocial care and Outpatient Center	90	17.3	70	12.2	27	4.9	60	12.1	
General death	11	2.1	21	3.6	13	2.4	7	1.4	
Male death	8	72.7	14	66.7	8	61.5	3	42.9	
Female death	3	27.3	7	33.3	5	38.5	4	57.1	
TOTAL	520	100.0	576	100.0	550	100.0	496	100.0	

Table 2 - Frequency of suicide attempts admitted to Urgent and Emergency Hospital Dr. Daniel Houly between 2009 and 2012.

DIAGNOSIS	2009		2010		2011		2012	
	N	%	N	%	N	%	N	%
Hanging	2	0.4	7	1.2	2	0.4	7	1.4
Drowning	0	0	1	0.2	2	0.4	0	0
Exogenous poisoning	514	98.8	540	93.8	536	97.5	448	90.3
Melee weapon	14	2.7	24	4.2	14	2.5	7	1.4
Firearm	1	0.2	4	0.7	1	0.2	3	0.6
Fall from height	2	0.4	6	1.0	1	0.2	2	0.4
Burn	0	0	0	0	1	0.2	2	0.4
TOTAL	520	100.0	576	100.0	550	100.0	496	100.0

Table 3 – Frequency of suicide attempts treated in Urgent and Emergency Hospital Dr Daniel Houly by surrounding cities and neighborhood of Arapiraca city between 2009 and 2012.

CITY	2009		2010		2011		2012	
	N	%	N	%	N	%	N	%
Arapiraca	243	46.8	274	47.6	276	50.2	233	47.0
Craíbas	19	3.6	20	3.5	18	3.3	23	4.6
Feira Grande	14	2.7	22	3.8	23	4.2	18	3.6
Girau do Ponciano	35	6.7	2	0.3	37	6.7	23	4.6
Lagoa da Canoa	20	3.8	24	4.2	21	3.8	17	3.4
Limoeiro de Anadia	14	2.7	18	3.1	16	2.9	26	5.2
Taquarana	16	3.1	18	3.1	33	6.0	24	5.0
Other	157	30.2	194	33.7	126	22.9	132	26.6
Without registration	2	0.4	4	0.7	0	0	0	0
NEIGHBORHOOD	2009		2010		2011		2012	
	N	%	N	%	N	%	N	%
Brasília	16	6.6	13	4.7	9	3.3	9	3.9
Cacimbas	11	4.5	16	5.8	18	6.5	1	0.4
Centro	36	14.8	37	13.5	18	6.5	40	17.2
Planalto	15	6.2	13	4.7	11	4.0	10	4.3
Primavera	8	3.3	24	8.8	29	10.5	17	7.3
Zona rural	38	15.6	143	52.2	121	43.8	101	43.3
Other	119	49.0	28	10.2	70	25.4	55	23.6
Total	243	100.0	274	100.0	276	100.0	233	100.0

Table 4 – Frequency of suicide attempts treated in Urgent and Emergency Hospital Dr. Daniel Houly by month, season, and time between 2009 and 2012.

MONTH	2009		2010		2011		2012		TOTAL
	N	%	N	%	N	%	N	%	N
January	38	7.3	45	7.8	97	17.6	47	9.5	227
February	49	9.4	38	6.6	3	0.5	49	9.9	139
March	51	9.8	32	5.6	40	7.3	75	15.1	198
April	54	10.4	51	8.8	41	7.4	82	16.5	228
May	43	8.3	42	7.3	32	5.8	40	8.1	157
June	40	7.7	36	6.2	37	6.7	17	3.4	130
July	33	6.4	26	4.5	43	7.8	15	3.0	117
August	28	5.4	51	8.8	41	7.5	10	2.0	130
September	46	8.8	52	9.0	36	6.5	60	12.1	194
October	47	9.0	73	12.7	62	11.3	34	6.8	216
November	41	7.9	70	12.2	70	12.8	45	9.1	226
December	50	9.6	60	10.4	48	8.8	22	4.4	180

Station/Year	2009		2010		2011		2012		
	N	%	N	%	N	%	N	%	
Autumn	149	28.6	133	23.1	101	18.4	174	35.1	
Winter	109	21.0	129	22.4	120	21.8	70	14.1	
Spring	133	25.6	193	33.5	171	31.1	109	22.0	
Summer	129	24.8	121	21.0	158	28.7	143	28.8	

Days of the week	2009		2010		2011		2012		Total
	N	%	N	%	N	%	N	%	TOTAL
Sunday	97	18.7	94	16.3	120	21.8	84	16.9	395
Monday	81	15.6	82	14.2	94	17.1	75	15.1	332
Tuesday	63	12.1	79	13.7	60	10.9	76	15.3	278
Wednesday	63	12.1	83	14.5	67	12.2	67	13.5	280
Thursday	79	15.2	72	12.5	51	9.3	56	11.3	258
Friday	50	9.6	72	12.5	64	11.6	52	10.5	238
Saturday	87	16.7	94	16.3	94	17.1	86	17.4	361

HOUR	2009		2010		2011		2012		
	N	%	N	%	N	%	N	%	
0 – 5h59	40	7.7	56	9.7	41	7.4	55	11.1	
6 – 11h59	95	18.3	103	17.9	99	18.0	103	20.8	
12 – 17h59	186	35.8	205	35.6	178	32.4	124	25.0	
18 – 23h59	190	36.5	210	36.4	227	41.3	206	41.5	
Without registration	9	1.7	2	0.4	5	0.9	8	1.6	
TOTAL	520	100.0	576	100.0	550	100.0	496	100.0	

Parte 2 - Resultados genéticos

Review

Associations between genetic polymorphisms and bipolar disorder

Associação entre polimorfismos genéticos e transtorno bipolar

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Abstract

Bipolar disorder (BD) is a common disorder that affects approximately 1% of the population. It is associated with both chronic and acute severe features, such as low remission rates and a high prevalence of clinical and psychiatric comorbidities. The aim of the present article is to synthesize data from various articles that investigated genetic polymorphisms associated with BD. The 129 articles selected identified 79 (85.87%) genes associated with BD. This analysis identified the five genes that are the most cited in the literature: CANAC1C, DAOA, TPH2, ANK3 and DISC1. Of the 92 genes identified in these articles, 33 (35.87%) showed no association with BD. This analysis showed that, despite recent advances with respect to the role of genetic polymorphism in predisposition to BD, further research is still required to elucidate its influence on this disorder.

Alves VM, et al. / Rev Psiq Clín. 2012;39(1):34-9

Keywords: Bipolar disorder, genes, polymorphisms, heredity, gene ontology, association with bipolar disorder.

Resumo

Transtorno bipolar (TB) é uma doença comum que afeta aproximadamente 1% da população. Apresenta características crônicas e agudas graves, com índices de remissão de baixa e alta prevalência de comorbidades clínicas e psiquiátricas. O objetivo do presente artigo é sintetizar dados de vários artigos que investigaram polimorfismos genéticos associados com TB. Dentre os 129 artigos selecionados, identificaram-se 79 (85,87%) genes associados com TB. Essa análise identificou cinco genes que são os mais citados na literatura: CANAC1C, DAOA, TPH2, ANK3 e DISC1. Dos 92 genes identificados nesses artigos, 33 (35,87%) não mostraram associação com TB. Essa análise mostrou que, apesar dos avanços recentes com relação ao papel do polimorfismo genético na predisposição para TB, mais pesquisas ainda são necessárias para elucidar sua influência sobre esse transtorno.

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Palavras-chave: Transtorno bipolar, genes, polimorfismos, hereditariedade, ontologia genética, associação com transtorno bipolar.

Introduction

The evolution of the concept of bipolar disorder is ongoing. Its roots can be found in the work of Araeteus of Capadocia, who assumed that melancholia and mania were two forms of the same disease. The modern understanding of bipolar disorder began in France, through the work of Falret and Baillarger. The pivotal concepts of Emil Kraepelin changed the basis of psychiatric nosology, and Kraepelin's unitary concept of manic-depressive insanity was largely accepted. Kraepelin and Weigandt's ideas on mixed states were the cornerstones of this unitary concept. After Kraepelin, however, the theories of Kleist and Leonhard in Germany, as well as the work of Angst, Perris and Winokur, emphasized the distinction between unipolar and bipolar forms of depression. More recently, the emphasis has shifted again to the bipolar spectrum, which, in its mild forms, has been expanded to the limits of normal temperament^{1,2}. Because the introduction of the concept of the bipolar spectrum broadened the boundaries of the disease, the estimated rates of BD have been found to be substantially higher. These estimates still need to be validated by population-based studies³.

Bipolar disorder (BD) is a complex, multifactorial and polygenic condition characterized by episodes of mania/hypomania and depression^{4,5}. Several genes potentially involved in the pathophysiology of BD have been studied relative to their association with severity, age at onset, number of hospitalizations, vulnerability to the disorder and other clinical aspects.

The genetic characterization of BD will enable (A) the identification of parents that are especially predisposed to having bipolar descendants, (B) the early detection of individuals that are prone to developing BD, (C) the identification of bipolar patients that are likely to be non-responsive to lithium therapy and (D) the identification of patients that are likely to suffer severe episodes. There is currently only a preliminary knowledge of genes that are associated with BD. However, the increasing understanding of gene expression regulation by epigenetic mechanisms and the dimensional approach to mental disorders suggest new directions for further research in psychiatric genetics⁶. Because the complexity in mode of transmission of BD and its phenotypic heterogeneity many difficulties have emerged in the identification of these genes⁵.

In the recent years, advances on techniques of neuroimaging, molecular biology and genetics has provided new insights about the biology of bipolarity⁷. Several studies have identified genes that are associated with triggering BD. Work in molecular genetic epidemiology has shown the influence of inherited factors in mental disorders and begun to characterize their genetic interactions with environmental factors⁸. Research focused on major pathophysiological disorders has defined a number of candidate genes, focusing on functional polymorphisms and identified variant sequences that change relevant proteins or enzymes⁸. Despite numerous studies, much of the genetic variation that may underlie the disease pathology is still unknown⁹. Analyses of changes in DNA and the molecular mechanisms

by which environmental factors can act on the genome may lead to the identification of genes whose expression is involved in the etiology of mental disorders¹⁰. A large number of genes with small effects, combined with environmental factors, are responsible for the etiology of BD¹¹.

In pharmacogenomic analyses, the success of mood stabilizers is affected by genetic factors that may change the response phenotype; for most drugs, there is still insufficient information about the mechanism by which these effects occur¹². Lithium is the most commonly used drug for BD treatment and has been the target of studies on genetic susceptibility to BD and subsequent therapeutic response¹³. Research on polymorphism and BD is relevant because the disease is heritable, as is resistance to treatment with lithium¹⁴.

Given this context, the identification of genetic polymorphisms may provide evidence for the cause of BD and will also identify genes that are strong candidates for further study. Candidate genes are selected based on their linkage to a characteristic of interest (e.g., circadian rhythm). The expression of these genes has also been studied and associated with BD; in this way, the presence of polymorphisms can be detected. Detection of polymorphism enables the identification of risk factors or protective factors that affect the development of BD.

A more successful approach would be to search for associations with more restricted phenomena, such as personality traits, symptoms or small groups of symptoms, and, preferentially, endophenotypes. The search for genetic susceptibility of mental disorders is warranted specially under new paradigms such as their interaction with the environment and other endophenotypic variables which have been investigated through neuropsychological and neuroimaging evaluations. Thus, this research seeks to identify articles that investigated the presence of genetic polymorphisms that are associated with BD¹⁵.

Methods

Original articles published in the database PubMed/Medline were selected by means of the following associations: Thbipolar disorder

and SNPT and Thbipolar disorder and polymorphism. A PubMed gene ontology search was used to determine the function of each gene identified. The references of the selected articles were not used as a source in this review.

The inclusion criteria were as follows:

- Published between 2005 and 2011;
- Written in English;

- Included codes identifying the location of polymorphisms (e.g., rs 1006737 – Gene CACNA1C);
- Described genes associated with bipolar disorder;
- No association with BD.

Results

We selected 129 original articles that identified genetic polymorphisms as associated or not associated with BD and were published between 2005 and 2011. We selected only those that included an identification code for the locations of the polymorphisms. Together, these articles identified 92 genes (Table 1).

Genes and polymorphisms associated with demonstration

The 129 articles selected, 79 (85.87%) genes associated with BD (Table 1). An analysis of these articles associated identified five genes as the most cited in the literature: CACNA1C¹⁶⁻²⁴, DAOA²⁵⁻³², TPH2^{30,33-37}, ANK3^{21,38-39} and DISC1⁴⁰⁻⁴³ (Table 2). These five genes account for 29 original articles that showed association with BD. The 29 articles represent research from several countries: United States^{16,17,21,28,41}, Germany^{8,20,39}, Australian²¹, UK^{19,23,24,32}, Africa^{25,26}, Romania^{23,33}, Scotland³⁰, Finland^{31,41}, China^{29,33,43}, Sweden³⁴, Russia⁸, France³⁷, Ireland³⁵, Canada³⁸, Japan⁴², Italy¹⁸ and the Netherlands²². Some articles related the genetic polymorphism specifying the classification of TBI^{8,25,27,32,35,36,39,41}, in addition to TBI and II³⁷. The population studied by the authors of the articles are mostly from occidental^{18,20,22,26,28,30,32,34-38} and a lower part are the oriental^{25,27,33,43}.

Among the 196 functions of these 92 polymorphic genes, according to gene ontology, the most common were the following: protein binding, appearing in 32.61% (30) of genes, metal ion binding (19.56%, 18), AT-binding (18.48%, 17), receptor activity (17.39%, 16) and nucleotide binding (16.3%, 15) (Table 2).

Among the five most cited genetic polymorphisms in the literature, it was possible to identify three genes, ANK3, CACNA1C and DISC1, with protein binding functions. TPH2 has metal ion binding activity. The DAOA gene was not associated with any function in the PubMed gene ontology database. None of these genes have a common gene ontology. The ANK3, CACNA1C and DISC1 genes were annotated as components of the cytoplasm, and the ANK3 and DISC1 genes encode components of the cytoskeleton.

The articles discussing the CACNA1C gene investigated BD patient sample populations that numbered between 282 and 2,021 individuals.

Table 1. Genetic polymorphisms associated with bipolar disorder, published between 2005 and 2011

GENES	GENES	GENES	GENES	GENES	GENES
ANK3*	G72/G30 DAOA* ^a	GABRB2*	ADCY8*	hNP*	NCAM1* ^a
Bcl-2*	NR1D1*	EGR3*	ST3GAL1*	QDPR*	PREP*
CACNA1C*	GPR50* ^a	GRIA2*	PDLIM5* ^a	CLOCK*	CHRNA2*
P2RX7* ^a	GRM3*	GRIA1* ^a	DGKH*	BHLHB2*	CHRNA5*
GSK3E*	LACE1*	AKT1*	PPARD*	CSNK1E*	CHRNA1*
AANAT*	CHRNA7* ^a	SP4*	PALB2*	BDNF* ^a	CHRNA4*
DOK5*	ITIH1*	PI4K2B*	COMT*	SIAT4A*	TBX1*
CRY2*	RORB* ^a	DFNB31*	TPH2* ^a	TACR1*	IMPA2*
NR4A3* ^a	PPARGC1B*	SORCS2*	PCDH *	DISC1*	SST*
GRIN2B* ^a	TEF*	SCL39A3* ^a	PCNT*	TSNAX*	ARNTL*
HSP-70*	DHHC*	IGF1*	ATPIA3*	ATPIA1*	NOS1*
OTX2* ^a	SLC6A3*	NAPG*	HTR2A*	ATPIA2*	KIAA0564*
SCN8A*	YWHAH*	ERG3*	DTNBP1* ^a	PACAP/ADCYAP1*	NRG1*
5-HT1A* ^a	TSPAN8*	NPAS2* ^a	TRPM2*	VAPA* ^a	CHMP1.5*
5-HT6*	DARPP-32*	NDUFV2*	RGS4*	MPPE1* ^a	BRCA2*
VMAT1 (Thr136Ser)*	Per3*	MAOA*			

* Genes associated with BD. ^a Genes not associated with BD.

Table 2. Study details for candidate bipolar disorder genes most often cited in the literature between 2005 and 2011

Genes	Designation	Function	Case/control	Authors	Polymorphism
CACNA1C	D-1C subunit calcium channel L – type voltage-dependent	Calmodulin Binding, protein binding, voltage-gated calcium, channel activity voltage-gated ion channel activity	90 cDNA	Quinn et al., 2010	rs1006737
			585	Franke et al., 2010	rs1006737
			1.868/2.938	Green et al., 2010	rs1006737
			282/440	Bigos et al., 2010	rs1006737
			110	Erk et al., 2010	rs1006737
			2.021/1.840	Dao et al., 2010	rs2370419 rs2470411
			1.213	Cassamassina et al., 2010	rs10848635 rs1006737
			1.098/1.267	Ferreira et al., 2009	rs1006737
			77	Kempton et al., 2009	rs1006737
DAOA	D-amino acid oxidase	No description	191/188	Dalvie et al., 2010	rs701567
			198/180	Grigoriu-serbanescu et al., 2010	rs3916965 rs1935057 rs3916967 rs2391191
			248/188	Gawlik et al., 2010	rs2391191 rs1935062 rs3916966
			475/588	Zhang et al., 2009	rs778293
			555/564	Maheshwari et al., 2009	rs1935058
			706/1416	Soronen et al., 2008	rs2391191 rs3916966
			723	Williams et al., 2006	rs391695 rs1341402 rs1935058 rs2391191 rs778294 rs954581 rs1421292
			213/197	Prata et al., 2008	rs2111902 rs3918346 rs746187 rs3916972
TPH2	Tryptophan hydroxylase 2	Function iron ion binding, metal ion binding, tryptophan 5-monoxygenase activity	151	Roche e Mckee, 2009	rs1386482 rs1386486 rs4290270
			883/1.300	Cichon et al., 2008	rs17110563 rs11178997 rs11178998 rs7954758
			198/180	Grigoriu-Serbanescu et al., 2008	rs17110563
			105/106	Lin et al., 2007	rs4570625 rs11178997 rs11178998 rs11179003 rs171110747
			225/221	Harvey et al., 2007	rs4290270
			182/364	Bogaert et al., 2006	rs4131348
ANK3	Ankyrin G	Protein binding	47/67	Ruberto et al., 2011	rs10994336
			90 cDNA	Quinn et al., 2010	rs10994336
			1.098/1.267	Ferreira et al., 2009	rs10994336
			923/774	Schulze et al., 2009	rs10994336 rs9804190
DISC1	Disorder of schizophrenia 1	Protein binding	506/507	Xiao et al., 2011	rs2738864 rs16841582
			379	Perlis et al., 2008	rs10495308 rs2793091 rs2793085
			723 members of 179 families with BD	Palo et al., 2007	rs821616
			373/717	Hashimoto et al., 2006	rs821616

Control sample populations ranged in size between 440 and 2.938 healthy individuals. Four studies worked only with healthy people or with cDNAs (derived from lymphoblastic cells) from the HapMap database. Four codes describing the location of a polymorphic gene associated with BD were identified (Table 2). This gene is located on chromosome 12p13.3 (Figure 1).

Articles related to the DAOA gene sampled between 191 and 704 individuals with BD and between 180 and 1.416 healthy individuals. Only one study contained only healthy individuals. These studies identified 17 codes for the location of a genetic polymorphism associated with BD (Table 2). This gene is located on chromosome 13q34 (Figure 1).

Articles related to the TPH2 gene sampled between 105 and 883 individuals with BD and between 106 and 1.300 healthy controls. Only one study did not include control samples. These studies identified 11 codes for the locations of polymorphisms associated with BD (Table 2). This gene is located on chromosome 12q21.1 (Figure 1).

Articles related to the ANK3 gene sampled between 47 and 1.098 individuals with BD and between 67 and 1.267 control individuals. One article studied cDNAs (derived from lymphoblastic cells) from the HapMap database. These studies reported four codes representing the location of the polymorphism associated with BD (Table 2). This gene is located on chromosome 10q21 (Figure 1).

Articles related to the DISC1 gene sampled between 373 and 506 patients with BD. One article did not include control samples, and another studied members of families affected with BD. These studies identified six codes indicating the location of the polymorphism associated with BD (Table 2). This gene is located on chromosome 1q42.1 (Figure 1).

The functionality of the polymorphisms identified was observed made to analyze the variation in the expression of genetic polymorphism in association with some variables: cognitive assessment³⁹, memory^{39,41}, making decision³⁹. Psychotic illness after the use of alcohol, drug dependence, intravenous drug abuse, psychotic illness secondary to medicamentos²⁰. Emotional memory, emotion on the face, the work memory¹⁷. Episodes of hospitalization disease^{25,27}. Age of first hospitalization^{26,34}. First age³⁶, number of episodes, family history of disease psychiatric^{8,36} on first and second grau²⁵. Attention⁴¹. These variables have been showing greater respect of the polymorphisms and episodes of TB, which when studied polymorphism with TB diagnosis.

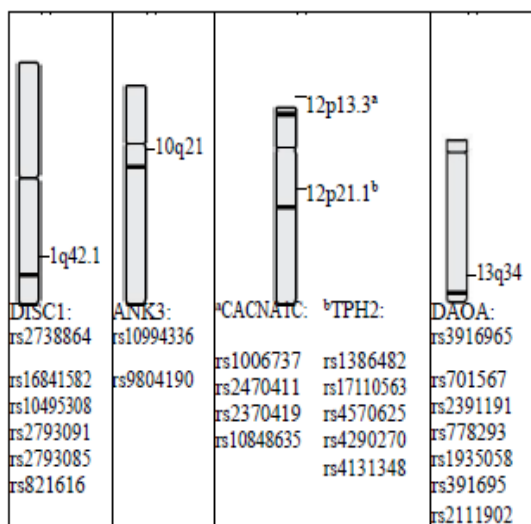


Figure 1. Chromosomal locations of the five genes most commonly associated with BD and their polymorphisms.

Genes/polymorphisms lacking association with BD

Of the 92 genes identified, 33 (35.87%) specifically showed no association with BD (Table 1). DAOA, TPH2, P2RX7, NR4A3, GPR50, CHR-NA7, RORB, GRIA1, PDLIM5, BDNF, NCAM1, VAPA, DTNBP1, SLC6A3, 5-HT1 and OTX2 were described both as associated with BD and not associated with BD by different studies (Table 1).

Discussion

The study of genetic polymorphism associated with TB raises the possibility that mental illness is mainly associated with common genetic variants is outdated. Is now plausible that multiple rare variants each have a potent effect on disease risk and that they could accumulate to become a substantial component of mental disease risk⁴⁴. The search for genetic information that are associated with the outbreak of TB involves structural and environmental factors. Among the genes associated with BD, those with protein binding activity may be especially relevant. Because the biological properties of a cell are determined by the active proteins expressed, these genes may be involved in BD through changes in protein structure, thereby increasing or decreasing some feature/function that can cause major cellular changes. Alternatively, these genes may still be active, along with other proteins, but with changes in their functions that trigger BD.

Adenosine triphosphate (ATP) is a key energy-transferring molecule that is used in many biological processes. It is involved in the active transport of molecules, the synthesis and secretion of substances, locomotion and cell division. Genes involved in ATP synthesis may therefore interfere in one or more of these biological processes, promoting the onset of BD. Genes involved in receptor function may increase or decrease the receptor activities and thereby modify some function/action that may then contribute to the onset of BD. Changes in nucleotide (adenine, guanine, cytosine, thymine and uracil) synthesis may result in mutations or polymorphism, depending on the effect of the structural change. This may contribute to BD.

Studies of the five most cited genes show their influence in the etiology of BD. Several articles confirmed the association of polymorphisms in CACNA1C with BD. The strong expression of CACNA1C in BD patients suggests an increased activity of calcium channels. Thus, calcium channel inhibitors may have clinical value for the treatment of BD. One of these studies further identified a potential mechanism for bipolar disorder risk¹⁶. A decrease in CACNA1C expression can protect against the development of mood disorders¹⁷. Two polymorphisms in the CACNA1C gene (rs10848635, rs1006737) had a protective effect on BD episodes. The polymorphism rs1006737 was also correlated with reduced severity of depression and insomnia. However, both alleles were associated with an increased risk of suicide during treatment for depression¹⁸. This is a clear demonstration that there is an overlap between genes in the biological basis of susceptibility to mental illness across the clinical spectrum¹⁹.

Research conducted by Erk et al.²⁰ suggests a gene-environment interaction mechanism for BD, i.e., a dysfunctional adaptation to stress. CACNA1C has been established as a drug target because of its binding site for calcium channel blockers (verapamil); these drugs have shown some evidence of effectiveness in mood stabilization of BD patients. Calcium channel subunit expression is decreased in the mouse brain in response to lithium, one of the most effective bipolar therapies²¹. Genetic variation in CACNA1C is associated with the volume of the brainstem that modulates central control over the motor, cognitive, affective and arousal, providing a psychiatric risk factor²². Magnetic resonance imaging showed that there was significant correlation between CACNA1C mutation and the total volume of gray matter, but not in regional grey matter volume, white matter volume, or cerebrospinal fluid or volume²³.

Several highly cited articles regarding the DAOA gene confirm its association with BD. An initial study by Dalvie et al.²⁵ provided preliminary evidence that ancestral DAOA gene alleles (rs701567) have a protective effect, lessening the chances of having severe BD (psychosis and repeated hospitalizations). Haplotypes of DAOA/G30 are associated with affective psychoses, but do not contribute to the pathogenesis of affective disorders²⁶. Different SNPs that potentially indicate membership in the DAOA/G30 haplotype were found to be correlated with psychotic episodes and mood changes with delusions in Romanian BD patients²⁷. Other studies suggest that DAOA does not have a major effect on susceptibility to BD, but can contribute to susceptibility in some families²⁸. In contrast, multiple sensitizing (and perhaps protective) variants of the DAOA/G30 gene are present in different populations²⁹. Additional evidence supports the involvement of DAOA/G30 and DAO in the etiology of bipolar disorder, but none indicated any interaction between these genes³⁰. DAOA thus may play an important role in the predisposition of individuals with a mixed phenotype of psychosis and mania and lead to changes in the expressed characteristics of these psychological illnesses³¹. Williams et al.³² suggested that depression is associated with greater glutamate-tergic function. Patients with mutations in the DAOA gene, which is associated with affective disorders, have symptoms that should be associated with reduced activity and/or frontal activation of DAO.

An analysis of the articles related to TPH2 shows that this gene may influence the risk of BD³³. A study performed in a population of Swedish descent provides preliminary evidence for the association of the TPH2 gene with protection against the pathogenesis of affective disorders³⁴. An examination of the functional effects of TPH2 provided evidence for the lower thermal stability and solubility of the mutant enzyme, suggesting that the reduced production of 5-HT in the brain may serve as a pathophysiological mechanism of BD³⁵. Studies carried out by Grigoriu-Serbanescu et al.³⁶ also support the involvement of TPH2 variability in the etiology of BD. The polymorphism rs17110563, which lies in the TPH2 protein coding region, was detected in a Romanian patient but not in control individuals, supporting the hypothesis that it represents a risk factor for a rare form of BD. The BD susceptibility locus in TPH2 shows a statistically significant association with BD at both a locus-specific SNP and haplotype marker SNPs³⁷.

The ANK3 protein is found in the initial segment of the axon and governs the localization of voltage-dependent sodium channels. The mRNA expression levels of ANK3 and CACNA1C are affected by local genetic variation²⁴. ANK3 is reduced in the mouse brain in response to lithium, one of the most effective bipolar therapies. Significant literature suggests that bipolar disorder is an illness of ion channels²¹. The ANK3 gene has a selective effect on sensitivity to signals that affect an individual's sustained attention and thus can even contribute to the risk of BD³⁸. Regions close to the rs9804190 and rs10994336 polymorphisms will be jumping off points for future studies that aim to define functional variants that are responsible for susceptibility to BD³⁹. A small sample of article related to the ANK3 gene may show little significance of its association with TB³⁸.

The involvement of DISC1 in the etiology of BD was first suggested by Palo et al.⁴⁰. These authors suggested that polymorphisms in DISC1 contribute to variations in the psychotic features of bipolar spectrum disorder. DISC1 may represent a new target for the development treatments and diagnostic tools for bipolar disorder⁴¹. DISC1 is associated with lowered biological activity of ERK (extracellular regulated kinase), reduced grey matter volume in the brain and increased risk for major depressive disorder⁴³. A

haplotype [rs2738864 (C)-rs16841582 (C)] was associated with BD. This discovery provides of the role of DISC1 in BD⁴³.

Conclusion

This study shows that, despite advances with respect to the role of genetic polymorphisms in predisposition to BD, significant research must still be performed to elucidate the roles of specific genes and their variants in this disorder.

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Genetic Polymorphisms Might Predict Suicide Attempts in Mental Disorder Patients: A Systematic Review And Meta-Analysis

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Abstract: The aim of the present study was to analyze if the genetic polymorphisms might predict suicide attempts in mental disorder patients. The literature review and meta-analysis were conducted using the PubMed/Medline, Web of science and Scopus database using the terms: “5-HTT or SLC6A4 or 5-SERT and suicide, suicidal ideation or suicidal behavior or suicidal attempt”. Thirty articles were analyzed. We found 17 articles that showed association and 13 articles that showed no association between LPR serotonin transporter polymorphism and suicide. A higher study of suicide identified the serotonin transporter polymorphism in patients with schizophrenia, mental disorder, major depression and bipolar disorder. There is an association between the serotonin-transporter-linked polymorphic region and suicidal behavior. The mental disorders with greater relationship with the suicide were the bipolar disorder, major depression and schizophrenia. The L allele had higher risk for suicide.

Keywords: Candidate gene, polymorphism, serotonin, suicidal behavior.

1. INTRODUCTION

The suicidal behavior is classified in three different categories: suicidal ideation, suicide attempt and suicide [1]. Suicide is a preventable cause of death [2]. After approximately two centuries of suicide prevention research, several effective interventions have been demonstrated and various risk factors have been incorporated [2]. Brief intervention may be an important part of suicide prevention programs for under resourced low- and middle-income countries [2]. Among risk factors emphasize the physical or sexual abuse, death of a friend or family member, unemployment, shame or dishonor, heartache, the presence of mental illness and attempted suicide in the family history of mental disorder and suicide attempt by the individual [3].

In addition, study shows differences in relation to feelings of hopelessness, about these patients with major depressive disorder are more likely to be anxious temperament and hopelessness, while patients with bipolar disorder often present more cyclothymic and irritable temperament [4].

Because of the stigma associated with suicide, survivors may feel they are unable to secure enough support from friends or family. However, survivors may benefit from attending support groups with other survivors, who uniquely share their experiences and offer a haven for survivors to feel understood [5].

Family, adoption and twin studies demonstrate that genetics play a role in suicidal behavior [6]. In fact, the influence of genetic variants on human behavior may be relevant to the symptomatology involved in psychiatric disorders [7]. For instance, genetic variants in the serotonin transporter have been associated with vulnerability to affective disorders. Mounting evidence supports the association between a polymorphism in the promoter region of the LPR serotonin transporter polymorphism (5-HTTLPR) and suicidal behavior [8-10].

The gene serotonin transporter (5-HTT) encodes a membrane protein responsible for reuptake of this neurotransmitter in the synaptic cleft. This gene has been described as a candidate in the serotonergic abnormalities observed in people with a history of suicide attempts [11]. The 5-HTT gene (also known as SERT or SLC6A4, and mapped on chromosome 17q11.1-q12) presents a functional insertion/deletion variant (5-HTTLPR) located in the promoter region of the gene with two alleles designated as ‘long’ (L) and ‘short’ (S). This variant would be associated to suicidal behavior [12].

5-HTTLPR has previously been shown to strongly associate with violent suicidal behavior in BD patients [13]. These results could be vital to creating a genetic tool for long-term suicide prediction [13]. Biological markers, such as 5-HTTLPR, could aid in identifying potential suicide attempters [13].

Previous work has not suggested a role for 5-HTT in the predisposition to suicidal behavior [14]. However, another study suggested that, despite efforts taken to assess this correlation, the exact effect and role of 5-HTTLPR in the

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genetics of suicide remains unclear, thus prompting future endeavors [8]. In a study of patients with one or more suicidal attempts, the 5-HTT gene was unlikely to be associated with suicidal behavior of psychotic patients in Han Chinese [15].

Because duality of information regarding the existence of an association between 5-HTT and suicidal behavior this study has proposed to do a systematic review and meta-analysis to assess if genetic polymorphisms might predict suicide attempts in mental disorder patients. This study also proposes to identify which mental disorder has been showing greater association with this gene and suicide; what is the ethnic group that has been most extensively studied; what is the allelic frequency found for polymorphism 5-HTTLPR; and what is the contribution from it, in people with mental disorder and suicidal behavior.

2. METHODS

2.1. Literature Search

We identified eligible studies for systematic review and meta-analysis by searching PubMed/Medline, Web of Science and Scopus database using the following key words: “5-HTT and suicide”, “SLC6A4 and suicide” or “5-SERT and suicide”, “5-HTT and suicidal ideation”, “SERT and suicidal ideation”, “SLC6A4 and suicidal ideation”, “5-HTT and suicide attempt”, “SERT and suicide attempt”, “SLC6A4 and suicide attempt”, “5-HTT and suicidal behavior”, “SERT and suicidal behavior” and “SLC6A4 and suicidal behavior”. Only articles in English in which human beings were studied were selected for analysis. Case-control studies were selected if data were available regarding the roles of 5-HTTLPR polymorphism in behavior suicide. The review took place in September 2014.

2.2. Inclusion Criteria

In our study, the inclusion criteria were as follows: (1) articles that described a relationship between 5HTT or 5-HTTLPR and suicidal behavior - suicidal ideation, suicide attempt and suicide, (2) studies that examined suicidal behaviors in subjects characterized as either having committed suicide or having a history of at least one suicide attempt, (3) a case-control study design, and (4) articles that provided sufficient genotype data for estimating an odds ratio (OR) with a 95% confidence interval (CI). We excluded articles that do not researched suicide and the association of this, with the gene 5-HTT; review articles; meta-analysis; and articles without information of ethnic group, the mean age of the controls and cases and quantity of cases and controls specified.

Those subjects without suicidal behavior were considered as a control group. All cases had a mental disorder, while the controls showed or not the mental disorder.

We collected the following information in the researched articles: year of publication, study population, polymorphism, case control, type of disorder and the presence of association or not between the polymorphism 5-HTTLPR and attempt/suicidal/suicidal behavior. Meta-analysis was conducted of selected studies to analyze the power of each

study compared to other. Meta-analysis was made

through the program R (Oswaldo Cruz Foundation, Rio de Janeiro, 2013).

For definition of descriptors, we opted for the PICOS strategy (6): Participants: patients with suicidal attempt/ideation; Intervention: 5HTTLPR polymorphism identification; Compared to control groups: absence of 5HTTLPR polymorphism in the control group; Outcome: presence of 5HTTLPR polymorphism in the group of patients with suicidal attempt/ideation; Study design: genetic association study [16].

3. RESULTS

One hundred and eighty articles and related reference were identified with the search terms. One hundred and fifty were excluded. Only thirty articles were included in the analysis. Were found 32 duplicate articles, 23 reviews, 10 meta-analysis and 85 articles weren't part of the criteria for inclusion to read your summary and full text (Fig. 1). The flow diagram of selection of articles was made based on the PRISMA document (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [17]. Fig. (1) shows the flow diagram of PRISMA.

We found 17 articles that showed association and 13 articles that showed no association between 5-HTTLPR polymorphism and suicide (Table 1).

The average number of people surveyed in the studies that displayed an association with mental disorders and suicide were 140.5 ± 92.6 cases and 175.9 ± 105.5 controls ($t(12) = 5.471$, $p = 0.000$). For studies without either association, there were 278.8 ± 275.7 cases and 357.2 ± 373.4

controls ($t(16) = 4.159$, $p = 0.001$). In total, 14,916 people were analyzed, and 6,556 of them were cases and 8,360 were controls. We found some studies that demonstrated an association, whereas others did not, between genetic polymorphisms, suicide and mental disorder.

Studies have proposed the association between polymorphisms and mental health every year since 1998, except for 1999 and 2002. In 2004, 2007, 2010, 2011, 2012 and 2013 several articles demonstrated a positive association, whereas in 1998, 2005, 2009 and 2012 several articles demonstrated no association (Table 1).

The distribution of the 5-HTT gene linked to suicide attempt/ideation ratified by ethnicity demonstrated a predominance of studies involving a Caucasian European population, followed by Brazilian, Han Chinese/Japanese, African, Croatian and Scandinavian populations in association studies (Table 1). Studies without a significant association between the polymorphism and suicide behavior also predominantly employed a Caucasian European population over Han Chinese/Japanese, Brazilian and African populations (Table 1).

We also performed the association between the 5-HTTLPR polymorphism and suicidal behavior (Table 1). The 5-HTTLPR polymorphism, allele L, displayed a larger frequency in both cases and controls, whereas allele S exhibited a larger frequency in cases without suicide

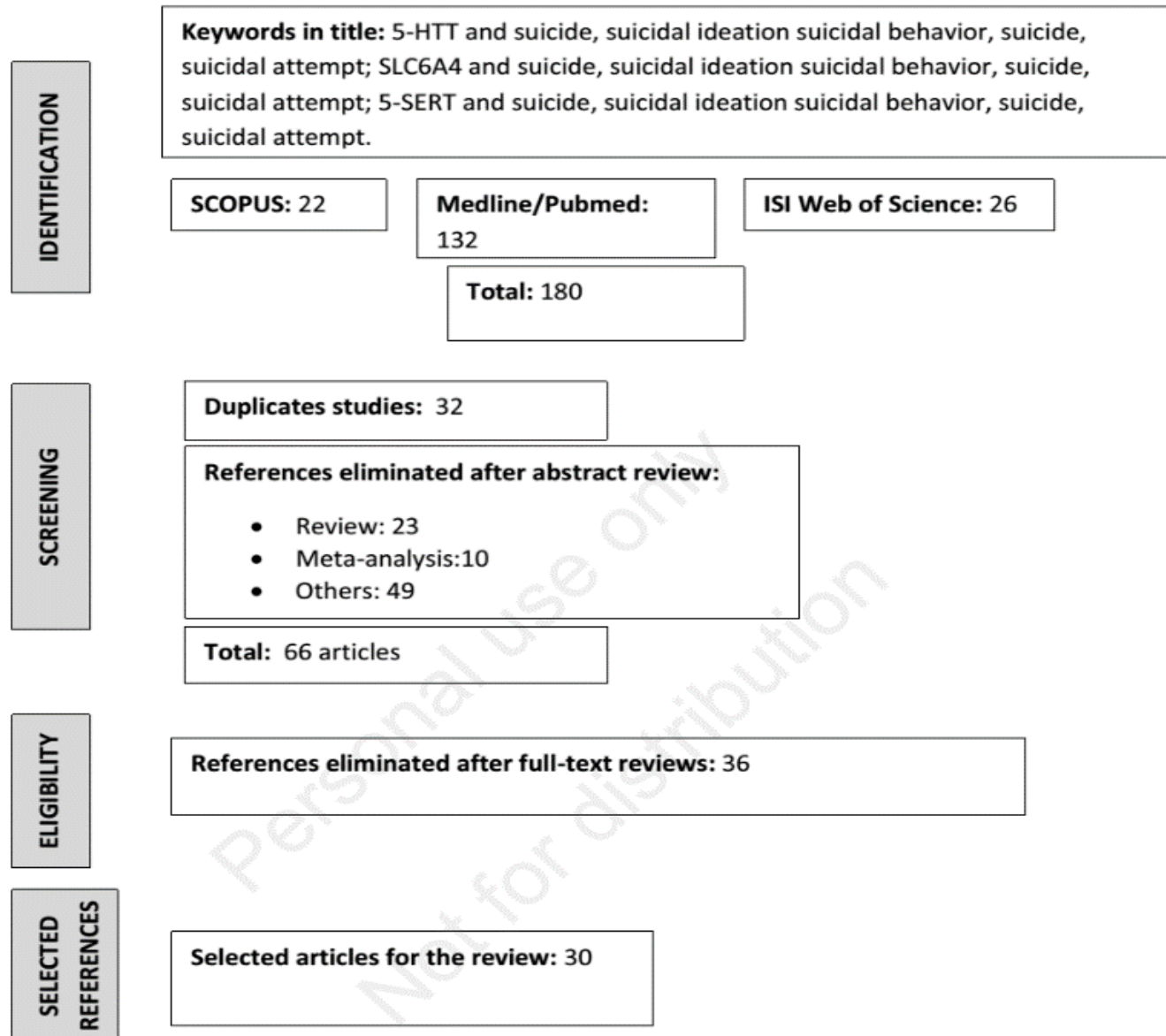


Fig. (1). Results of the review.

attempts. The difference in allele frequencies of cases without suicide attempts in comparison to controls was statistically significant (χ^2 : 6.54, p = 0.0106) (Table 2). Only one study has previously demonstrated a statistically significant difference in allele frequencies in a case control design [18]. Only 17 studies have described the allelic frequency of the polymorphism 5-HTTLPR. The presence of L allele represents a higher risk for attempt/suicidal or suicidal behavior in patients with mental disorder (Table 2).

Through analyzing studies, we observed that the most frequently studied associations between genetic polymorphisms and suicide in mental disorder patients were psychiatric disorder, bipolar disorder, major depression and schizophrenia.

show evidence of statistical heterogeneity Q (df = 29)= 3.6565, p = 1.000. Value of I^2 = 0.00% also highlights the no heterogeneity between studies. Two studies [9, 19] presented a greater measure of effect, showing a study of greater weight. One study [20] presented a larger confidence interval, demonstrating greater variability within the study (Fig. 2).

4. DISCUSSION

Studies have demonstrated that larger sample sizes of cases and controls display greater associations compared to studies with smaller sample sizes [9, 10, 21, 22].

Forest plot of meta-analysis identified that studies don't

Table 1. Study characteristics from published studies on the relation of the 5-HTT gene and suicide.

Population Studied	SNP	Case	Average Case	SD	Control	Average Control	SD	Type of Disorder	Association	Authors
Japanese.	5-HTTLPR	80	46.6	16,4	92	35.2	14,5	BD	N	Ohara <i>et al.</i> , 1998 [25]
Hispanics, African Americans and Asians	5-HTTLPR	82	43	20	138	42	16	MD	N	Mann <i>et al.</i> , 2000 [26]
Caucasian, African-American, Hispanic, Indian, Asian	5-HTTLPR	51	38	15	51	41	13	PD	S	Russ <i>et al.</i> , 2000 [22]
Chinese	5-HTTLPR	76	41.2	10,6	262	48.8	10,8	Schiz	N	Chong <i>et al.</i> , 2000 [27]
German	5-HTTLPR	124	39.2	14,8	185	47.7	0	PD	N	Rujescu, <i>et al.</i> , 2001 [23]
Caucasians	5-HTTLPR	163	41	8,3	117	46	8,1	AD	S	Preuss <i>et al.</i> , 2001 [20]
European Caucasians	5-HTTLPR	51	38.6	13,2	139	45.2	13,2	MD	N	Courtet <i>et al.</i> , 2001 [14]
European Caucasians	5-HTTLPR	166	35.57	13,45	139	45.2	13,2	PD	N	Courtet <i>et al.</i> , 2003 [28]
Croatian/southern Slavic	5-HTTLPR, VNTR	135	51	19	299	41	12	PD	S	Hranilovic <i>et al.</i> , 2003 [29]
Caucasians	5-HTTLPR	104	30.45	0	21	63.4	0	RMC	S	Baca-Garcia <i>et al.</i> , 2003 [24]
French Caucasian	5-HTTLPR	185	32	9	159	35	10	Schiz	S	Bayle <i>et al.</i> , 2003 [17]
Caucasians	5-HTTLPR	101	34.6	11,7	101	35.8	13,2	Had	S	Gerra <i>et al.</i> , 2004 [18]
Croatian	VNTR-2	192	52	19	377	43	2	PD	S	Jernej <i>et al.</i> , 2004 [30]
Han Chinese	5-HTTLPR	272	46.5	13,1	903	38,25	11,2	First ESB	S	Shen <i>et al.</i> , 2004 [13]
Jewish Ashkenazi	5-HTTLPR	32	17	2,1	28	16.8	2,0	PD	N	Zalsman <i>et al.</i> , 2005 [31]
Caucasian	5-HTTLPR	191	39.8	15	125	34.6	16,8	BD	N	Zalsman <i>et al.</i> , 2006 [32]
French-Canadian	5-HTTLPR	106	41.8	14,7	152	41.7	10,2	MD	N	Lara <i>et al.</i> , 2006 [33]
Brasilian	5-HTTLPR	84	35.39	13	152	35.65	10	D	S	Segal <i>et al.</i> , 2006 [34]
Chinese	5-HTTLPR	94	27.5	6,7	294	27.2	7,1	Map	S	Chen <i>et al.</i> , 2007 [35]
Caucasians	5-HTTLPR	447	43.2	13,1	370	44.2	11	BD	S	Vincze <i>et al.</i> , 2008 [15]
Caucasian	5-HTTLPR	193	35.6	12,5	420	40.6	11,3	PD	N	Saiz <i>et al.</i> , 2008 [10]
Han Chinese	5-HTTLPR	297	46.1	12,76	329	43.22	12,8	PD	N	Zhang <i>et al.</i> , 2008 [12]
European-Brazilian	5-HTTLPR	94	35.8	10,4	94	35.9	10,4	MD	N	Segal <i>et al.</i> , 2009 [6]
Turkish population	5-HTTLPR	182	33,77	1,37	181	35.89	1,40	PD	S	Akar <i>et al.</i> , 2010 [7]
Brasilian	5-HTTLPR	95	41	12	94	32	13	BD	S	Malloy-Diniz <i>et al.</i> , 2011 [19]
Caucasian	5-HTTLPR	168	38.3	9,9	302	50.1	8,6	Schiz	S	Hung <i>et al.</i> , 2011 [8]
Spanish Caucasian	5-HTTLPR	913	38,9	12,85	420	41,1	11,5	PD	S	Saiz <i>et al.</i> , 2011 [16]
Scandinavian	Rs16965628	837	45,1	12,7	1473	44,1	10,7	Schiz	S	Carlstrom <i>et al.</i> , 2012 [36]
Croatian	5-HTTLPR, 5-HTTVNTR	335	32,5	11,6	184	35,9	11,7	Schiz	N	Bozina <i>et al.</i> , 2012 [37]
African Americans	5-HTTLPR	706	45,2	7,9	759	34,3	10,1	CT	S	Enoch <i>et al.</i> , 2013 [21]

ABBREVIATIONS: SD (Standard Deviation), BD (Bipolar Disorder), MD (Major Depression), First ESB (First Episode of Suicidal Behavior), Had (Heroin Addicts), Map (Methamphetamine Abuse), PD (Psychiatric Disorder), RMC (Regular Menstrual Cycles), Schiz (Schizophrenic), AD (Alcohol Dependent), (D) Depressed, (CT) Childhood Trauma.

Although research assessing the association between genetic polymorphisms, suicidal behavior and mental disorder has been continuous between 1998 and 2013, a definitive conclusion about whether polymorphisms can predict suicide attempts in mental disorder patients remains elusive.

When results were evaluated according to ethnicity, we observed that the European population dominated the study samples [22-24]. Maybe this is due to presence of large hospitals and more study centers. However, the existence of more cases that are suicidal and their association with certain polymorphisms remains unresolved. Additionally, whether the risk of suicide increases depending on race (in this case the Caucasian population), based on particular genetic or environmental backgrounds is unanswered.

The majority of studies have focused on patients diagnosed with general mental disorder. However, some studies aimed at assessing more detailed disorders [10, 21, 23, 25]. Studies with patients with mental disorder specific are rare, thus it is necessary to carry out studies that use cases and controls of mental disorder more specific for better association of the polymorphism with the suicidal behavior. Multicenter studies allow for a greater access to necessary sample size for analysis.

The small sample sizes for the controls without suicide attempts likely precluded statistical insignificance of S and L allelic proportions observed between cases. To assess the influence of the S or L allele polymorphisms at 5-HTTLPR in people with mental disorder that exhibited a suicidal attempt/ideation, a larger sample size is necessary. Thus, the lack of statistical significance may be attributable to the few

studies that have been performed with sample cases without attempted suicide. The control samples outnumbered cases, which may have contributed to the statistical significance when comparing the frequency of this allele.

Association studies between 5-HTTLPR polymorphism and suicide in mental disorder patients showed that bipolar disorder, major depression and schizophrenia are disorders where this polymorphism are present. Because of the difficulty of obtaining a considerable sample that shows a kind of mental disorder for evaluation of genetic polymorphisms, psychiatric disorder generally, end up being the most studied. Evaluate psychiatric disorders generally contributes to identification of polymorphisms with characteristics of wider influence. Hence the need for studies that address specifically a certain type of disorder in relation to suicidal behavior. Studies with a kind of disorder could offer greater reliability of influence of polymorphism on the triggering of suicidal behavior. Besides, could offer bigger possibilities of correlations in this polymorphism with the characteristics of disorder type studied and their pharmacological interaction.

A brief critical discussion about the studies analyzed follows:

4.1. Association of Genetic Polymorphisms and Suicidal Behavior

The described results above underscore the importance of studies assessing associations between genetic polymorphisms and

Table 2. Allele frequencies of 5-HTTLPR polymorphisms.

Alleles	Attempt of Suicide				Control				Without Attempt of Suicide				Control and Cases		
	S		L		S		L		S		L				
	N	%	N	%	N	%	N	%	N	%	N	%			
Ohara <i>et al.</i> , 1998 [25]	124	77,5	36	22,5	140	76,1	44	23,9	#	#	#	#	0,77	1	0,77
Chong <i>et al.</i> , 2000 [27]	108	71,1	44	28,9	148	71,8	58	28,2	372	71	152	29	0,510	2	0,775
Rujescu, <i>et al.</i> , 2001 [23]	98	40	150	60	142	38	228	62	#	#	#	#	0,015	1	0,91
Courtet <i>et al.</i> , 2001 [14]	57	56	45	44	#	#	#	#	118	42	160	58	5,42	1	0,02*
Courtet <i>et al.</i> , 2003 [28]	155	47	177	53	#	#	#	#	118	42	161	58	1,1	1	NS
Hranilovic <i>et al.</i> , 2003 [29]	91	34	177	66	239	40	357	60	#	#	#	#	#	#	0,0959
aca-Garcia <i>et al.</i> , 2003 [24]	38	37	17	16	3	14	8	38	#	#	#	#	2,8	1	0,09
Bayle <i>et al.</i> , 2003 [17]	38	20,5	48	25,9	36	22,6	40	25,2	106	47,3	118	52,7	6,13	1	0,015
Shen <i>et al.</i> , 2004 [13]	393	72,2	139	25,6	885	70,5	329	26,2	396	72	140	25,5	2.337	#	0,674
Zalsman <i>et al.</i> , 2006 [32]	160	41,9	222	58,1	111	44,4	139	54,6	#	#	#	#	1,08	2	0,58
Lara <i>et al.</i> , 2006 [33]	83	41,9	115	58,1	126	41,4	178	58,6	#	#	#	#	0,011	1	0,917
Segal <i>et al.</i> , 2006 [6]	80	47,6	135	44,4	88	52,4	169	55,6	#	#	#	#	2,48	#	0,115
Chen <i>et al.</i> , 2007 [35]	131	69,7	57	30,3	427	72,6	161	27,4	#	#	#	#	#	#	0,435
Vincze, <i>et al.</i> , 2008 [15]	39	50	39	50	295	41,4	417	58,6	#	#	#	#	#	#	0,08
Saiz <i>et al.</i> , 2008 [10]	192	50	194	50	389	46	451	54	#	#	#	#	1,25	1	0,264
Malloy-Diniz <i>et al.</i> , 2011 [19]	#	#	30	31,6	#	#	24	25,5	#	#	#	#	0,178	#	NS
Bozina <i>et al.</i> , 2012 [37]	204	63	118	37	158	43	210	57	146	42	202	58	4.995	4	0,082

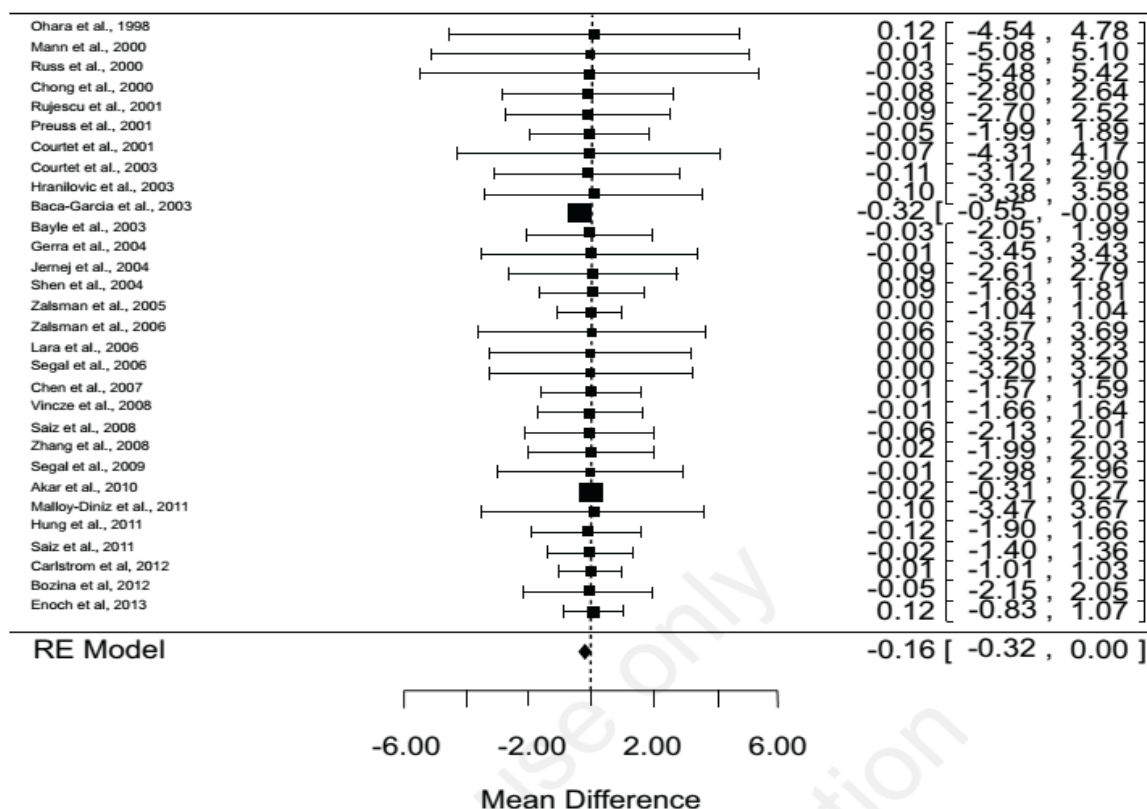


Fig. (2). Distribution of the number of sample averages and standard deviation of the age of the studies selected.

suicidal attempt/ideation/behavior in larger samples of cases and controls. Only four studies [9, 20, 23, 26] have employed uniform samples. Another study used the most individuals for both cases and controls [21]. A larger sample size permits a validation of observed results.

4.2. Not Association of Genetic Polymorphisms and Suicidal Behavior

In the same way that studies that showed an association need to be replicated by analyzing a uniform sample, the same parameters must be employed to confirm a lack of association between 5-HTTLPR and suicide attempt [8].

The discrepancy between the case sample size and the control sample size in some study evokes doubts about the relevance of conclusions. Therefore, a larger case sample size must be used in its replication.

One of the studies [9] that submitted largest measure effect has a sample of case and similar control; and averages of similar age. Other study [19] presents a number of sample cases higher than control, and the average age of the controls is twice the average of the cases. This may have influenced the presentation of measurement of effect of this study in relation to other.

One study involved considerable case and control samples and revealed associations between suicide, mental disorder and 5-HTTLPR [9]. Another study assessed a smaller sample of cases and controls but was able to demonstrate an association between suicide, mental disorder and 5-HTTLPR [27]. Two studies were not included in this analysis because standard deviations of averages were not

available [19, 28].

Heterogeneity of data shows that studies show differences between them. This is result of the presence of studies with samples from cases and controls varied. In studies presented a higher measure of effect observed that the samples are more uniform [9, 19]. The largest measure of effect of these studies suggests a reliable result. This result reinforces the need for studies with a larger sample and more uniform

CONCLUSION

This study identified that there is an association between polymorphism 5-HTTLPR and suicidal behavior. The ethnic group more studied was the European Caucasian population. The mental disorders identified were bipolar disorder, major depression and schizophrenia. The L allele had higher risk for suicide.

Studies that present a lack of association employ uniform, but still small, case and control sample sizes than studies that do suggest an association. It reinforces the need for studies to employ uniform and larger samples. Studies that have exhibited these characteristics tend to show consistent results that are more definitive and conclusive. Furthermore, our analysis underscores the need for more studies of specific mental disorders to gain a better understanding of the relationship between genetic polymorphisms and suicide.

LIMITATIONS

This study covers only the association studies case-control samples. This restricts participation of this polymorphism in suicidal behavior. Studies of gene expression, in family and in twins would be interesting in grounds of the influence of this polymorphism in triggering of suicidal behavior.

LIST OF ABBREVIATIONS

5-HTT = Gene Serotonin Transporter
 5-SERT = Gene Serotonin Transporter
 BD = Bipolar Disorder
 CI = Confidence Interval
 L = Long
 LPR = Serotonin-Transporter-Linked Polymorphic Region
 OR = Odds Ratio
 PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses
 S = Short
 SLC6A4 = Gene Serotonin Transporter

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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Suicide attempt in mental disorders: their association with 5-HTT, IL-10 and TNF-alpha polymorphisms

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Abstract

Objectives: It is to evaluate the relationship among SA, quality of life, MD and the presence of rs2020933 (5-HTT), rs1800871 (IL-10) and rs1800629 (TNF- α) polymorphisms. **Methods:** A total of 161 patients with MD and SA, 145 with MD and no SA, and 175 subjects in the control group were enrolled in the study. DNA was obtained using buccal mucosa swab samples, and genotyping was performed using real-time polymerase chain reaction. **Results:** The C allele of rs1800871 polymorphism is associated with MD without SA in females. The A/T genotype in rs2020933 polymorphism appeared as a factor of protection for the number of SA. The absence of the T allele of rs2020933 polymorphism is related to the presence of any family with

MD. **Conclusion:** Rs2020933 is associated with SA. Rs2020933 and rs1800871 is associated with MD.

Introduction

Mental disorder (MD) is a major precedent for suicide. Approximately 90% to 98% of the people who commit suicide have a MD (Almeida et al. 2009). Family history or relatives with MD are a risk factor for suicide (Bertolote et al. 2010), and this finding may justify the presence of genetic influence. Several studies involving major depression and suicidal behavior, with regard to familial and environmental risk factors, have suggested that genetic factors for suicidal behavior may exist (Mandelli and Serretti 2013). Studies involving twins have suggested a higher concordance in monozygotic pairs (13.2%) than in dizygotic twins (0.7%) in relationship to suicidal behavior (Mann et al. 2001). Other genetic studies have found 18.5% concordance for monozygotic twins as opposed to 0.7% concordance for dizygotic twins (Joiner et al. 2005). These studies have demonstrated a likely genetic component of suicidal behavior; however, the data are still inconsistent.

The role of immunologic dysfunction in the pathophysiologic mechanism of many MD has been investigated (Black and Miller 2015), and the results are inconclusive. There are few published studies on the role of genetic polymorphisms of pro- and anti-inflammatory cytokines in suicide in persons with major depressive disorders (Kim et al. 2013). Interleukin (IL)-10, an anti-inflammatory cytokine, whose gene is located on chromosome 1 between 1q31 and 1q32 (Clerici et al. 2009), limits inflammation by inhibiting proinflammatory cytokines as tumor necrosis factor- α (TNF- α) (Mesa et al. 2014). The TNF- α has its gene located on chromosome 6 (6p21.1–21.3) (Clerici et al. 2009). Several studies have shown that polymorphisms in TNF- α can be associated with depression (Kim et al. 2013) and suicide (Kim et al. 2013; Omrani et al. 2012). Studies have also identified an IL-10 association with schizophrenia (Sun et al. 2013; Almoguera et al. 2011; Lung et al. 2011).

An earlier study has suggested that the over-activation of proinflammatory cytokines may cause inflammation in the central nervous system (Dowlati et al. 2010). These proinflammatory cytokines may produce physiological and behavioral effects, thus suggesting that they can be produced by their interaction with the serotonergic systems (Yamada et al. 2000). The serotonin transporter (5-HTT) might play an important role in the pathophysiology of mood disorders and may also be involved in

suicidal behavior because its binding is decreased in the brain of suicide victims (Pinto et al. 2011).

The solute carrier family 6 neurotransmitter transporter member 4 (5-HTT or SLC6A4) is located on chromosome 17 (17q11.1–q12) and contains the rs2020933 polymorphism (Kenna et al. 2012). Some polymorphisms in 5-HTT can significantly affect the regulation of serotonergic neurotransmission (Kenna et al. 2012). The 5-HTT gene has been implicated in the pathology of several psychiatric disorders and suicide (Kenna et al. 2012; Martin et al. 2007; Ryding et al. 2008; Antypa et al. 2013; Huezo-Diaz et al. 2009).

Despite studies that have shown the participation of the 5-HTT, TNF- α and IL-10 in several MD and suicide, research clarifying this relationship is required. Thus, the present study aimed to evaluate the relationship among suicide attempts (SA), quality of life, MD and presence of rs2020933 (5-HTT), rs1800871 (IL-10) and rs1800629 (TNF- α) polymorphisms in patients in the health service municipality of Arapiraca, Alagoas, a city in the northeast of Brazil.

Methods

A total of 161 patients with MD and history of SA, 145 patients with MD and no history of SA, and 175 subjects in the control group (without MD and no history of SA) were enrolled in the current study. All of the patients were recruited from the Center of Psycho-Social Attention and Family Health Units located in the city of Arapiraca, Alagoas, Brazil. The local ethics committee approved the study design, and all of the subjects provided their informed consent.

a) Data collection procedure: The questionnaire of identification and general data, questionnaire of quality of life assessment brief (WHOQOL-brief), scale of suicide ideation of Beck and the MINI International Neuropsychiatric Interview (MINI 5.0.0) were completed by the patient after enrollment in the study.

The questionnaire of identification and general data were used to identify the profile of the participants. The WHOQOL-brief allowed us to evaluate quality of life by analyzing the following four domains: physical, psychological, social relations and environment. The WHOQOL-brief was validated in Portuguese (Fleck et al. 2000). The scale of suicidal ideation of Beck is self-applied (Beck and Steer 1993), and one Brazilian version was validated in a sample of patients hospitalized for SA (Cunha et al. 1997). In this study, the following definition was adopted: presence of suicidal ideation

when there was an affirmative response to questions 4 or 5. The MINI is a structured interview for assessing psychiatric symptoms and disorders based on the Diagnostic and Statistical Manual of the American Psychiatric Association (DSM-IV-TR), which has a high diagnostic concordance with the Structured Clinical Interview for DSM-IV (Sheehan et al. 1998).

b) DNA Genotyping: DNA was obtained from buccal mucosal swab samples that were collected using a cytology brush applied to both sides of the inner surface of the cheek. The collected samples were placed in a microtube (2 mL) containing TES solution (10 mM Tris HCl, 1 mM EDTA and 0.6% SDS). Genomic DNA was extracted using a salting out procedure following the modified protocol by Abrão et al (2005). The DNA sample was stored in a tube containing TE solution (10 mM Tris HCl, 1 mM EDTA). The samples were stored in a freezer at -20°C in the laboratory of Molecular Biology and Gene Expression of the Federal University of Alagoas. The integrity of the DNA sample was analyzed in agarose gel (1%). The DNA concentration in all of the samples was determined using UV spectrophotometry, adjusted to a concentration of 4 ng/ μL with sterile distilled water, and stored at -80°C .

Genotyping of three polymorphisms in 5HTT (rs2020933), IL-10 (rs1800871) and TNF- α (rs1800629) was performed using the method of TaqMan allelic discrimination assay and a reagent kit (Applied Biosystem, Foster City, CA, USA) on Steep One Plus instrument real (Applied Biosystems, USA). Genotype calls were made using Steep One Plus software and visually checked. Primers used for PCR amplification of three polymorphisms were 5'-TCAGTTTTGTCCAGAAAAGTGAACC-3' (forward) and 5'-GGTCAATGGATTATTTATGAGCCTG-3' (reverse) for 5HTT gene, 5'-GTGTACCCTTGTACAGGTGATGTAA-3' (forward) and 5'-ATCTCTGTGCCTCAGTTTGCTCACT-3' (reverse) for the IL-10 gene, and primers were 5'-GAGGCAATAGGTTTTGAGGGGCATG-3' (forward) and 5'-GGACGGGGTTC AGCCTCCAGGGTCC-3' (reverse) for the TNF- α gene.

c) Statistical analysis: The analysis of the study was performed using SPSS (Statistical Package for the Social Sciences) program version 20. The Pearson χ^2 test was used to compare the proportions between the groups and among the general samples. The calculations of the odds ratio and 95% confidence interval were conducted using the risk option of Crosstabs. The onset ages from the patients of different genders were analyzed using the *t*-test. Student's *t*-test and ANOVA were used to analyze the quality

of life among the groups and between the general samples, through Welch test. *Cramer's V* was used to identify whether there was evidence of a correlation between the study groups. The level of significance for all of the statistical tests was 0.05.

d) Test of Hardy-Weinberg Equilibrium: Each genetic polymorphism was tested for Hardy-Weinberg equilibrium. For χ^2 analysis of each polymorphism in the group studied, a degree of freedom equal to 1 ($df = 3 - 1 \text{ genotypes} - 2 \text{ alleles} = 1$) was used. For χ^2 analysis of the three polymorphisms in the overall sample, a degree of freedom equal to 3 ($df = 9 \text{ genotypes} - 6 = 3 \text{ alleles}$) was used. All of the analyses considered an α of 5%.

Results

a) General characteristics

There is homogeneity between the variances of age in 3 studied groups, where Fisher's exact test = 3.742; $df = 2.478$; $p = 0.123$. ANOVA identified a significant difference in the average age of the 3 groups ($p = 0.024$) (Table 1).

The majority of the subjects interviewed were female, likely because women tend to look for more health services than men (Table 1). The group with MD and SA showed a lower likelihood of being married than the group without SA ($OR = 0.5$; $\chi^2 = 8.9$; $p = 0.002$) (Table 1).

The group with MD and SA showed a lower educational level than the control group. The majority of the subjects received elementary school education ($OR = 4.8$; $\chi^2 = 4.8$; $p = 0.000$), followed by high school education ($OR = 0.4$; $\chi^2 = 10.4$; $p = 0.001$) and higher education ($OR = 0.2$; $\chi^2 = 23.7$; $p = 0.000$). The group with MD without SA presented fewer years of education than the control group. Most of them received elementary school education ($OR = 2.8$; $\chi^2 = 19.5$; $p = 0.000$), high school education ($OR = 0.6$; $\chi^2 = 3.8$; $p = 0.05$) and higher education ($OR = 0.4$; $\chi^2 = 10.1$; $p = 0.001$) (Table 1).

The majority of the subjects in the three groups claimed to have a religion; however, the group with MD and SA showed a higher frequency of individuals without religion (Table 1). Regarding family income, the group MD disorder and SA ($OR = 2.5$; $\chi^2 = 15.8$; $p = 0.000$) and the group with MD without SA ($OR = 1.7$; $\chi^2 = 5.1$; $p = 0.020$) had a lower income level compared with the control group (Table 1).

Unemployment in the group with MD and SA ($OR = 0.3$; $\chi^2 = 18.3$; $p = 0.000$) and in the group with MD without SA ($OR = 0.2$; $\chi^2 = 36.7$; $p = 0.000$) was greater than in the control group (Table 1).

b) Attempt, ideation and suicide risk

Among the 161 people who were interviewed for MINI and who had SA, 56 (34.8%) presented with current suicidal ideation; and 131 subjects (81.4%) presented with a suicide risk; the mild risk ($n= 60$; 45.8%) and the severe risk ($n= 65$; 49.6%) occurred more frequently (Table 1).

There is a significant relationship between SA in the group with MD and suicide attempt compared with the group without SA and the control group (*Cramer's* $V= 0.960$; $\chi^2_{(2)}= 443.6$; $p= 0.000$).

c) Genetic polymorphisms

All three groups — controls, MD and SA and MD without SA — were successfully genotyped. We were unable to identify the alleles and genotypes (degraded sample) in 5-HTT in only one DNA sample in the MD and SA group. All of the allelic and genotypic frequencies were found to be in Hardy-Weinberg equilibrium (HWE).

The genotypic and allelic frequencies of all of the polymorphisms of genes were not different between the MD and SA group and the MD without SA group, the MD and SA group and the control group as well as the MD without SA group and the control group (Table 2). Notably, there were no individuals in the MD without SA group in our study sample carrying homozygote single nucleotide polymorphism (SNP) of TNF- α A/A (Table 2).

The C allele of rs1800871 (IL10) polymorphism is associated with MD without SA in females (Table 3). The most common MD (major depression, manic episode and generalized anxiety disorder) in the group with MD and SA were analyzed; however, no association with the polymorphisms studied was found (Table 4). The A/T genotype appeared as a factor of protection for the number of SA (2-3 times) in relation to the control groups ($OR=0.91$; $\chi^2= 0.000$; $p= 0.000$), in rs2020933 (5-HTT) polymorphism (Table 4). There is an evident correlation between the absence of the T allele of rs2020933 (5-HTT) polymorphism and the presence of any family with MD in the general sample (*Cramer's* $V= 0.117$; $p= 0.038$) (Table 4).

d) Quality of life

The Welch test shows that the quality of life is influenced by the domains physical, psychological, social and environmental relationship between in the 3 studied groups ($p= 0.000$). ANOVA identified that there is a statistically significant difference in the media of the domains studied and general quality of life in the 3 groups ($p= 0.000$). The post-hoc Bonferroni test ($p= 0.000$) and Tukey ($p= 0.000$) confirm this

significance between the domains of quality of life in the three groups. The ‘environment’ domain presented the lowest media, and the ‘social relationship’ domain presented the higher media in the three groups and in the general sample (Table 5).

e) Mental Disorder

The individual with psychotic syndrome ($OR= 3.9$, $x^2= 29.7$), obsessive-compulsive disorder (3.9 , $x^2= 12.0$), post-traumatic stress disorder ($OR= 3.0$, $x^2= 7.5$), depressive episode ($OR= 2.7$, $x^2=17.5$), manic episode ($OR= 2.7$, $x^2= 14.2$), panic disorder ($OR= 2.2$, $x^2= 7.5$), social phobia ($OR= 2.0$, $x^2= 4.7$), generalized anxiety disorder ($OR= 1.9$, $x^2= 7.3$), and alcohol dependence/abuse ($OR= 1.4$, $x^2= 0.01$) showed a higher risk to SA (Table 6).

There is a significant relationship between having a first-degree relative with MD in the group with MD and SA compared with the group without SA and control ($x^2_{(4)}= 29.0$; *Cramer's V*= 0.173; $p= 0.000$).

The subject with MD and SA showed the highest risk of having psychiatric co-morbidity than the subject with MD without SA ($OR= 4.0$; $p= 0.000$) (Table 6).

Discussion

The etiology of suicidal behavior is multifactorial and involves genetic, environmental and psychological factors (Mandelli and Serretti 2013).

a) Genetic factors

Among the underlying biological changes, studies have indicated that a dysregulated immune system can be a contributing factor to depression and suicidality (Muller 2014). The SNPs in IL-10 (rs1800871), 5HTT (rs2020933) and TNF- α (rs1800629) were examined for associations with the risk of suicide in people with MD.

IL-10

Our study identified that C allele of rs1800871 (IL-10) polymorphism is associated with MD without SA in females. A study conducted in Spanish with the rs1800896 (IL-10) polymorphism identified that the A allele was associated with schizophrenia in women (Almoguera et al. 2011).

Another study identified that there were no differences in the allele of IL-10 (rs1800896) between depressed patients who had SA and those who had not (Kim et al. 2013); however, a study in Spain identified that the AA genotype is associated with schizophrenia in women (Almoguera et al. 2011). Another study did not identify the

participation of two polymorphisms of IL-10 (rs1800872 and rs72393728) in patients with schizophrenia with tardive dyskinesia but identified the association with positive and negative symptoms of schizophrenia in these patients (Sun et al. 2013). Another study examined two polymorphisms (rs1800871 and rs1800896) in patients with schizophrenia and found no association (Lung et al. 2011). There are few studies in the area, suggesting the need for new research focusing on specific MD and the IL-10 gene.

5-HTT

The proinflammatory cytokine activation in the central nervous system causes inflammation (Dowlati et al. 2010) and interferes with the serotonergic system (Yamada et al. 2000). Several studies have demonstrated that abnormalities in the functioning of the serotonergic system are related to the pathogenesis of suicidal behavior (Martin et al. 2007; Ryding et al. 2008; Antypa et al. 2013). Genes, such as the 5-HTT, that code for proteins regulating the neurotransmission of serotonin have been considered to be candidates in association studies of suicidal behavior (Antypa et al. 2013).

A correlation exists between the absence of the T allele of rs2020933 polymorphism and the presence of any family with MD in the general sample. However, an earlier study showed that the A allele was associated with greater serotonin transporters and transcription that may interfere with the positive imbalance with the long allele of the 5-HTTLPR (Huezo-Diaz et al. 2009), affecting the presence of MD. A previous systematic review with meta-analysis identified an association between 5-HTTLPR (serotonin-transporter-linked polymorphic region) polymorphism and suicidal behavior (Alves et al. 2015).

The rs2020933 polymorphism is located in the first intron, 870 bp, approximately 2.5 kb 3' to the 5-HTTLPR, and this location contributes to the variation of serotonin transporter expression (Martin et al. 2007). Recently, it has been discussed that the analysis of 5-HTTLPR is incomplete because other polymorphisms have been found in the proximity of the Ins/Del locus, such as rs2020933 (Wendland et al. 2008; Bozina et al. 2012), suggesting participation in the presence of MD and suicidal behavior.

The A/T genotype in rs2020933 polymorphism presented an association and appeared as a factor of protection for the number of SA (2-3 times) in the control groups in our study. The proximity of rs2020933 could be related to SA in people with MD. This rs2020933 polymorphism had the strongest influence in mood disorders, depressive symptoms and anxiety (Huezo-Diaz et al. 2009).

TNF- α

Our study presented low frequency of the genotype AA. We do not identify any allele or genotype in rs1800629 polymorphism associated with SA in people with MD. This situation reinforces the need for new studies to evaluate the association of these polymorphisms in samples of people with SA and MD, aiming at confirming participation in this event.

The G/G genotype of the TNF- α was found to significantly increase the risk for SA (Kim et al. 2013). Another study reported that the G/G genotype of TNF- α appeared significantly more frequently in those who had SA compared to the normal controls (Omran et al. 2012). Another study identified that the A/A genotype of TNF- α represented a risk factor for those persons with major depression disorder and SA (Kim et al. 2013). Furthermore, several studies have identified that the TNF- α as an independent risk factor for those persons have had SA in major depression disorders (Kim et al. 2013; Janelidze et al. 2011). In contrast, our study did not identify this polymorphism associated with depression or SA, which reinforces the need for new studies with this focus.

The development of more sophisticated and advanced methods for investigating the interplay between biological factors (genetics, biomarkers, among others) and environmental risk and their integration with advanced techniques of investigation would be helpful in the future to advance research, potentially leading to more effective, preventative, diagnostic and therapeutic opportunities (Mandelli and Serretti 2013).

a) Epidemiological characteristics

SA are violent self-inflicted events that present serious repercussions to both the attempter, family and friends (Alves et al. 2014). Psychological, biological, economic, and sociocultural factors make suicide a complex phenomenon (Brzozowski et al. 2010). Thus, the present study aimed to show genetic and epidemiological characteristics regarding suicide and MD.

A previous study conducted in Ceará, a state in the northeast region of Brazil, with people who SA, identified 64.6% of the sample as females; 76.0% were between the ages of 30 and 59 years and 75.2% had no formal education or elementary school education (Oliveira et al. 2013). Another study conducted in Arapiraca showed that women between the ages of 10 and 19 years and men between the ages of 60 and 69 years exhibited the most significant number of SA (Alves et al. 2014). The highest rate

(65.5%) of SA occurred among single/divorced patients. There was a predominance of religious affiliations (96.5%) (Brzozowski et al. 2010). Another study conducted in São Paulo, Brazil showed that the suicide risk was higher among singles and divorced/widowers compared with married people (Bando et al. 2013). In our study, the majority of the participants were women, young adults, with low educational level, singles, with a religion and family history of MD in the group who had SA. A second study conducted in southern Brazil identified that the greatest number of people who SA were female, aged 30-39 years, married and with 5 to 8 years of formal education (Ferreira and Trichês 2014). These findings were similar to our research results.

The social isolation caused by the presence of MD can be increased by their difficulties in dealing with daily problems. The desire to the divine, to religiosity, regardless of belief, the glimpse of possible solutions and the relief of suffering (Câmara and Pereira 2010) and participate in a church community could contribute to relieve their suffering and promote social inclusion. In our study, this situation would be a likely justification for the large number of people with a religion.

Women who were employed were more susceptible to SA (Bernardes et al. 2010); however, our study identified that unemployment was more common among women with SA.

Suicide is a complex phenomenon and an important indicator of the population's quality of life (Heck et al. 2012). An earlier study identified that those individuals with depression and risk of suicide showed a lower quality of life than individuals with depression without suicide risk (Lopez et al. 2011). In our study, we identified that those patients with MD and SA showed a lower quality of life than those patients with MD but no SA. We have identified that the quality of life of the patients interviewed with MD and SA is committed to all domains assessed: physical, psychological, social relations and environmental. The 'environment' domain may have introduced smaller media because of the precarious conditions in finance, security, transportation, housing and health care in the population living in the city. The domain 'social relationship' may have presented greater media because of the culture of this place to maintain good ties with friends and neighbors, thus facilitating interpersonal relationships.

The presence of a MD is one important risk factor for suicide.² Suicidal behavior can occur in different psychopathological conditions (Bertolote et al. 2010; Mandelli and Serretti 2013; García-Rábago et al. 2010). Mood disorders, particularly depressive

syndromes, represent the most frequent diagnosis among those who have committed suicide (Bertolote et al. 2010).

A study conducted in Mexico, involving people with SA, identified that generalized anxiety disorder and dysthymia were the most common MD (García-Rábago et al. 2010). The major depressive disorder seems to be an established risk factor for suicidal behavior (Mandelli and Serretti 2013; Muller 2014). Our study identified that psychotic syndrome, obsessive-compulsive disorder, post-traumatic stress disorder, depressive episode, manic episode, panic disorder, social phobia, generalized anxiety disorder and alcohol dependence/abuse presented statistical significance in the group with MD and SA.

A recent study conducted in Alagoas, Brazil identified the relationship of psychiatric co-morbidities with the risk of suicide (Vasconcelos et al. 2015). Our study identified that co-morbidity is a risk factor for SA. However, a study conducted in Minas Gerais, Brazil identified that there was no relationship between psychiatric co-morbidities and SA (Barbosa et al. 2011). Psychiatric co-morbidity uses a therapeutic approach because it requires the treatment of more than one MD. The medical treatment or psychotherapy will take longer to produce an effective result, which may favor in the meantime the SA.

The present study aimed to illustrate the genetic and epidemiological characteristics associated with suicide and MD in patients living in the city of Arapiraca, Brazil. There was no association of alleles and genotypes of rs1800871 (IL-10), rs1800629 (TNF- α) and rs2020933 (5-HTT) polymorphism in the groups. The C allele of rs1800871 (IL-10) polymorphism is associated with MD without SA in females. The A/T genotype in rs2020933 (5-HTT) polymorphism appeared as a factor of protection for the number of SA (2-3 times) in the control group. There is a correlation between the absence of the T allele of rs2020933 (5-HTT) polymorphism and the presence of any family with MD in the general sample.

Our study interviewed, for the most part, women and young adults with the following: a low educational level; single subjects; unemployment; religion; and family history of MD among those who have a history of SA. The suicide risk most frequently found in patients was the mild and severe risk. The quality of life of patients interviewed with MD and SA is committed to all domains assessed.

The limitation of the study is related to the presence of the largest female sample, and the study does not need to be focused on a particular type of MD. We

interviewed, for the most part, women because these subjects are more accessible in the health service studied. A homogeneous sample of men and women could present different results. Additionally, genetic studies addressing a particular type of MD would be more accurate; however, it is difficult to obtain the appropriate sample of individuals with some type of MD to conduct these genetic studies.

Conflict of Interest: None

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Table 1. General characteristics of the sample (n= 481).

General Data	Mental disorder and SA n= 161	Mental disorder without SA n= 145	Control n= 175
Age			
General media (SD)	37.9 (11.3)	40.7 (13.5)	36.8 (13.1)
Sex			
Female (n)	130	126	153
Marital status			
Married	76 (47.2%)	94 (64.8%)	100 (57.1%)
Not married	85 (52.8%)	51 (35.2%)	75 (42.9%)
Education			
University	9 (5.6%)	16 (11.0%)	45 (25.7%)
High school	30 (18.6%)	35 (24.0%)	61 (34.9%)
Elementary	122 (75.8%)	94 (65.0%)	69 (39.4%)
Religion			
With	150 (93.2%)	137 (94.5%)	166 (94.9%)
Without	11 (6.8%)	8 (5.5%)	9 (5.1%)
Family income			
Up to US\$200.00	89 (55.3%)	67 (46.2%)	58 (33.1%)
More than US\$200.00	72 (44.7%)	78 (53.8%)	117 (66.9%)
Work			
Yes	37 (23.0%)	68 (46.9%)	98 (56.0%)
No	124(77.0%)	77 (53.1%)	77 (44.0%)
Mental disorder in the family			
Yes	90 (55.9%)	61 (42.1%)	56 (32.0%)
No	68 (42.2%)	66 (45.5%)	94 (53.7%)
Unknown	3 (1.9%)	18 (12.4%)	25 (14.3%)
Number of suicide attempt			
1 time	71 (44.1%)	-	-
2 to 3 times	32 (19.9%)	-	-
More than 4 times	45 (27.9%)	-	-
Not reported	13 (8.1%)	-	-
Current suicidal ideation			
Yes	56 (34.8%)	7 (4.8%)	-
Risk of suicide (MINI)	131 (81.4%)	22 (15.2%)	-
Mild	60 (45.8%)	9 (40.9%)	-
Moderate	6 (4.6%)	4 (18.2%)	-
Severe	65 (49.6%)	9 (40.9%)	-

SA: suicide attempt; SD: standard deviation.

Table 2. Allelic and genotypic frequencies of polymorphisms located in the gene IL-10, TNF- α and 5-HTT.

Genetics factors	Mental disorder and SA n= 161*		Mental disorder without SA n= 145		Control n= 175		Mental disorder and SA vs. Mental disorder without SA		Mental disorder and SA vs. Control		Mental disorder without SA vs. control		HWE <i>x</i> ²	HWE <i>p</i>
IL 10	N	%	N	%	N	%	<i>x</i> ²	<i>p</i>	<i>x</i> ²	<i>p</i>	<i>x</i> ²	<i>p</i>	0.023	0.880
C	141	87.6	128	88.3	148	84.6	0.000	0.988	0.305	0.581	0.378	0.538		
T	94	58.4	84	57.9	111	63.4								
CT	74	46.0	67	46.2	84	48.0								
CC	67	41.6	61	42.1	64	36.6	0.036	0.982	1.163	0.0559	1.459	0.482		
TT	20	12.4	17	11.7	27	15.4								
TNF alpha	N	%	N	%	N	%	<i>x</i> ²	<i>p</i>	<i>x</i> ²	<i>p</i>	<i>x</i> ²	<i>p</i>	1.265	0.261
A	28	17.4	25	17.2	43	24.6	0.001	0.971	1.346	0.246	1.535	0.215		
G	157	97.5	145	100.0	171	97.7								
AG	24	14.9	25	17.2	39	22.3								
AA	4	2.5	0	-	4	2.3	3.862	0.145	2.997	0.223	4.864	0.088		
GG	133	82.6	120	82.8	132	75.4								
5-HTT	N	%	N	%	N	%	<i>x</i> ²	<i>p</i>	<i>x</i> ²	<i>p</i>	<i>x</i> ²	<i>p</i>	2.658	0.103
A	159	99.4	144	99.3	173	98.9	0.002	0.963	0.004	0.952	0.017	0.897		
T	45	28.1	40	27.6	51	29.1								
AA	115	71.9	105	72.4	124	70.9								
TT	2	1.2	1	0.7	3	1.7	0.246	0.884	0.142	0.931	0.701	0.704		
AT	43	26.9	39	26.9	48	27.4								

Test of Hardy-Weinberg equilibrium (HWE χ^2) and associated p (HWE p).

*A degraded DNA sample; thus, it was not possible to identify the alleles and genotypes in 5-HTT (mental disorder and SA group).

Table 3. Allelic and genotypic frequencies of polymorphisms located in the gene IL-10, TNF- α and 5-HTT, by gender.

Male													Female											
Genetics factors	Mental disorder and SA n= 31		Mental disorder without SA n= 19		Control n= 22		Mental disorder and SA vs. Mental disorder without SA		Mental disorder and SA vs. Control		Mental disorder without SA vs. control		Mental disorder and SA n= 130*		Mental disorder without SA n= 126		Control n= 153		Mental disorder and SA vs. Mental disorder without SA		Mental disorder and SA vs. Control		Mental disorder without SA vs. control	
	N	%	N	%	N	%	χ^2	p	χ^2	p	χ^2	p	N	%	N	%	N	%	χ^2	p	χ^2	p	χ^2	p
IL 10																								
C	28	90.3	17	89.5	18	81.8	0.025	0.874	0.010	0.918	0.048	0.827	113	86.9	111	88.1	130	85.0	0.000	0.000	0.287	0.592	0.414	0.520
T	19	61.3	12	63.2	13	59.1							75	57.7	72	57.1	98	64.0						
CT	16	51.6	10	52.6	9	49.9							58	44.6	57	45.2	75	49.0						
CC	12	38.7	7	36.9	9	40.9	0.022	0.989	1.033	0.597	0.754	0.686	55	42.3	54	42.9	55	36.0	0.036	0.982	1.163	0.559	1.459	0.482
TT	3	9.7	2	10.5	4	18.2							17	13.1	15	11.9	23	15.0						
TNF α																								
A	7	22.6	4	21.1	5	22.7	0.038	0.846	0.087	0.768	0.041	0.839	21	16.1	21	16.7	38	24.8	0.020	0.886	1.680	0.195	1.610	0.204
G	30	96.8	19	100.0	21	95.5							127	97.7	126	100.0	150	98.0						
AG	6	19.4	4	21.1	4	18.2							18	13.8	21	16.7	35	22.9						
AA	1	3.2	-	-	1	4.5	0.633	0.729	0.069	0.966	0.910	0.634	3	2.3	-	-	3	2.0	3.862	0.145	2.997	0.223	4.864	0.088
GG	24	77.4	15	78.9	17	77.3							109	83.9	105	83.3	115	75.1						
5-HTT																								
A	31	100.0	18	94.7	22	100.0	0.001	0.972	0.331	0.565	0.569	0.451	128	99.2	126	100.0	150	98.0	0.000	0.983	0.169	0.681	0.324	0.569
T	10	32.3	7	36.8	4	18.2							35	27.1	33	26.2	47	30.7						
AA	21	67.7	12	63.1	18	81.8							94	72.9	93	73.8	106	69.3						
TT	-	-	1	5.3	-	-	1.671	0.434	1.312	0.252	2.393	0.302	2	1.5	-	-	3	2.0	0.246	0.884	0.142	0.931	0.701	0.704
AT	10	32.3	6	31.6	4	18.2							33	25.6	33	26.2	44	28.7						

*A degraded female DNA sample; thus, it was not possible to identify the alleles and genotypes in 5-HTT (mental disorder and SA group).

Table 4. Allelic and genotypic frequencies of polymorphisms located in the gene IL-10, TNF- α and 5-HTT, by the types of mental disorders, presence of mental disorder in the family and history of suicide attempt.

Genetics factors	Current major depressive episode n= 105*		Manic episode n= 68		GAD n= 74		Family history of mental disorder n= 90*		Number of suicide attempts**						Control n= 175	
	N	%	N	%	N	%	N	%	1 n= 71		2 – 3 n= 32		> 4 n= 45*		N	%
IL 10									N	%	N	%	N	%	N	%
C	90	85.7	62	91.2	64	86.5	78	86.7	62	87.3	27	84.4	39	86.7	148	84.6
T	62	59.0	44	64.7	47	63.5	57	63.3	40	56.3	17	53.1	29	64.4	111	63.4
CT	47	44.8	38	55.9	37	50.0	45	50.0	31	43.7	12	37.5	23	51.1	84	48.0
CC	43	40.9	27	39.7	27	36.5	33	36.7	31	43.7	15	46.9	16	35.6	64	36.6
TT	15	14.3	3	4.4	10	13.5	12	13.3	9	12.6	5	15.6	6	13.3	27	15.4
TNF alfa	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
A	19	18.1	12	17.6	13	17.6	17	18.9	9	12.7	6	18.7	9	20.0	43	24.6
G	102	97.1	65	95.6	71	95.9	88	97.8	71	100.0	30	93.7	44	97.8	171	97.7
AG	16	15.2	9	13.2	10	13.5	15	16.7	9	12.7	4	12.5	8	17.8	39	22.3
AA	3	2.9	3	4.4	3	4.1	2	2.2	-	-	2	6.2	1	2.2	4	2.3
GG	86	81.9	56	82.4	61	82.4	73	81.1	62	87.3	26	81.3	36	80.0	132	75.4
5-HTT	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
A	103	99.0	67	98.5	74	100.0	88	98.9	71	100.0	32	100.0	44	100.0	173	98.9
T	30	28.8	21	30.9	21	28.4	30	33.7	20	28.2	8	25.0	13	29.5	50	28.9
AA	74	71.1	47	69.1	53	71.6	59	66.3	51	71.8	24	75.0	31	70.5	123	71.1
TT	2	2.0	1	1.5	1	1.4	2	2.2	1	1.4	-	-	-	-	3	1.7
AT	28	26.9	20	29.4	20	27.0	28	31.5	19	26.8	8	25.0	13	29.5	47	27.2

*A degraded DNA sample; thus, it was not possible to identify the alleles and genotypes in 5-HTT (current major depressive episode, family history of mental disorder and >4 suicide attempt groups).

**Thirteen people not reporting the number of suicide attempts.

GAD, generalized anxiety disorder. The χ^2 was conducted comparing current major depressive episode vs. control, manic episode vs. control, GAD vs. control, family history of mental disorder vs. control and number of suicide attempts vs. control. Only the A/T genotype (2-3 suicide attempts vs. control) of 5-HTT presented statistical significance ($p < 0.05$).

Table 5. Media and standard deviation (SD) of the domains of quality of life in the three groups.

Group	Domains					<i>p</i>
	Physical	Psychological	Social relations	Environment	General quality of life	
	Media (SD)	Media (SD)	Media (SD)	Media (SD)	Media (SD)	
Mental disorder and SA n= 161	51.2 (18.4)	52.0 (18.8)	57.9 (18.6)	47.6 (15.0)	54.1 (21.9)	0.000
Mental disorder without SA n= 145	61.9 (16.1)	64.4 (13.6)	66.0 (15.7)	52.5 (12.8)	64.3 (19.1)	0.000
Control n= 175	72.6 (12.7)	74.6 (10.9)	74.5 (14.2)	60.4 (12.9)	73.1 (15.9)	0.000
General n= 481	62.2 (18.2)	64.0 (17.5)	66.4 (17.6)	53.7 (14.6)	64.1 (20.6)	0.000

SA: suicide attempt

Table 6. Mental disorders in patients with and without suicide attempts.

Mental disorder	Mental disorder and SA		Mental disorder without SA		OR	χ^2	p
	N	%	N	%			
Current major depressive episode	105	65.2	59	40.7	2.7	17.5	0.000
Recurrent major depressive episode	73	45.3	46	31.7	1.8	5.4	0.020
MDE with melancholic features	77	47.8	41	28.3	2.3	11.5	0.000
Dysthymic disorder	12	7.4	5	3.4	2.2	1.6	0.201
Manic episode	68	42.2	31	21.4	2.7	14.2	0.000
Hypomanic episode	23	14.3	16	11.0	1.3	0.5	0.497
Panic disorder	52	32.3	26	17.9	2.2	7.5	0.006
Agoraphobia	80	49.7	64	44.1	1.2	0.7	0.392
Social phobia	39	24.2	20	13.8	2.0	4.7	0.030
Obsessive compulsive disorder	33	20.5	9	6.2	3.9	12.0	0.000
Post traumatic stress disorder	29	18.0	10	6.9	3.0	7.5	0.006
Addiction/Abuse of Alcohol	20	12.4	7	4.8	2.8	4.6	0.033
Addiction/Abuse of substance	3	1.9	2	1.4	1.4	0.01	0.906
Psychotic syndrome	88	54.7	34	23.4	3.9	29.7	0.000
Mood disorder with psychotic features	49	30.4	4	2.8	15.4	38.9	0.000
Anorexia nervosa	0	-	0	-	-	-	-
Bulimia nervosa	2	0.8	1	0.7	1.8	0.008	0.927
Generalized anxiety disorder	74	46.0	44	30.3	1.9	7.3	0.007
Antisocial personality disorder	2	1.2	1	0.7	1.8	0.008	0.927
Comorbidade	127	78.9	70	48.3	4.0	29.8	0.000

SA: Suicide attempt.

4 DISCUSSÃO

O suicídio é influenciado pela situação econômica, grau de desigualdade, gastos com saúde pública, região geográfica, idade e sexo do indivíduo, transtorno mental, nível educacional, grau de urbanização, taxa de desemprego, problema de identidade sexual, exposição a armas de fogo, situações de perda, exposição a situações de estresse extremo (abuso sexual, instabilidade familiar) e histórico familiar¹¹. Por ser um tema relevante, esta tese buscou apresentar artigos que permitissem conhecer melhor a complexidade desse problema na cidade de Arapiraca, Alagoas.

As tentativas de suicídio em pacientes atendidos no Hospital de Urgência e Emergência mostrou predominância no sexo feminino⁵⁴. A menor ocorrência de suicídio entre as mulheres está relacionada a baixa prevalência de dependência do álcool; maior religiosidade e ao envolvimento social e papel de mãe, esposa e filha. As mulheres conseguem ainda, reconhecer precocemente sinais de riscos para depressão, suicídio e transtorno mental e buscam mais ajuda em momentos de crise⁵⁵.

A ingestão de medicamentos foi o método mais frequente para as mulheres; e o envenenamento, objetos pontiagudos e enforcamento para os homens⁵⁴. Estudo realizado na Bahia, entre 2006 e 2010, identificou que as tentativas de suicídio foram mais frequentes no sexo feminino (53,4%) e utilizaram como meio a queda de altura (69,2%)⁵⁶.

O artigo de revisão sistemática identificou que os homens idosos têm uma maior taxa de morte por tentativa de suicídio⁵⁷. Isso condiz com os estudos atuais que mostram que as mulheres tentam mais, mas os homens, ao utilizarem meios mais agressivos, têm um êxito maior na tentativa de suicídio^{58,59}.

Estudos sugerem que há diferenças entre as variações climáticas e o comportamento suicida⁶⁰. As tentativas de suicídio atendidas no serviço pré-hospitalar foram mais frequentes em mulheres, no outono, dia de domingo e no período vespertino. O domingo, principalmente no período vespertino, pode ter apresentado um maior número de tentativas de suicídio, pelo fato das pessoas estarem mais sozinhas em suas residências⁵⁴. Estudo realizado no serviço hospitalar de Arapiraca identificou que a primavera e outono, dia de sábado, domingo e segunda e o período matutino apresentaram maior número de tentativas

de suicídio. Estudo realizado na Bahia, entre 2006 e 2010 identificou que as tentativas de suicídio ocorreram, mais frequentemente, no outono e primavera, nos dias de sábado e terça-feira, nos turnos da manhã e noite⁵⁶.

Os estudos epidemiológicos realizados no hospital estudado não identificaram a relação do suicídio com a presença de transtorno mental. Isso porque não haviam registros nos prontuários sobre uso de medicações ou acompanhamento psiquiátrico anterior a tentativa de suicídio, que permitisse identificar essa relação. O acesso ao tratamento adequado, ao ser conduzido de forma compatível à realidade de cada indivíduo com tentativa de suicídio, reduz os números de mortes²¹, mas o serviço de saúde mental dessa cidade não está articulado com o hospital de urgência e emergência estudado. Quando os pacientes com tentativa de suicídio têm alta, eles saem com o encaminhamento dado pela psicóloga ou médico, mas isso não garante que eles irão procurar um serviço de saúde para acompanhamento do transtorno mental ou ainda se vão ter acesso a esse atendimento em tempo hábil. As ações de cuidado deveriam estar articuladas com os demais serviços existentes no sistema de saúde, permitindo o adequado encaminhamento dos pacientes aos serviços competentes⁶¹.

O estudo sobre ideação suicida e cronotipo em militares e enfermeiros identificou características semelhantes. Ambos trabalham em turnos e com pessoas em sofrimentos emocionais ou vítimas de violência. Os resultados apontaram que os enfermeiros e militares estudados na cidade de Arapiraca apresentaram sintomas de ansiedade com nível leve, moderado e grave e risco para depressão; ideação suicida ao longo da vida; e cronotipo indiferente⁶². Estudos mostram que o cotidiano da atividade policial pode gerar sofrimento psíquico em razão da contínua pressão pela qual esses profissionais passam^{63,64}. O enfermeiro, por interagir na maior parte do tempo com pessoas que necessitam de ajuda, está mais propenso a apresentar sofrimento psíquico⁶⁵. Além disso, o trabalho noturno altera o ritmo circadiano, provocando estresse, que gera, entre outras coisas, alterações no padrão do sono, promovendo uma retroalimentação da situação. O sono diurno não possui a mesma qualidade e capacidade reparadora do sono noturno, gerando nesses trabalhadores um débito cumulativo de sono, o que resulta em diminuição da capacidade produtiva⁶⁶. Dessa forma, uma atenção especial deveria ser oferecida aos enfermeiros e militares em busca de uma melhor qualidade de vida laboral.

Estudo realizado em unidades de saúde da família e centro de atenção psicossocial de Arapiraca identificou que a presença de transtorno mental com risco de suicídio pode ser um fator que está contribuindo para uma menor qualidade de vida dos pacientes. A avaliação da qualidade de vida permite identificar se as pessoas entrevistadas estão satisfeitas com alguns aspectos da sua vida. Quando analisamos as médias de acordo com os grupos (transtorno mental com tentativa de suicídio, transtorno mental sem tentativa de suicídio e controle) e os domínios físico, relação social, psicológico e meio ambiente para QV, o grupo com transtorno mental e risco para tentativa de suicídio apresentou QV mais baixa em todos os domínios. O domínio 'meio ambiente' foi o menor e o domínio 'relação social' foi maior em todos os grupos. Estudo realizado com a população baiana geral identificou que o domínio 'relação social' apresentou maior escore o domínio 'meio ambiente' apresentou-se menor⁶⁷, semelhante ao nosso estudo. Estudo realizado com a população iraniana geral identificou que o domínio 'meio ambiente' também se apresentou menor, seguidos do domínio psicológico, relação social e físico⁶⁸.

O Brasil tem diferenças regionais econômicas e culturais muito grande. Alagoas tem um Índice de Desenvolvimento Humano (IDH) de 0,63, o pior indicador do país⁶⁹. O IDH mede dimensões como renda, educação e saúde. Isso retrata as condições desfavoráveis em que vivem a maior parte da população desse Estado. A cidade de Arapiraca/Alagoas apresenta pouco atrativo cultural, tem apenas um cinema e apresenta IDH de 0,64⁶⁹. A diversão das pessoas está relacionada a ir ao bar com amigos e familiares. A qualidade de vida de pessoas que vivem numa cidade com essas características provavelmente não seria boa. Isso foi refletido no baixo escore do domínio 'meio ambiente' que está relacionado com o oferecimento de segurança física e proteção, ambiente no lar, recursos financeiros, cuidados de saúde e sociais: disponibilidade e qualidade, oportunidades de adquirir novas informações e habilidades, participação em/e oportunidades de recreação/lazer, ambiente físico (poluição/ruído/trânsito/clima) e transporte⁴⁷.

A renda mensal dos pacientes estudados é baixa, com pouca escolaridade e se encontram recebendo benefícios do governo ou aposentados. As características pessoais como gênero, status sócio-econômico, idade, educação e personalidade são fatores que estão associados com comportamento suicida³². A escolaridade é fator de risco para tentativa e ideação suicida⁷⁰. O fato deles se aposentarem mais

cedo é um indicador de pobreza na função social, gerando uma carga psicológica negativa e ainda, um impacto na QV dos mesmos⁷⁰.

Os transtornos mentais que apresentaram maior risco para o suicídio foram o transtorno obsessivo-compulsivo, transtorno do estresse pós-traumático, transtorno depressivo, episódio maníaco, transtorno do pânico, fobia social, transtorno de ansiedade generalizada e dependência/abuso de álcool. Estudos mostram que a maioria dos suicídios está relacionado com transtorno do humor (depressão), alcoolismo, abuso de drogas, esquizofrenia e ansiedade generalizada^{1,71-73}.

A maioria dos entrevistados com transtorno mental e tentativa de suicídio relatou ter parentes com transtorno mental. A herdabilidade para o comportamento suicida depende em parte da presença de transtornos mentais, mas também estes últimos podem aparecer independente do primeiro⁷⁴. O comportamento suicida está relacionado com a combinação de fatores como as comorbidades psiquiátricas, doenças médicas, fatores psicológicos, biológicos e genéticos⁷⁵.

Quanto a contribuição genética, esse estudo identificou a participação de alguns polimorfismos no transtorno mental. O artigo de revisão sistemática sobre os genes relacionados ao transtorno bipolar serviu de embasamento para a escolha dos genes selecionados para a pesquisa genética dessa tese (5-HTT, IL10 e TNF- α)⁷⁶. Inicialmente, a pesquisa tinha a proposta de selecionar apenas pacientes bipolares, mas devido a dificuldade de se conseguir pacientes com esse diagnóstico e ao tempo que seria despendido para isso, foram selecionados pacientes com transtornos mentais generalizados.

O artigo de metanálise sobre o polimorfismo 5-HTTLPR, localizado no gene 5-HTT, identificou que existe associação com comportamento suicida. Além disso, verificou-se que o alelo L estava relacionado ao maior risco de suicídio⁶². Outro estudo com o gene 5-HTT não apresentou associação com comportamento suicida³¹, mas isso pode ser resultado do pequeno número de amostra desse estudo.

Nosso estudo genético apresentou uma maior amostra feminina. Isso pode interferir nos resultados dessa pesquisa, mas não invalida o estudo. As unidades de saúde da família estudadas são frequentadas, principalmente, por mulheres e tal fato influenciou essa composição da amostra.

Não encontramos associação entre os alelos e genótipos dos polimorfismos rs1800871 (IL10), rs1800629 (TNF- α) e rs2020933 (5-HTT) com os grupos

estudados (transtorno mental com tentativa de suicídio, transtorno mental sem tentativa de suicídio e controle).

O alelo C do polimorfismo rs1800871 estava associado com transtorno mental sem tentativa de suicídio em mulheres. Não encontramos estudo analisando a relação do transtorno mental e/ou tentativa de suicídio com esse polimorfismo. Estudo realizado na Espanha com outro polimorfismo (rs1800896) do gene IL10 identificou que o alelo A está associado com esquizofrenia em mulheres³⁷. Percebemos que existem poucos estudos sobre a relação de polimorfismos no gene IL10 e a presença de transtorno mental e suicídio.

O genótipo A/T do polimorfismo rs2020933 apareceu como fator de proteção para o número de tentativa de suicídio (2 – 3 vezes). Estudo mostrou a participação do alelo A no transporte e transcrição da serotonina³⁹, o que pode estar interferindo na presença do transtorno mental, mas nosso estudo identificou o alelo T do polimorfismo rs2020933 correlacionado com história familiar de transtorno mental.

Nosso estudo apresentou uma pequena frequência de genótipos A/A no polimorfismo rs1800629. Nós não identificamos associação desse polimorfismo com tentativa de suicídio em pessoas com transtorno mental. Estudos mostram a participação do genótipo GG como fator de risco para tentativa de suicídio^{33,77}. Outro estudo identificou o genótipo A/A como fator de risco para depressão maior e tentativa de suicídio³³.

Apesar das evidências encontradas em nosso estudo genético, a participação dos polimorfismos rs2020933 (5-HTT) e rs1800871 (IL10) nos transtornos mentais e tentativa de suicídio ainda precisa ser melhor elucidada.

5 CONCLUSÃO

O levantamento das tentativas de suicídio atendidas no serviço hospitalar e pré-hospitalar identificaram que as mulheres apresentam mais tentativas de suicídio, sendo a ingestão de medicamentos o método mais frequente; e o envenenamento, objetos pontiagudos e enforcamento os mais utilizados pelos homens. No idoso identificou-se que o suicídio predomina no sexo masculino.

Sintomas de ansiedade e depressão em enfermeiros e militares, além de casos de ideação suicida ao longo da vida apontam para a necessidade de cuidados médicos e psicológicos ofertados a esses profissionais.

O cronotipo mais presente entre os militares e enfermeiros foi o indiferente. Pessoas que não pertencem a este cronotipo tem mais dificuldades na atividade laboral. Assim, um plano de trabalho voltado para as especificidades do ciclo sono-vigília deveria ser seguido favorecendo a realização de atividades laborais livres de desgastes e desatenção causados pela inadequação de turnos de trabalho.

O grupo com transtorno mental e risco de suicídio apresentou QV mais baixa em todos os domínios. O domínio 'meio ambiente' apresentou menor escore e o domínio 'relação social' apresentou maior escore. Aumentar o nível de escolaridade, a renda mensal, a oferta de emprego e o acesso ao serviço de saúde dos pacientes com transtorno mental e tentativa de suicídio pode contribuir com a melhora na QV dos mesmos.

O transtorno obsessivo-compulsivo, transtorno do estresse pós-traumático, transtorno depressivo, episódio maníaco, transtorno do pânico, fobia social, transtorno de ansiedade generalizada e dependência/abuso de álcool apresentaram maior risco para tentativa de suicídio. Reforçar a atenção quanto ao risco de suicídio no cuidado a esses pacientes pode contribuir com a diminuição de tentativas de suicídio.

No estudo genético, a maioria dos pacientes eram do sexo feminino, adultos jovens, com baixo nível educacional, solteiros, desempregados, com uma religião, história de transtorno mental na família e baixa qualidade de vida. Não encontramos associação dos alelos e genótipos dos polimorfismos rs1800871 (IL10), rs1800629 (TNF- α) e rs2020933 (5-HTT) nos grupos estudados. O alelo C do polimorfismo rs1800871 (IL10) está associado com transtorno mental sem tentativa de suicídio em mulheres. O genótipo A/T do polimorfismo rs2020933 (5-HTT) representa fator

de proteção para o número de tentativas de suicídio (2-3 vezes). Existe correlação entre a ausência do alelo T do polimorfismo rs2020933 e a presença de história de transtorno mental na família.

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