


Symptoms without Medical Explanation associated with depression and anxiety in the general population

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ABSTRACT

Introduction: The association between Medically Unexplained Symptoms (MUS) and depressive and anxious conditions, named Common Mental Disorders (CMD) has been studied, but there are few studies in Brazil. Aims: To estimate prevalence of four MUS

(irritable bowel, dyspepsia, chronic fatigue, and dizziness), its relationship with sociodemographic characteristics and co-occurrence with CMD. Method: The sample consists of 764 individuals, a subsample clinically evaluated by physicians, from the population survey 'São Paulo Megacity Mental Health Survey'. Psychiatric diagnoses were obtained through the SCID interview, according to DSM-IV. Information on the presence of MUS were obtained from validated scales in our country. Multivariable logistic regression model was used to study association of MUS and CMD. Results: Half of the sample presented at least one MUS, being more frequent in women, those aged between 35-49 years, 'low average' income and among married people. Chronic fatigue was the most frequent symptom (30.4% in the total sample; 22.9% women; 7.5% men), followed by dyspepsia (26.8%; 19.3% in women and 7.5% in men), vertigo (19.6%; 15% in women and 4.5% in men), and irritable bowel (6%; 4.5% in women and 1.3% in men). There was an association between SEM and depression (RC 3.4; 95% CI, 2.4-4.8) and anxiety (RC 2.2; 95% CI, 1.5-3.0). The likelihood of these common mental disorders increased with increasing numbers of Mus. Conclusion: We confirm the association between MUS and CMD in this sample of the largest Brazilian city, indicating the need of a comprehensive approach in treatment.

Keywords: Common mental disorders, Medically unexplained symptoms, Epidemiology, Somatization, Cross-sectional studies, Irritable bowel syndrome, Dyspepsia, Chronic fatigue, Dizziness, Depression, Anxiety.

1 INTRODUCTION

The term Symptom without Medical Explanation (SEM), known as *Medically Unexplained Symptoms (MUS)*, appeared after the observation of patients who attended secondary care clinics and who presented symptoms that could not be well explained by some pathology or biological dysfunction. In this situation, it began to be used by professionals and researchers when they needed to appeal to name

something undefined, observed from what they were treating and/or researching. ⁽¹⁾ According to Bransfield & Friedman⁽²⁾, SEM often fall into a category that difficulties arise from its differentiation between psychosomatic, somatopsiquic and multisystemic diseases, and the differential diagnosis is increasingly challenging with the intense specialization of current medicine. Requer the knowledge of general medicine, psychiatry and the systems that connect the body and the brain, which makes it difficult to measure them in the population as a single category.

The terminology has been undergoing changes over time, now based on the description and symptomatic specificity now in the process of falling ill of the pain somatize somatizeas as a whole, generating high costs for the health system. ⁽³⁾ The process of identification and the search for the integration of references that descrevam these clinical frameworks was constituted in nomenclatures that promoted, as far as possible, more refined clinical analyses, with less time proposals for a new classification that is not purely somatic or mental. ⁽⁴⁾

The association of SEM with Common Mental Disorders (CMD), a concept created by Goldberg and Huxley⁽⁵⁾ to designate a set of non-psychotic symptoms, which are usually related to subclinical conditions of anxiety, depression and stress, designating situations of mental suffering with higher prevalence among users of Primary Care (PA) services was recognized decades ago. Kroenke et al. ⁽⁶⁾ demonstrated that the most prevalent physical symptoms in PA were somatoform, associated with high prevalence of depressive disorder (50 to 75%) and anxious (40 to 50%) in these patients. In the study by Kirmayer et al. ⁽⁷⁾, around 80% of patients in PA clinics, with depressive and/or anxious symptoms, presented somatic manifestations, which hindered the recognition of associated psychiatric conditions. In one the sample of almost 8.000 patients in AP, Roca et al. ⁽⁸⁾ found 11.5% of patients presenting affective, anxiety and somatoform disorders concomitantly. In a recent study conducted with a Brazilian sample of patients seen in PA, more than 80% had somatic symptoms associated with anxiety and depression. ⁽⁹⁾ For Bombana, Leite and Miranda⁽¹⁰⁾, reports of symptoms and psychiatric diagnoses are not well recorded in the medical practice performed in PA in Brazil, which makes it difficult for epidemiological studies to investigate the association of SEM and CMD.

Our objective is to reduce *this gap* by evaluating the prevalence of four symptoms in a population sample in the Metropolitan Region of São Paulo, Brazil, its relationship with sociodemographic characteristics and comorbidity with depressive and anxiety disorders. For this, scollectsthefour symptoms based on: (i) its high prevalence; (ii) the great impairment of the quality of life associated with them; (iii) because they are not linked to specific pathologies; (iv) and be present at the AP. They are: 1) Irritable Bowel Syndrome (IsI) or irritable colon, characterized as functional gastrointestinal disease due to abdominal pain or discomfort associated with changes in the characteristic of bowel movements; ⁽¹¹⁾ 2) Dyspepsia, a persistent or recurrent pain or discomfort in the upper abdomen, with no organic disease justifying such symptoms; ⁽¹²⁾ 3) Fadig a, the manifestation of tiredness or exhaustion associated with

impairments in the development of the common activities of the day to day; ⁽¹³⁾ 4) Dizziness, a frequent symptom of multiple causes such as labyrinthopathy, postural hypotension, neurogenic síncope, convulsion, hearing problems . ⁽¹⁴⁾

2 METHOD

2.1 SAMPLE

The data are from the *epidemiological study 'São Paulo Megacity Mental Health Survey (SPMHS)'*, conducted by researchers from the Psychiatric Epidemiology Center of the Institute of Psychiatry of the Hospital das Clínicas of the Faculty of Medicine of the University of São Paulo (IPq-HCFMUSP).

The overall response rate of São Paulo Megacity (SPM) was 81.3% and the final sample was 5,037 individuals living in Região Metropolitana of São Paulo. This is a population-based cross-sectional study divided into two phases: the first, a home interview and the second, the object of this study, an evaluation of a subsample in the hospital environment. The objective of the first phase was to identify prevalence rates of psychiatric disorders in individuals aged 18 years or older in a multistratified probabilistic sample of the population living in households of Região Metropolitana of São Paulo. ⁽¹⁵⁾

For the second phase, a subsample of the 5. 037 individuals from the research were selected and invited to attend ipq-hcfmusp to perform complementary clinical and psychiatric evaluation. The selection of this subsample was as follows: todos individuals with psychiatric disorder during life (2,236 participants) and 20% of the 2,801 participants without diagnosis (corresponding to 55.6% of the total household sample, which corresponds to a total of 584 individuals) were selected by simple draw. Thus, 2,820 individuals were eligible to participate in the second phase of the survey.

Contact with 1,349 individuals was not possible. Of the 1,471 contacted, 780 (53%) attended IPq. Cinco were referred to the Emergency Room (ER), because they needed urgent care, and three gave up the evaluation. Thus, 772 individuals composed the sample. Of this total, 8 were excluded for not presenting information in sociodemographic variables, totaling 764 individuals at the end.

2.2 SOCIODEMOGRAPHIC VARIABLES

The sociodemographic variables were categorized as follows: a) sexo (female and male); b) gage rupes (18-34, 35-49 and 50-64 years); c) schooling (0-4 years of schooling, partial or complete elementary school, called 'low schooling'), (5-8 years of schooling, partial or complete elementary school, called 'low-middle schooling'), (9-11, years of study, partial or complete high school, called 'middle-high school') and (12 years or more of study, higher or completed education, called 'high schooling'); d) *per capita family income* defined in four categories: 'low' (0.5 minimum wage or less), 'low-average' (0.5-1.0 minimum wage), 'medium-high' (1.0-2.0 minimum wages), and 'high' (higher than 2.0 minimum wages); e) marital status classified as: 'married/live together', 'previously married/separated/widowed/divorced' and 'never

married (single)'; f) occupation in: 'workers' (including self-employed, owners, employees, temporarily removed from service, sick leave and maternity leave, and students), 'home workers', 'retired and unemployed' (including disabled, looking for jobs and others).

2.3 DIAGNOSTIC EVALUATION

The 764 individuals who composed the sample were reevaluated through the Structured Clinical Interview for DSM-IV Axis I Disorder, patient version (SCID-I/P),⁽¹⁶⁾ applied by experienced psychiatrists trained by (YPW, GLS, BMC), with the objective of obtaining greater reproducibility of psychiatric diagnosis. The following lifelong disorders were considered in the area: (1) depressive: major depression, minor depression and persistent depressive disorder (dysthymia); (2) anxious: agoraphobia, panic disorder, specific and social phobia and generalized anxiety disorder (GAD).

To evaluate the four SEM surveyed, evaluation scales and questionnaires were applied by experienced general practitioners (IB and DB), during clinical anamnesis and physical examination:

Irritable colon: the adapted version for WMH-CIDI⁽¹⁷⁾ composed for five questions (abdominal pain or discomfort; improvement with evacuation; increased frequency of evacuation; change in the shape of feces; distended abdomen in the absence of pain). The positive answer of the first question was necessary for continuity of application of the scale.

Dispepsia: we used the questionnaire by Moayyedi et al.⁽¹⁸⁾ of the University of Leeds, translated and validated by the General Practice Service of the Hospital das Clínicas of the Faculty of Medicine of the University of São Paulo (HC-FM USP), with a correlation coefficient beyond the chance $[\kappa] = 0.7$. This questionnaire is the Rome III⁽¹⁹⁾ criteria. It is an increasing ordinal scale, with the possibility of responses from 0 to 3 for each item: 0 for 'no symptom' from; 1 to 'up to once a week', 2 for 'more than once a week' and 3 scores for 'every day'. The final score ranges from 0 to 18. Null results mean absence. Individuals with final scores between 1 and 18 are considered as dyspeptic, and the scores of 1 to 4 are 'very light', from 5 to 8 'mild', from 9 to 15 'moderate' and greater than 15 'very severe'.

Fatigue: The Chalder scale et al.⁽²⁰⁾, composed of 11 items measured by a Likert scale of 4 points, going from "less fatigue than normal" to "much more fatigue than normal". A score of 29 or more on the fatigue scale discriminates, with more than 95% accuracy, that the individual has less than 5% chance of not presenting the feeling, and can therefore be used reliably as an indicator of the probability of clinical severity and, more importantly, as a need for reference to treatment.

Dizziness: the reduced version of the *Dizziness Handicap Inventory* (DHI) modified by Tesio et al.⁽²¹⁾ was used. The instrument comprises 12 questions with three possibilities of answers. Only questions 1 were used, 2, 5, 7, 9, 10 and 12, the first of which corresponds to the presence of vertigo, the 2nd is related to labyrinthopathy, the 5th and 7th had their results allocated together since they correspond to

postural hypotension, the 9th neurogenic syncope, the 10th to the convulsion and, finally, the 12th related to the presence of the Syndrome or Menière's Disease (DM) linked to hearing problems.

2.4 STATISTICAL ANALYSIS

The description of the sample and the estimates of prevalence of symptoms are obtained with descriptive statistical analysis through a cross-section table controlled by sociodemographic variables. In the case of the prevalence of depressive and anxiety disorders, the estimates were controlled using the variable of presence/absence of SEM (positive score for at least one of the four SEM analyzed).

Multivariate logistic regression model was used to study correlates of prevalence of depressive and anxiety disorders and their association by amount of SEM. The analyses of the correctors, which determined the odds ratio (RC) of the associations, were performed as follows: first, the presence of any depressive disorder and any anxiety disorder was added to examine the association with the presence of SEM; in the second model, the disorders, also separated by categories, were associated with the amount of symptoms; sociodemographic variables were used as control in both regressions.

The software used was the *SAS Enterprise Guide 5.1*. Statistical significance ($p < 0.05$) was examined using Pearson's χ^2 test, which included a 95% Confidence Interval (CI) of 95% in all analyses.

2.5 ETHICAL PROCEDURE

All individuals were interviewed only after signing the Term of Free and Informed Consent (TCLE). Full confidentiality of the data was guaranteed and the interviewers were prepared to provide information about mental health services available in the individual's area of residence if requested. The SPMHS was approved by the Ethics and Research Committee of the Hospital das Clínicas of the Faculty of Medicine of the University of São Paulo under protocol number 234/03 (on April 24, 2003).

3 FINDINGS

3.1 DESCRIPTIVE ANALYSES

The sample of 764 participants consists of 56.5% of women. Most adults were adults, 47% aged between 35 and 49 years and 46% between 0 and 8 years of schooling and 20% belonging to the low income stratum. Most individuals are married (64.4%), and more men than women reported having a company ($p = 0.014$) and more than 70% performing some work activity. (Tabela 01)

The prevalence of SEM by sociodemographic variables are presented in Tabela 2. Approximately half of the sample (50.3%; 35.7% of women and 14.5% of men) reported at least one of the four SEM surveyed, with the prevalence of the four SEM being higher in women. Fatigue was the most frequent symptom, with a prevalence of 30.4% in the total sample (22.9% women; 7.5% men) and 17.5% among married individuals. Secondly, dyspepsia (26.8%; 19.3% in women and 7.5% in men), more frequent in

individuals aged between 35 and 49 years (12%). Approximately 20% of the total sample presented the tinnitus symptom (19.6%; 15% in women and 4.5% in men), being more common among individuals in the two lowest income quartiles. When the subcategories of this symptom were evaluated, the female sample had a higher prevalence in three of the five subcategories described: labyrinthopathy (11.1%), postural hypotension (11.9%) and neurogenic syncope (2.2%) (data not shown in the table). Finally, almost 6% of the sample had Irritable Bowel Syndrome (ISS) or irritable colon, 4.5% of women and 1.3% of men.

Lifetime prevalence of depressive disorder was higher in subjects with SEM than in those who did not have SEM (28.4% vs 10.1%). The same happened in relation to anxiety disorders (27% in those with SEM vs. 13.3% in those without SEM). Major depression present in 25.9% of the sample, specific phobia (14.1%), social phobia (10%) and generalized anxiety disorder (9.4%) were the most frequent disorders in those who presented SEM. (Tabela 3)

3.2 ASSOCIATION ANALYSES

Table 4 exposes the association between SEM and CMD, controlled by socio-demographic variables estimated by means of probability ratios, obtained by logistic regression. Those with SEM were more likely to have some depressive disorder in life, with CR of 3.4 (95% CI, 2.4-4.8), and twice as likely to have some anxiety disorder in life (2.2; CI 95%, 1.5-3.0), compared to those who did not present SEM. Women (3.7; 95% CI, 2.5-5.5), young adults (1.9; CI 95%, 1.1-3.2) and with medium income is low day (2.1; 95% CI, 1.3-3.5) were those who were more likely to present at least one SEM, controlled by the other variables of the model.

Table 5 shows that there is a dose-response relationship between the number of SEM and the presence of depression and anxiety. The greater the amount of SEM, the higher the ratio of chance for concomitant presence with depressive disorders, ranging from 2.2 (95% CI, 1.5-3.4) for the presence of a symptom, to 6.9 (95% CI, 3.5-13.7) for the presence of 3 or 4 symptoms. Regarding the association with anxiety disorders, the reasons for chance range from 2.0 (95% CI, 1.3-2.9) to one symptom, reaching 3.2 (95% CI, 1.7-6.2), for individuals who have between 3 or 4 symptoms.

4 DISCUSSION

In this study conducted in adults living in Região Metropolitana in São Paulo, approximately 50% had at least one of the SEM surveyed, being the tinnitus the most common symptom. The four SEM surveyed were more common in women and young adults, when we controlled for the presence of depressive and anxious disorders and other socio-demographic variables. Moreover, we confirm that comorbidity with depressive and anxiety disorders is frequent in individuals with SEM, and the higher the number of SEM, the stronger the association.

Our findings corroborate previous studies. According to Coelho and Ávila⁽²²⁾, about 20 to 60% of patients with ISIs had the concomitant presence with depressive and anxiety disorders. This same

association is also described for the other symptoms emphasizing that the genesis of this comorbidity may be based on inflammatory processes, common both in somatoform conditions and in depressive-anxiety syndromes. ⁽²³⁾ The presence of SEM and anxious-depressive syndromes has already been described in Brazil common process, particularly in population contexts with social disadvantages.

The four SEM surveyed were three times more frequent in women compared to men, which is consistent with the literature, and specific hypotheses exist for this phenomenon. The higher prevalence of ISS in younger age groups and in women can be explained by hormonal cycle changes in fertile ages, and may be associated with a decreased sensory threshold for rectal distension. ⁽²⁴⁾ The hormonal hypothesis has also been suggested to explain the higher prevalence of dyspepsia in women: sex hormones would be involved in modulating the response to pain in women, besides affecting gastric mobility. ⁽¹²⁾ In relation to fatigue, the association with neuropsychological symptoms, such as impaired memory and concentration and depressive symptoms, establishes a highly disabling clinical picture. ⁽²⁵⁾ In addition to the hormonal and inflammatory hypothesis, social factors such as work activities with double/triple working hours, inside and outside the home, would relate overwork, stress, excessive concern to you, family members and others as a triggering factor for symptom manifestation in women. ⁽¹³⁾

The symptom dizziness, one of the SEM most closely associated with anxiety and depressive disorders is paradigmatic of the intersection between the physical and the mental, since it comes from biological and/or psychological causes. Chronic anxiety and dysthymia are part of the differential diagnosis, but they can also coexist. In addition, the use of antidepressant medication can give rise to feelings of dizziness and vertigo, as many of these medications cause orthostatic hypotension. ⁽²⁶⁾

It should be taken into account that, as already discussed by Kirmayer et al. ⁽⁷⁾, the symptomatic descriptive presentation of the patient to the professional directs to criteria for recognition of the disorders associated with them. In the study by Kroenke et al. ⁽⁶⁾ the symptomatic presentation of patients in PA was somatic, and the higher the number of physical symptoms, the greater the chance of being SEM, being often associated with depressive and anxiety disorders. For the author, the recognition of this association for the therapeutic approach is necessary, because these conditions are potentially treatable.

The intersection between the identification and diagnosis process was discussed with different approach perspectives. For example, Roca et al. ⁽⁸⁾ argue that in view of the overlap between SEM and CMT, the separation between the two entities should be reconsidered. Bombana et al. ⁽²⁷⁾ point to the need for increasingly integrated approaches, especially in the care of THE. Burton et al. ⁽²⁸⁾ propose that dysfunctional somatic syndromes, an umbrella term for various conditions characterized by persistent and problematic physical symptoms, should occupy a neutral place within the diagnostic classifications and subclassified by area, i.e., multisystemic, single system, or single symptom, thus promoting dual parenthood, such as, for example, in the case of irritable colon, belonging to both the classification of gastrointestinal disorders and functional somatic disorders.

The current classifications take into account the difficult conceptualization of these symptoms, because they are characterized by the absence of objective clinical signs. The diagnosis is based on subjective complaints, clinical history and differential diagnosis. Aspects such as the Committee for the Review of the International Classification of Diseases (ICD-11) to coin the term "Bodily Distress Disorder" to replace the concept related to SEM defined as one of the general syndromes characterized as due to concern and suffering regarding symptoms that cause excessive discomfort, and which may or may not be known. Four subtypes were included in this general syndrome: cardiovascular, gastrointestinal, musculoskeletal, and general symptoms/fatigue. ⁽²⁸⁾

We should consider the following strengths: 1) the sample of this study is composed of subjects from a sample of the general population - it is known that comorbidity is common in samples of subjects seeking services; 2) the clinical psychiatric evaluation was performed through a standardized interview, applied by trained psychiatrists and with years of clinical experience; 3) the subjects were evaluated in person by experienced general practitioners, who, although they used a self-report questionnaire, the presence of depression and SEM was clinically decided. In fact, a diagnostic interview conducted by trained physicians may better delimit individuals with clinically relevant disorders of individuals with SEM, because the use of self-report questionnaires can induce errors in classification of both false positives and false negatives.

The study has some limitations. The absence of biological markers and the impossibility of doing a detailed prospective investigation prevented us from obtaining more information about the somatization process. The perspective of the subject himself regarding the process of falling ill, because it is not susceptible to operationalization was not recorded. Only four SEM were surveyed and many others are probably prevalent in our population. ⁽²⁹⁾ Therefore, these cannot and should not be taken as unique, and further research describing other than these is necessary. Although the research subjects came from a sample of the general adult population of the Metropolitan Region of São Paulo, there was friction when the recruitment of the subsample to be clinically evaluated in the premises of the Hospital das Clínicas of the Faculty of Medicine of the University of São Paulo, with the possibility that those who agreed to be evaluated have higher physical and mental morbidity. Moreover, the findings of this research are not representative of the entire Brazilian adult population, being restricted to residents of the largest metropolis in the country. Regional differences are expected in a continental country like Brazil.

Despite the limitations, this study confirms the strong association between SEM and depressive and anxiety disorders in a sample of the general population with a description of prevalence and odds ratio. For authors such as Guo et al. ⁽³⁰⁾, this association hinders the diagnosis and therapeutic approach of these disorders that are persistent and disabling, with negative consequences, because although there is a common denominator, when classifying patients with diagnoses entitled nonspecific, are left aside

specificities of cadto SEM . It is necessary that, because of this complex and multifaceted etiology of SEM, a comprehensive approach is incorporated into therapy and treatment.

REFERENCES

- Creed F, Henningsen P, Fink P. Medically Unexplained Symptoms, Somatisation and Bodily Distress [Internet]. Creed F, Henningsen P, Fink P, organizadores. London: Cambridge University Press; 2011 [citado 5 de março de 2017]. 253 p. Available at: <https://books.google.com.br/books?hl=pt-BR&lr=&id=UQjdZrkyWkoC&oi=fnd&pg=PR5&dq=per+fink+medically+unexplained+symptoms&ots=R1-TbrW3bd&sig=7tK2HNqQqK158Ypap7hlZfvGyEg#v=onepage&q=per+fink+medically+unexplained+symptoms&f=false>
2. Bransfield RC, Friedman KJ. Differentiating Psychosomatic, Somatopsychic, Multisystem Illnesses and Medical Uncertainty. *Healthcare*. 2019;7(114):1–28.
 3. De Gucht V, Fischler B. Somatização: uma revisão crítica do conceito e questões metodológicas. *Psicossomática*. 2002;43:1–9.
 4. Burton C, Fink P, Henningsen P, Rief W. Desordens somáticas funcionais : artigo de discussão para uma nova classificação comum para pesquisa e uso clínico. 2020;1–8.
 5. Goldberg DP, Huxley P. Common mental disorders: a bio-social model. London: Tavistock/Routledge; 1992. 194 p.
 6. Kroenke K, Spitzer RL, Williams JBW, Linzer M, Hahn SR, Degruy F V., et al. Physical Symptoms in Primary Care: Predictors of Psychiatric Disorders and Functional Impairment. *Arch Fam Med*. 1994;
 7. Kirmayer LJ, Robbins JM, Dworkind M, Yaffe MJ. Somatization and the recognition of depression and anxiety in primary care. *Am J Psychiatry*. 1993;
 8. Roca M, Gili M, Garcia-Garcia M, Salva J, Vives M, Garcia Campayo J, et al. Prevalence and comorbidity of common mental disorders in primary care. *J Affect Disord*. 2009;
 9. Fortes S, Ziebold C, Reed GM, Robles-Garcia R, Campos MR, Reisdorfer E, et al. Studying ICD-11 primary health care bodily stress syndrome in Brazil: Do many functional disorders represent just one syndrome? *Rev Bras Psiquiatr*. 2019;41(1):15–21.
 10. Bombana JA, Leite ALSS, Miranda CT. Como atender aos que somatizam? Descrição de um programa e relatos concisos de casos. *Rev ista Bras Psiquiatr*. 2000;22(4):180–4.
 11. Catapani WR. Conceitos atuais em síndrome do intestino ir ritável irritável Current concepts in irritable bowel syndrome. 2004;29(1):19–21.
 12. Kim YS, Kim N. Functional dyspepsia: A narrative review with a focus on sex-gender differences. *J Neurogastroenterol Motil*. 2020;26(3):322–34.
 13. Mota DDC de F, Cruz D de ALM da, Pimenta CA de M. Fadiga: uma análise do conceito. *Acta Paul Enferm*. 2007;18(3):285–93.
 14. Handa PR, Kuhn AMB, Cunha F, Schaffleln R, Ganança FF. Qualidade de vida em pacientes com vertigem posicional paroxística benigna e/ou doença de Ménière. *Rev Bras Otorrinolaringol*. 2006;71(6):776–83.
 15. Andrade LH, Viana MC, Teixeira MG, Beraldi F, Bassani I de S. São Paulo Megacity Mental Health Survey – A population-based epidemiological study of psychiatric morbidity in the São Paulo Metropolitan

Area: aims , design and field implementation. *Revista Brasileira de Psiquiatria*. setembro de 2009;31(4):375–86.

16. First MB, Spitzer RL, Gibbon M, Williams JBW. Structured clinical interview for DSM-IV-TR Axis I disorders, research version, non- patient edition (SCID-I/NP). New York: Biometrics Research, New York State Psychiatric Institute. 2002;
17. Kessler RC, Üstün TB. The World Mental Health (WMH) Survey Initiative version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). *Int J Methods Psychiatr Res* [Internet]. 2004;13(2):93–121. Available at: <http://dx.doi.org/10.1002/mpr.168>
18. Moayyedi P, Duffett S, Braunholtz D, Mason S, Richards IDG, Dowell AC, et al. The Leeds dyspepsia questionnaire: A valid tool for measuring the presence and severity of dyspepsia. *Aliment Pharmacol Ther*. 1998;
19. Drossman DA, Corazziari E, Delvaux M, Spiller R, Talley NJ, Thompson WG, et al. Rome III: the functional gastrointestinal disorders. In: *Arq Gastroenterol*. 3^o ed Degnon Associates; 2006. p. 885–93.
20. Cella M, Chalder T. Measuring fatigue in clinical and community settings. *J Psychosom Res* [Internet]. 2010;69(1):17–22. Available at: <http://dx.doi.org/10.1016/j.jpsychores.2009.10.007>
21. Tesio L, Alpini D, Cesarani A, Perucca L. Short form of the dizziness handicap inventory: Construction and validation through Rasch analysis. *Am J Phys Med Rehabil*. 1999;78(3):233–41.
22. Coelho CL de S, Ávila LA. Controvérsias sobre a Somatização. *Revista de Psiquiatria Clínica*. abril de 2007;34(8):278–84.
23. Irwin MR. Inflammation at the intersection of behavior and somatic symptoms. *Psychiatr Clin North Am* [Internet]. 2011;34(3):605–20. Available at: <http://dx.doi.org/10.1016/j.psc.2011.05.005>
24. Ferreira AI, Garrido M, Castro-Poças F. Irritable Bowel Syndrome: News from an Old Disorder. *GE Port J Gastroenterol*. 2020;27(4):255–68.
25. Rivera CM, Mastronardi C, Silva-Aldana CT, Arcos-Burgos M, Lidbury BA. Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: A Comprehensive Review. *Diagnostics*. 2019;9(91):2–34.
26. Kim HA, Bisdorff A, Bronstein AM, Lempert, T. Rossi-Izquierdo M, Staab JP, Strupp, M. Kim J-S. Hemodynamic orthostatic dizziness/vertigo: Diagnostic criteria Consensus document of the Committee for the Classification of Vestibular Disorders of the Bárány Society. *J Vestib Res*. 2019;29:45–56.
27. Bombana JA. Sintomas somáticos inexplicados clinicamente: um campo impreciso entre a psiquiatria e a clínica médica. *J Bras Psiquiatr* [Internet]. 2006;55(011):308–12. Available at: <http://www.scielo.br/pdf/jbpsiq/v55n4/a07v55n4.pdf>
28. Burton C, Fink P, Henningsen P, Löwe B, Rief W. Functional somatic disorders: Discussion paper for a new common classification for research and clinical use. *BMC Med*. 2020;18(1):1–7.
29. Tófoli LF, Andrade LH, Fortes S. Somatização na América Latina: uma revisão sobre a classificação de transtornos somatoformes , síndromes funcionais e sintomas sem explicação médica. *Revista Brasileira de Psiquiatria*. maio de 2011;33:59–69.
30. Guo D, Kleinstäuber M, Johnson MH, Sundram F. Evaluating commonalities across medically

unexplained symptoms. *Int J Environ Res Public Health*. 2019;16(5).

Tabela 1 - Perfil sociodemográfico da amostra por sexo: São Paulo Megacity - Fase Hospitalar N=764

	Feminino (%)	Masculino (%)	Total	p
	N= 432	N= 332	N= 764	
	56,5	43,4	100	
Idade				
18 - 34	32,4	30,4	31,5	0.0066
35 - 49	46,7	46,9	46,8	
50 - 64	20,8	22,5	21,6	
Educação				
0-4 anos	18,2	15,6	17,1	0.2872
5-8 anos	28,7	30,1	29,3	
9-11 anos	34,0	37,3	35,4	
12+ anos	18,9	16,8	18,0	
Renda				
Baixa	23,6	15,0	19,9	0.0061
Média Baixa	26,1	28,0	26,9	
Média Alta	23,8	27,1	25,2	
Alta	26,3	29,8	27,8	
Estado Civil				
Casado(a)	56,7	74,4	64,4	0.0135
Casado(a) anteriormente; Viúvo(a); Divorciado(a)	21,3	8,7	15,8	
Solteiro(a) (nunca casou)	21,9	16,8	19,7	
Ocupação				
Trabalhador(a); Estudante	59,2	87,9	71,7	0.6321
Do lar	24,3	0,3	13,8	
Aposentado(a); Outros	16,4	11,7	14,4	

Fonte: Pesquisa São Paulo Megacity, realizada na Região Metropolitana de São Paulo - 2005 a 2007

Tabela 2 - Prevalência de Sintoma sem Explicação Médica (SEM) por variáveis sociodemográficas: São Paulo Megacity - Fase Hospitalar N=764

	Qualquer SEM*		Cólon Irritável	p	Dispesia	p	Fadiga	p	Tontura	p
	Sexo									
Feminino	35,7	4,5	0.0031	19,3	0.0001	22,9	0.0001	15,0	0.0001	
Masculino	14,5	1,3		7,5		7,5		4,5		
Idade										
18 - 34	18,4	1,9		10,4		10,0		6,5		
35 - 49	22,2	2,7	0.9487	12,0	0.0148	14,2	0.7574	9,4	0.6116	
50 - 64	9,5	1,1		4,4		6,1		3,6		
Educação										
0-4 anos	9,5	0,9		5,3		6,2		3,6		
5-8 anos	14,5	1,3	0.6534	8,2	0.3960	8,5	0.4176	6,6	0.2539	
9-11 anos	16,4	2,3		8,3		10,3		6,6		
12+ anos	9,6	1,3		4,9		5,3		2,6		
Renda										
Baixa	11,2	0,9		6,1		7,5		5,1		
Média Baixa	15,4	1,8	0.8446	8,2	0.0558	8,6	0.0712	6,8	0.0025	
Média Alta	11,5	1,5		6,9		6,6		3,8		
Alta	12,0	1,5		5,6		7,5		3,9		
Estado Civil										
Casado(a)	29,8	3,6		16,3		17,5		11,5		
Casado(a) anteriormente; Viúvo(a); Divorciado(a)	8,9	0,5	0.1731	4,0	0.1640	6,2	0.0180	3,9	0.1993	
Solteiro(a) (nunca casou)	11,5	1,7		6,5		6,6		4,1		
Ocupação										
Trabalhador(a); Estudante	35,9	4,5		18,7		22,2		13,2		
Do lar	7,4	1,0	0.1314	4,4	0.4412	4,4	0.5820	3,4	0.3287	
Aposentado(a); Outros	6,8	0,2		3,8		3,8		3,0		

Fonte: Pesquisa São Paulo Megacity, realizada na Região Metropolitana de São Paulo - 2005 a 2007

* Sintoma sem Explicação Médica

Tabela 3 - Prevalência de transtornos depressivos e ansiosos por presença/ausência de Sintoma sem Explicação Médica (SEM): São Paulo Megacity - Fase Hospitalar N=764

	Sem SEM*	Com SEM*	Total	<i>p</i>
Transtornos Depressivos	10,1	28,4	39,1	0.0001
Depressão Maior	9	25,9	34,9	0.0001
Depressão Menor	1,7	2,3	4	0.3750
Transtorno Depressivo Persistente (Distímia)	0,1	3,1	3,2	0.0001
Transtornos Ansiosos	13,3	27	40,3	0.0001
Agorafobia	1,9	6,6	8,6	0.0001
Fobia Específica	6,1	14,1	20,2	0.0001
Fobia Social	7,3	10	17,4	0.0527
Transtorno de Ansiedade Generalizada (TAG)	2,3	9,4	11,7	0.0001
Transtorno do Pânico	1,4	5,2	6,6	0.0001

Fonte: Pesquisa São Paulo Megacity, realizada na Região Metropolitana de São Paulo - 2005 a 2007

*Sintoma sem Explicação Médica

Tabela 4 - Razão de chances da associação de Sintoma sem Explicação Médica (SEM) com transtorno depressivos e ansiosos na vida. Regressão logística multivariável, controlada por variáveis sociodemográficas da amostra total: São Paulo Megacity - Fase Hospitalar N=764

	RC (95% IC)	<i>p</i>
Tipo de Transtorno		
Depressivo	3,4 (2,4-4,8)	0.0001
Ansioso	2,2 (1,5-3,0)	0.0001
Sexo		
Feminino	3,7 (2,5-5,5)	0.0001
Masculino	1,0	-
Idade		
18 - 34	1,9 (1,1-3,2)	0.0200
35 - 49	1,0 (0,7-1,6)	0.8251
50 - 64	1,0	-
Educação		
0-4 anos	1,0	-
5-8 anos	0,7 (0,4-1,2)	0.2683
9-11 anos	0,5 (0,3-0,9)	0.0276
12+ anos	0,8 (0,4-1,6)	0.6036
Renda		
Baixa	1,6 (0,9-2,8)	0.0779
Média Baixa	2,1 (1,3-3,5)	0.0021
Média Alta	1,1 (0,7-1,8)	0.6148
Alta	1,0	-
Estado Civil		
Casado(a)	1,3 (0,8-2,1)	0.2260
Casado(a) anteriormente; Viúvo(a); Divorciado(a)	1,0	-
Solteiro(a) (nunca casou)	1,4 (0,8-2,6)	0.2509
Ocupação		
Trabalhador(a); Estudante	1,5 (0,9-2,5)	0.1073
Do lar	0,7 (0,4-1,4)	0.3905
Aposentado(a); Outros	1,0	-

Fonte: Pesquisa São Paulo Megacity, realizada na Região Metropolitana de São Paulo - 2005 a 2007

Tabela 5 - Associação do número de Sintomas sem Explicação Médica (SEM) com transtornos depressivos e ansiosos. Regressão logística multivariável controlada por variáveis sociodemográficas: São Paulo Megacity - Fase Hospitalar N=764

	Quantidade de sintomas					
	1		2		3 e/ou 4	
	RC (95% IC)	p	RC (95% IC)	p	RC (95% IC)	p
Tipo de Transtorno						
Depressivo	2,2 (1,5-3,4)	0.0001	5,7 (3,5-9,3)	0.0001	6,9 (3,5-13,7)	0.0001
Ansioso	2,0 (1,3-2,9)	0.0006	2,4 (1,5-3,9)	0.0002	3,2 (1,7-6,2)	0.0002
Sexo						
Feminino	2,7 (1,8-4,0)	0.0001	4,4 (2,6-7,6)	0.0001	7,3 (3,2-16,7)	0.0001
Masculino	1,0	-	1,0	-	1,0	-
Idade						
18 - 34	2,0 (1,1-3,7)	0.0189	1,5 (0,7-3,1)	0.2705	2,6 (0,8-8,0)	0.0933
35 - 49	1,0 (0,6-1,6)	0.9432	1,0 (0,5-1,8)	0.9918	2,2 (0,8-6,0)	0.1285
50 - 64	1,0	-	1,0	-	1,0	-
Educação						
0-4 anos	1,0	-	1,0	-	1,0	-
5-8 anos	0,7 (0,4-1,2)	0.2375	0,8 (0,4-1,6)	0.5802	0,9 (0,3-2,3)	0.8214
9-11 anos	0,6 (0,3-1,0)	0.0879	0,4 (0,2-0,9)	0.0219	0,8 (0,3-2,2)	0.7286
12+ anos	1,1 (0,5-2,3)	0.7275	0,5 (0,2-1,2)	0.1398	0,6 (0,2-2,2)	0.4660
Renda						
Baixa	1,7 (0,9-3,1)	0.0915	1,3 (0,6-2,6)	0.5282	2,7 (1,0-7,4)	0.0511
Média Baixa	2,3 (1,3-4,0)	0.0034	1,7 (0,9-3,4)	0.1166	2,5 (0,9-6,5)	0.0680
Média Alta	1,1 (0,6-1,9)	0.6710	1,1 (0,6-2,1)	0.7857	1,2 (0,5-3,3)	0.6605
Alta	1,0	-	1,0	-	1,0	-
Estado Civil						
Casado(a)	1,2 (0,7-2,1)	0.4383	1,2 (0,6-2,3)	0.5198	1,8 (0,7-4,3)	0.2078
Casado(a) anteriormente; Viúvo(a); Divorciado(a)	1,0	-	1,0	-	1,0	-
Solteiro(a) (nunca casou)	1,1 (0,6-2,2)	0.7038	1,5 (0,7-3,4)	0.3003	2,3 (0,8-6,8)	0.1290
Ocupação						
Trabalhador(a); Estudante	1,4 (0,8-2,4)	0.2653	1,5 (0,8-3,0)	0.2303	2,4 (0,9-6,5)	0.0940
Do lar	0,6 (0,3-1,4)	0.2510	0,8 (0,3-1,9)	0.6438	1,2 (0,4-4,1)	0.7339
Aposentado(a); Outros	1,0	-	1,0	-	1,0	-

Fonte: Pesquisa São Paulo Megacity, realizada na Região Metropolitana de São Paulo - 2005 a 2007

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