RELATIONSHIP BETWEEN METABOLIC SYNDROME AND PARKINSON DISEASE PRODROMAL SYMPTOMS

RELAÇÃO ENTRE A SÍNDROME METABÓLICA E OS SINTOMAS PRODRÔMICOS DA SOENÇA DE PARKINSON

Ana Patrícia da Silva Souza
e-mail: patricia-asb@hotmail.com
Mariluce Rodrigues Marques Silva
Ana Beatriz Januário da Silva
Karollainy Gomes da Silva
Matheus Santos de Sousa Fernandes
Sandra Lopes de Souza
Waleska Maria Almeida Barros
Programa de Pós-graduação em Neuropsiquiatria e Ciências do Comportamento, Centro de Ciências da Saúde, Universidade Federal de Pernambuco, Recife - PE

Viviane de Oliveira Nogueira Souza
Núcleo de Nutrição, Centro Acadêmico de Vitória (CAV), Universidade Federal de Pernambuco
Vitória de Santo Antão - PE

Paulo Roberto Leite de Arruda
Taciane Silva do Carmo
Maria Eduarda Rodrigues Alves dos Santos
Roberta Karlize Pereira Silva
José Maurício Lucas da Silva
Mayara Luclécia da Silva
Centro Integrado de Tecnologias em Neurociência (CITENC), Centro Universitário FACOL - UNIFACOL
Vitória de Santo Antão - PE

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ABSTRACT

There is evidence that mechanisms involved in the systemic metabolic dysfunction that occur in Metabolic Syndrome (MS) and obesity, such as oxidative stress, inflammation caused by inadequate protein deposition, and changes in lipid pathways, have common elements with Parkinson's Disease (PD). The objective of this study was to investigate the frequency of MS in adult patients at basic health units in the city of Vitória de Santo Antão-PE, and relate it to possible symptoms experienced in the prodromal period of PD. This is a cross-sectional study, in which sociodemographic and blood data were collected to analyze the serum levels of fasting glucose, triglycerides, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol. The Epworth Sleepiness Scale, Patient Health Questionnaire-9, and the Montreal Cognitive Assessment were applied. In addition to performing anthropometry and measuring systemic blood pressure. A total of 179 individuals were evaluated, 78.8 % female, with a mean age of 49.64 (±6.0) years. For the allocation of groups with and without MS, a sample of 89 volunteers with a mean age of 48.6 years (±5.8) was obtained, among which 71.7 % were obese. The frequency of MS among those evaluated was 51.7 % and there was a relationship between its components and prodromal symptoms of PD, such as excessive daytime sleepiness and mild cognitive impairment, both in individuals with MS and in those without the syndrome.

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Keywords: Metabolic Syndrome; Parkinson's Disease; Prodromal Symptoms; Daytime Sleepiness; Depression.

RESUMO

Há evidências de que os mecanismos envolvidos na disfunção metabólica sistêmica que ocorrem na Síndrome Metabólica (SM) e na obesidade, como o estresse oxidativo, a inflamação causada por depósito inadequado de proteínas e alterações nas vias lipídicas, possuem elementos em comum com a Doença de Parkinson (DP). O objetivo deste estudo foi investigar a frequência de SM em pacientes adultos nas unidades básicas de saúde do município de Vitória de Santo Antão-PE e relacioná-la a possíveis sintomas experimentados no período prodrômico da DP. Trata-se de um estudo transversal, no qual foram coletados dados sociodemográficos e sanguíneos para análise dos níveis séricos de glicose em jejum, triglicerídeos, colesterol de lipoproteína de alta densidade e colesterol de lipoproteína de baixa densidade. Foram aplicadas a Escala de Sonolência de Epworth, o Questionário de Saúde do Paciente-9 e a Avaliação Cognitiva de Montreal. Além disso, foram realizadas medidas antropométricas e da pressão arterial sistêmica. Ao todo, 179 indivíduos foram avaliados, sendo 78,8 % do sexo feminino, com média de idade de 49,64 (±6,0) anos. Para a alocação dos grupos com e sem SM, foi obtida uma amostra de 89 voluntários com média de idade de 48,6 anos (±5,8), dos quais 71,7 % eram obesos. A frequência de SM entre os avaliados foi de 51,7 %, havendo relação entre seus componentes e sintomas prodrômicos da DP, como sonolência diurna excessiva e comprometimento cognitivo leve, tanto em indivíduos com SM quanto naqueles sem a síndrome.

Palavras-chave: Sindrome Metabólica; Doença de Parkinson; Sintomas Prodrômicos; Sonolência Diurna; Depressão.

1 INTRODUCTION

Metabolic Syndrome (MS) consists of a set of metabolic changes comprised of abdominal obesity, insulin resistance or impaired glucose metabolism, lipid disorders and hypertension [1]. There is a marked variation in prevalence around the world, between 8 % and 67 % [1,2] and generally equates to the prevalence of obesity. Such variation is based on age, race/ethnicity, sex and diagnostic criteria [3].

There is evidence that mechanisms involved in the systemic metabolic dysfunction that occur in MS and obesity, such as oxidative stress, inflammation caused by inadequate protein deposition, and changes in lipid pathways, have common elements with Parkinson's Disease (PD) [4–6] . In this conception, recent cohort and systematic review studies investigated the influence of MS on PD [7–9] and concluded that MS can be a risk factor for the disease.

In PD there are not only motor dysfunctions, but there is also the relevant presence of non-motor symptoms (NMS) such as sleep disturbances, depression, and cognitive deficit [10,11]. These symptoms can appear up to 20 years before the motor manifestations, progress with the disease and the prevalence varies among patients [12].

The identification of this prodromal phase of PD enables an early diagnosis and thus increases the chances of a treatment that delays or prevents the onset of the classic motor symptoms of the disease [13,14]. From this perspective, it is known that there is no specific NMS for PD, but the presence of several of these, together with biochemical studies and/or additional images, can help in anticipating the diagnosis to identify the individual in the prodromal period of the disease [15].

There is still little evidence in the literature highlighting that the presence of MS can facilitate the development of PD. Thus, it is relevant to investigate the prevalence of MS, as well as to relate it to the presence of symptoms that are experienced by individuals in the prodromal period of PD in the adult population, aged between 40 and 59 years. As these symptoms can occur up to 20 years before a clinical diagnosis [16]. Such investigations aim to develop educational and preventive intervention strategies for a population that is eventually more likely to develop neurodegenerative processes.

2 Meterial and Methods

2.1 Study Population

A cross-sectional study was carried out, including adult individuals of both sexes, aged between 40 and 59 years and 11 months, residing in the municipality of Vitória de Santo Antão, Pernambuco, Brazil and registered in basic health units in the urban area. Individuals with neurological or psychiatric disorders, those diagnosed with PD and pregnant women were excluded from the study.

2.2 Clinical Information Collection

The collection started on February 3rd and concluded on October 25th, 2021. According to data provided by the municipal health department in September 2020, in the urban area there were a total of 27 units, among which 20 were visited.

To understand aspects of income, housing and general health status, researchers applied a sociodemographic questionnaire with information about personal data, housing and income, general health status, lifestyle habits and anthropometric data.

For the diagnosis of metabolic syndrome, the International Diabetes Federation (IDF) Guideline was used, which establishes the following criteria: presence of abdominal obesity, verified by WC above: 94 cm for males and 80 cm for females; along with the presence of 2 or more of the following components: levels ≥ 100 mg / dl or diagnosed diabetes; Triglycerides (TG): ≥ 150 mg / dl or on medication; high-density lipoprotein cholesterol (HDL-C) levels <40 mg/dl in males and <50 mg/dl in females or in treatment; Systolic blood pressure (SBP): ≥ 130 mmHg or Dystolic blood pressure (DBP): ≥ 85 mmHg or under treatment.

Blood collection was performed on individuals for subsequent analysis of fasting serum glucose, TG, HDL-C and low-density lipoprotein cholesterol (LDL-C) levels. All exams were requested by a primary care physician, appointed by the municipal health department. The analyzes were carried out in Laboratories associated with the Municipal Health Department. After receiving the results of the exams, the individuals were instructed to make an appointment for a medical appointment.

To assess body composition, height was measured using 2 flexible and inextensible Merita® measuring tapes (glued to the wall). The barefoot volunteer leaned against the wall, and the highest point on the skull was used as a reference to mark the measurement. Weight was checked with a G-Tech® portable digital electronic scale (with a total capacity of 150 kg), the individual was instructed to climb barefoot, maintain the anatomical position and breathe normally. Waist circumference was used to diagnose abdominal fat accumulation. It was measured at the midpoint between the last rib and the iliac crest with a measuring tape, with no clothes on the waist (when possible). The subject remained with arms bent and crossed in front of the chest, feet apart, keeping the abdomen relaxed. The inspiration and release of air from the lungs were requested, remaining so until the measurement was taken. The values considered were: for Low accumulation, value less than 80 for females and lower than 94 for males; High accumulation values between 94 and 102 for males, between 80 and 88 for females; Very high values above 102 and 88 for males and females respectively.

Body mass index (BMI) was calculated by dividing weight (kg) by height (m) squared. The definition of overweight and obesity was defined according to the criteria of the World Health Organization [17], in which a BMI ≥ 18.5 to 24.9 is considered eutrophic; overweight a BMI ≥ 25 and obesity a BMI ≥ 30.

Systolic and diastolic blood pressure was checked with a Premium® brand tensiometer and sphygmomanometer with the patient in a sitting position, bladder empty, after 5 minutes of rest. In the present study, self-reported hypertension was considered, as well as the individual with normal or high blood pressure levels, who reported using antihypertensive drugs. After each measurement, the instrument was disinfected with 70 % alcohol rubbing.

To identify the presence of EDS, the Epworth sleepiness scale adapted and validated for use in Brazil was used [18] , which is comprised of 8 questions, with the possibility of the individual napping in different situations. Scored on a scale of zero to three, and a score above 10 indicates an SDE. After explaining the objective and response options, the scale was filled out by the volunteer, who could be guided again when requested. The pen used by the individual was disinfected with 70 % alcohol after use.

To verify symptoms suggestive of depression, the Patient Health Questionnaire9 (PHQ-9). This instrument is ideal for use in epidemiological studies, it can be applied as an interview (in this study, this modality was chosen, taking into account the possible low educational level of the population). It has 9 questions that assess the frequency of symptoms in the two weeks prior to application. It consists of a scale ranging from zero (never) to three (almost every day). It is validated for the general adult population in Brazil [19]. Its use as a continuous scale proved to be more useful in tracking, privileging the sensitivity of identifying those in need of care. It indicates individuals at higher risk of having a major depressive episode with a cutoff point ≥ 9.

To assess global cognitive function, the Brazilian version of the Montreal Cognitive Assessment - Montreal Cognitive Assessment (Moca-BR) - a cognitive assessment instrument to detect mild cognitive impairment was used [20]. The instrument contains 11 subtests that assess attention, executive functions, memory, language, visual-constructive skills and orientation. Adapted for use in Brazil, it is used to identify the risk of dementia, differentiating it from age-related cognitive impairment [21]. Originally the maximum Moca score was 30, and a value ≤ 25 indicates mild cognitive impairment [20]; for individuals with 12 years of schooling or less, one point should be added to the total. However, in the present study, the cutoff point suggested by a recent Brazilian study was used, with scores below 21 for elderly people with more than 12 years of schooling; and less than 20 for elderly people with education between 4 and 12 years, after the sum of 1 point in the investigation of impairment of cognition [22]. MOCA has been shown to be a reliable tool in predicting cognitive decline in early PD [23,24]. A neuropsychologist trained the team to apply the instrument, as well as performed the subsequent interpretation of the collected data.

2.3 Data Analysis

Statistical analyzes were performed using the GraphPad Prism 9® program (GraphPad Software, Inc., La Jolla, CA, USA). Attendance results were stratified by age, sex, individual monthly income, education level, marital status and self-reported pathologies. The MS diagnoses were analyzed, as well as the symptoms potentially related to the PD prodromal period. All results are displayed in the form of tables. The normal distribution of data was analyzed using the Kolmogorov Smirnov test. Comparison between groups (with and without MS) was performed using the Mann Whitney test. Correlations using the Pearson test for parametric data and Spearman for non-parametric data. For the analysis of frequency distribution, Pearson's chi-square test was applied with a significance level < 5 %.

3 Results

A total of 179 individuals were evaluated, among which the majority 141 (78.8 %) were female, with a mean age of 49.64 (±6.0) years. Of the total of those evaluated, 84 (46.9 %) claim to have an income that varies between half and a minimum wage, and 50 (27.9%) with an income less than half the minimum wage. Among the 39 (21.8 %) people who completed high school, 11 (6.1 %) have completed higher education (Table 1).

About the general health status, 90 (50.3%) reported being chronically ill, and with a diagnosis of anxiety disorder, 51 (28.5%) people reported having it. Relatives with PD only 11 (6.1%) people claimed to have it. Among female individuals, 74 (52.5%) are in menopause (Table 2).

The classification according to the BMI showed that the majority (44.4 %) of the volunteers are obese (Table 3).

Regarding the frequency of MS, many volunteers did not attend the blood collection, which was carried out in the week following the application of the other research procedures. Thus, it was possible to obtain the results of laboratory tests on 78 individuals. In addition, 11 diagnoses were closed without blood tests, as these volunteers had the 3 necessary components, according to the IDF guideline. Thus, a sample of 89 volunteers with a mean age of 48.6 years (±5.8) was obtained.

The mean age was 49.9 years (±5.9) in the MS group, and 47.3 years (±5.5) in the group without MS. It was found that elevated WC was the most frequent component, followed by an increase in SBP in both groups (Table 4).

Table 1. Sociodemographic data of volunteers

Variables	n	Relative Fr (%)
Sex		
Feminine	141	78.8
Masculine	38	21.2
Age group		
40 to 49 years old	90	50.3
50 to 59 yeras old	89	49.7
Color/race		
White	49	27.4
Black	16	8.9
Brunette	70	39.1
Brown	39	21.8
Didn't know	5	2.8
Marital status		
Single	55	30.7
Married or have a partner	92	51.4
Separate	14	7.8
Widower	18	10.1
Education		
No instruction	26	14.5
Elementay	82	45.8
Incomplete high school	18	10.1
Full medium	39	21.8
Incomplete higher	9	1.7
Graduated	11	6.1
Home		
Own	114	63.7
Leased	45	25.1
Assigned	19	10.6
Financed	1	0.6
Other	0	0
Employment status		
Employee	57	31.8
Unemployed	117	65.4
Pensioner or benefit	5	2.8
Income		
≤0.5 minimum wage	50	27.9
>0.5 and ≤1.0	84	46.9
>1.0 and ≤ 1.5	38	21.2
>1.5 and ≤2.0	5	2.8
>2,0	0	0
Did not answer	2	1.1

The frequency of some of the symptoms experienced by individuals who are in the prodromal period of PD was verified. Due to the level of education (less than four years or illiterate), some individuals (18) were excluded from daytime sleepiness and cognition assessments. Thus, in the MS group, 41 people completed the scale, and 30 individuals did so in the group without MS. In the interview to investigate the risk of depression, one volunteer refused to be evaluated. (Table 5).

Table 2. General health status of the evaluated

Feature	Yes n (Fr)	No n (Fr)
Drug use	109 (60.9%)	70 (39.1%)
Any chronic disease	90 (50.3%)	89 (49.7%)
Anxiety Disorder Diagnosis	51 (28.5%)	128 (71.5%)
Feels dizzy when getting up fast	67 (37.4%)	112 (62.6%)
Difficulty to urinate	17 (9.5%)	162 (90.5%)
Difficulty to evacuate	26 (14.5%)	153 (85.5%)
Relative with Parkinson's Disease	11 (6.1%)	168 (93.9%)
Practice physical activity	58 (32.4%)	121 (67.6%)
Smoker	Current smoker	17 (9.5%)
	Former smoker	44 (24.6%)
	Never smoked	118 (65.9%)
Alcohol consumption	Stopped drinking	40 (22.3%)
	Never drank	93 (51.9%)
	Once a month	41 (22.9%)
	Up to 3 times a week	5 (2.8%)

Table 3. Overweight or obesity according to BMI.

Classification BMI (Kg/m2)	Total individuals n=178	Fr (%)
Low weight	1	0.5
Eutrophic	45	25.3
Overweight	53	29.8
Obesity	79	44.4

Eutrophic the BMI ≥ 18.5 to 24.9; overweight a BMI ≥ 25, and obesity a BMI ≥ 30.

Table 4. Frequency of components for diagnosis between SM and non-SM Groups

Variable	MS (n 46) n (Fr)	Without MS (n 43) n (Fr)
Wigh WC (cm)	45 (97.8%)	27 (62.8%)
Hypertensive or taking antihypertensive	30 (65.2%)	10 (23.2%)
SBP: ≥ 130 mmHg	37 (80.4%)	11 (25.5%)
DBP: ≥ 85 mmHg	27 (58.7%)	8 (18.6%)
Diabetic or taking antiglycemic	17 (37%)	0
Blood glucose: levels ≥ 100 mg / dL	19 (41.3%)	2 (4.65%)
TG: ≥ 150 mg / dL or taking medicine	23 (50%)	9 (20.4%)
HDL-C levels <40 mg / dL in males and <50 mg / dL in female or in treatment	21 (45.6%)	5 (11.6%)

WC- waist circumference; SBP- systolic blood pressure; DBP – diastolic blood pressure; TG- Triglycerides; HDL- high density cholesterol

With regard to the correlations between the prodromal symptoms of PD and MS, significant correlations were found: between the scores of daytime sleepiness and triglycerides in the group without MS (n=28, r= 0.39, p=0.048); between cognitive assessment scores and DBP in the group without MS (n=30, r=0.47, p=0.017); and WC in the group without MS (n=30, r=-0.4, p=0.033); and glucose in groups MS n=32/ (r= 0.43, p= 0.019) and without MS (n=30, r=0.39, p= 0.037). There was no correlation between depression risk scores and MS components (Table 6).

4 Discussion

The objective of this research was to investigate the frequency of MS in adult patients registered in basic health units in the city of Vitória de Santo Antão-PE, and relate it to possible symptoms experienced in the prodromal period of PD. A total sample (179 volunteers) was evaluated, with a mean age of 49.64 (±6.0) years, mostly female, with a monthly income between half and a minimum wage, incomplete primary education, unemployed, with obesity and who reports not performing physical activity.

A considerable part of this sample did not attend the laboratory collection, and it was not possible to rule out or confirm the presence of MS in the total evaluated, however, the presence of predictors for the development of the syndrome was observed. In accordance with a Brazilian study that evaluated 942 participants, with a mean age of 59.8 (± 19.7), and found that older age, female sex, higher BMI and lower education independently increased the chance of the occurrence of the MS [25]. These results reaffirm the relevance of investigating the presence of MS in this population.

In the present study, it was found in the sample through which the closed diagnosis was obtained (89 volunteers), a frequency of 51.7 % of MS, in individuals with a mean age of 48.6 years (±5.8). This is a high frequency when compared to the prevalence of studies in other countries, such as Burkina Faso, an African country 10.9 % [26] or in Taiwan 6,23 % [27]. The difference between countries is probably due to cultural, nutritional, social and economic differences. However, the results of this research are similar to the prevalence of other studies carried out with adults in Brazil: 43 %, 47.5 % [25,28]. This outcome may be due to the fact that most of the sample is female, which has a higher prevalence than men [25,28]. Furthermore, socioeconomic characteristics and lifestyle habits such as physical inactivity, reported by those evaluated, represent predictors for MS. Furthermore, there are different criteria for diagnosis adopted by research. Different cutoff points can result in different prevalences in the same sample [29].

Table 5. Description of age groups, level of daytime sleepiness, symptoms suggestive of depression and cognitive function in the MS and without MS groups

Variables	MS n (Fr%)	Group average (SD)	Without MS n (Fr%)	Group average (SD)
Ages (n 89)				
40 to 49	23 (25.8%)	49.96 (±5.9)	28 (31.5%)	47.33 (±5.5)
50 to 59	23 (25.8%)		15 (16.9%)	
Day sleeping (n 71)		Scores		Scores
Normal	30 (42.3%)		22 (30.9%)	
EDS	11 (15.5%)	7.9 (±5.6)	8 (11.3%)	6.9 (±4.5)
PHQ-9 (risk of depression) (n 88)				
No risk	27 (30.7%)		33 (37.5%)	
Presence of Risk	18 (20.4%)	8.5 (±6.0)	10 (11.4%)	6.3 (±6.2)
MoCA (n 71)				
Normal Cognition	20 (28.2%)		12 (16.9%)	
Mild cognitive impairmen	21 (29.6%)	19.6 (±4.6)	18 (25.3%)	19.3 (±38)

EDS- Excessive day sleeping; PHQ9- Patient Health Questionnaire 9; MoCA- Montreal Cognitive Assessment

Table 6. Correlations between PD prodromal symptoms and MS components in the two groups.

Variables	MS n (Fr%)	Metabolic syndrome		No Metabolic syndrome	
	Component of Metabolic Syndrome	***r***	***p***	***r***	***p***
Epworth (Somnolence)	HDL	- 0.18	0.329	0.08	0.641
	Triglycerides	- 0.07	0.696	**0.39**	**0.048**
	Systolic Blood Pressure	0.04	0.795	- 0.00	0.972
	Diastolic Blood Pressure	- 0.00	0.991	- 0.06	0.724
	Waist Circumference	0.01	0.914	- 0.00	0.979
	Glucose	- 0.01	0.948	- 0.16	0.369
		r	***p***	***r***	***p***
Moca (Cognition)	HDL	- 0.02	0.883	0.07	0.675
	Triglycerides	0.07	0.674	0.04	0.829
	Systolic Blood Pressure	- 0.00	0.989	0.04	0.829
	Diastolic Blood Pressure	- 0.01	0.913	**- 0.47**	**0.017**
	Waist Circumference	- 0.11	0.534	**- 0.41**	**0.033**
	Glucose	**0.43**	**0.019**	**0.39**	**0.037**
		r	***p***	***r***	***p***
PHQ9 (Depression)	HDL	- 0.04	0.819	- 0.32	0.094
	Triglycerides	- 0.02	0.894	0.12	0.495
	Systolic Blood Pressure	0.01	0.944	- 0.06	0.739
	Diastolic Blood Pressure	0.19	0.302	0.00	0.999
	Waist Circumference	0.08	0.644	0.30	0.097
	Glucose	0.02	0.912	- 0.16	0.369

Correlations performed with the Pearson Test: Epworth-WMS x HDL; WMS x TG; WMS x Glucose; WMS x WC. MOCA-WMS x HDL; MS x HDL; WMS x TG; WMS x Glucose; MS x WC. The other correlations were performed using Spearman's test.
Caption: MS- Metabolic syndrome group; WMS- Group without metabolic syndrome

The individual components for the diagnosis were quantified, and considering the IDF criteria, the measure of elevated WC was identified as the most frequent component. Both in the MS group (97.8 %) and in the group without the syndrome (62.8 %). Similarly, a Brazilian survey of individuals with an average age of 45.6 years highlighted that among 8,854 people, elevated WC was also the most prevalent component [30]. The guideline used in this study, the IDF has high WC as a mandatory component, thus verifying a considerable part of the sample without the syndrome, presenting at least one criterion for diagnosis.

Regarding the classification of BMI, 71.7% of the volunteers in the MS group were obese. In this perspective, a study conducted by Brazilian researchers verified the prevalence of MS in adults, with a mean age close to that of the present study, 51.2 years (± 8.9). A sample of 12.313 people was evaluated, and it was found that the prevalence among eutrophic, overweight and obese was 13 %, 43.2 % and 60. 7% respectively [31], showing the trend that the prevalence of MS may be higher according to the BMI categories. In the present research, it was not possible to calculate the prevalence of MS in a representative sample to verify this propensity related to body mass, but it was

found that the frequency of obese patients with MS was accentuated.

With regard to hypertension, in the present study, it was the second most prevalent component in both groups. In a cohort carried out with 171,060 individuals divided into SM and non-SM groups, followed up on average for 7.23 years, with 819 incident cases of PD [8], it was found that hypertension was a component that increased the incidence of PD by 1.34-fold. Thus, the need for intervention for the prevention and treatment of MS and its components in the evaluated population is emphasized, with the objective of reducing the incidence of PD or other neurodegenerative diseases such as Alzheimer's.

Next, the relationship between the metabolic syndrome and the symptoms experienced by an individual who is in the prodromal period of Parkinson's disease will be discussed.

There was a correlation between the components of MS and the scores of daytime sleepiness and cognitive assessment, both in the MS group and in the group without MS. This outcome demonstrates that the presence of 1 or 2 components can already contribute to the association with the symptoms mentioned, since in the group without the syndrome the relationship was also identified. As verified in a cohort research with 17,163,560 individuals, aged over 40 years, allocated in groups with and without MS, followed for 5.3 years. Each component was positively associated with the risk for PD, however, in the MS group the risk was higher [32].

Regarding the relationship between MS components and daytime sleepiness scores, a positive correlation was found between sleepiness and triglycerides in the group without MS. Therefore, the higher the level of triglycerides, the greater the drowsiness presented. A study comprising 538 patients with obstructive sleep apnea (OSA), mean age 42.64 (± 10.23) who underwent physical examinations and blood biochemistry tests, also found a significant association between the two variables. People with high sleepiness scores, as assessed by the Epworth scale, and higher TG levels were at high risk for mixed sleep apnea events [33].

It is known that sleep disorders such as OSA can result in MS [34], as well as sleep deprivation can be a causative factor for obesity and DM2 [35]. Thus, the elevation of triglycerides is related to the risk of cardiovascular events, as well as being related to aspects related to sleep. Such evidence highlights the relevance of evaluating the quality of sleep of those individuals who did not have MS.

However, with regard to the risk for PD, in a cohort study carried out with 85,530 pairs with and without MS, followed for 7.23 years, a protective effect of hypertriglyceridemia for the incidence of PD was found, especially in men[8].

Regarding the presence of symptoms suggestive of depression in the sample, there was no correlation with MS, and the percentage of people at risk of developing depression was not high, but among the MS group, some other risk factors for PD were identified with high frequency, such as obesity (71.7 %) and physical inactivity (71.7 %). These data suggest that the adequate management of the population's emotional and physical health can collaborate to reduce the risk of developing PD.

Depression can also act on cognitive function, as well as cognitive decline can be a prodromal symptom of PD. When investigating the relationship between cognitive assessment and MS components between groups, a negative correlation was obtained with DBP in the group without MS, that is, worse MOCA scores had higher DBP. It has been observed that high blood pressure during middle age is a 1.19 to 1.55 times higher risk for cognitive impairment [36] and this may be related to structural changes in specific regions of the brain over the course of life [37].

Such evidence was proven in a study with 128 elderly people, divided into 2 groups, hypertensive and non-hypertensive, and among the instruments for assessing general cognitive function, the MOCA was used. Biochemical indicators of basal blood (total protein, fasting plasma glucose, HDL, LDL, cholesterol and triglycerides) and basal magnetic resonance data of the hippocampus and amygdala volume and thickness of the polar cortex were also examined. As an outcome, hypertensive individuals had worse general cognitive and executive function, and the authors believe that the mechanism may be related to the effect of hypertension on greater cortical thickness of the right temporal pole, affecting cognition [38].

These results emphasize the need for better blood pressure control, in addition to health education for this population, about the importance of regular medical appointments, for example, since reducing blood pressure with medications was associated by a recent meta-analysis with 14 trials randomized clinical trials at a lower risk for dementia or cognitive impairment [39].

A negative correlation was also found between cognitive performance and WC in the group without MS, that is, for the worst scores, WC was higher. This group had a mean score in the MOCA of 19.3 (±3.8) approximated to the MS group. A result that agrees with the literature, as an increase in WC can be considered a risk factor for dementia. As verified in a survey carried out with 297 individuals with DM2, mean

age 56.8 (±6.9). To assess cognition, the Clinical Assessment of Dementia, the Mini Mental State Examination and the MOCA were used. Anthropometric and biochemical analyzes were performed and it was found that cognitive impairment was common in these individuals. WC and diabetic retinopathy were evidenced as risk factors for dementia [40].

This relationship can be explained by the fact that dementias and DM2 share pathophysiological mechanisms such as oxidative stress, irregular enzyme activity, amyloidosis, endothelial dysfunction, resistance and insulin deficiency in the brain and the individual's genetics [41]. On the other hand, in the present study, a positive correlation was found between cognitive assessment and glucose levels in both groups. An outcome in disagreement with the literature, as high fasting glucose is associated with an increased risk of MCI [42]. Elevated glucose also demonstrates a relationship with a higher incidence of PD [8].

MCI may be the initial stage of dementia, and is defined as a noticeable and measurable decline in the assessment of cognitive performance, but one that does not harm daily life [43]. Hyperglycemia aggravates this cognitive impairment [44], however, studies are carried out with mean age and larger samples. Furthermore, in the current study only one measure of cognitive function was performed, which also depends on the individual's willingness to correctly perform the tasks proposed by the examiner. Such factors can contribute to the disagreement of the results.

When considering impairment to cognition as one of Parkinson's prodromes, a cohort study with 1,629 people related MCI with prodromal PD [45]. Lower cognitive performance was associated with prodromes such as daytime sleepiness, depression, urinary dysfunction, constipation and subliminal parkinsonism. The authors suggested that physicians carry out an early cognitive assessment of their patients.

However, another cohort research followed 3,777 volunteers, and observed in the 43 individuals who developed PD, preserved cognitive functions. There was also a decline in psychomotor speed in the two years before diagnosis, in addition to depressive symptoms 12 years before [46].

Therefore, it appears that the analysis of this variable requires a study with follow-up over time, and if possible with larger samples than the current study. Furthermore, early and routine assessment, with the identification and adequate intervention for patients with MCI, can contribute to reduce or delay the onset of dementia.

Some difficulties were encountered in carrying out the collection, as it started during a coronavirus pandemic period (February 2021). Thus, it was difficult to obtain patients in the units to carry out the research, both because of the fear of possible infection on the part of the population, and because of the reduced number of patients in the units. Furthermore, many volunteers did not attend the blood collection, even after exhaustive telephone contacts with the aim of rescheduling.

It is noteworthy that the research team valued the safety of everyone, following the rules imposed by the health authorities. In periods of stricter restrictions, collection was suspended and resumed after the established deadline. The entire team involved was vaccinated.

4 CONCLUSION

The frequency of MS is high among those evaluated and there is a relationship between its components and prodromal symptoms of PD, such as excessive daytime sleepiness and mild cognitive impairment, both in individuals with MS and without the syndrome. Such conditions are compatible with the literature, confirming the importance of implementing prevention and treatment strategies not only for MS, but also for its individual components. These, in addition to representing a cardiovascular risk factor, when added to the prodromal symptoms, can signal the beginning of a neurodegenerative disease.

DECLARATIONS

-The authors did not receive support from any organization for the submitted work. -The authors have no relevant financial or non-financial interests to disclose.

-This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Federal University of Pernambuco (Date. October 22, 2020 /37085720.2.0000.5208).

- Informed consent was obtained from all individual participants included in the study.

AUTHOR'S CONTRIBUTIONS

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [Ana Patrícia da Silva Souza], [Viviane de Oliveira Nogueira],[Paulo Roberto Leite de Arruda] [Taciane Silva do Carmo] [Maria Eduarda Rodrigues Alves dos Santos], [Mariluce Rodrigues Marques Silva], [Ana Beatriz Januário da Silva], [Karollainy Gomes da Silva], [Matheus Santos de Sousa Fernandes], [Roberta Karlize Pereira Silva], [José Maurício Lucas da Silva], [Mayara Luclécia da Silva],

[Sandra Lopes de Souza] and [Waleska Maria Almeida Barros]. The first draft of the manuscript was written by [Ana Patrícia da Silva Souza and Waleska Maria Almeida Barros] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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