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PRESENTATION

Knowledge is the foundation for transformation and progress in any field of study, especially when it comes to health and well-being. The pursuit of new perspectives, combined with critical reflection on practices and strategies, is essential for professionals, teachers, and students who seek to enhance their expertise and make a positive impact on society.

Health Promotion Studies brings together reflections and approaches that foster a deeper understanding of fundamental topics for those dedicated to the study and practice of health promotion. More than just a collection of content, this book serves as an invitation to continuous learning, constructive questioning, and the development of innovative solutions.

May this reading inspire new ideas, broaden horizons, and strengthen the commitment to building a healthier and more balanced future for all.

SUMMARY

CHAPTER 1

CLINICAL, EPIDEMIOLOGICAL PROFILE AND QUALITY OF LIFE OF CLIMACTERIC ASSOCIATED WITH OSTEOPOROSIS: A DESCRIPTIVE STUDY

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ABSTRACT: Climacteric is a biological process associated with symptoms that reduce well-being and a clinical picture compatible with important hormonal changes. Concomitantly, there is a decline in bone stiffness with posterior bone tissue fragility and a predisposition to fracture due to adjacent osteoporosis. Thus, this is a cross-sectional, exploratory and descriptive study designed to descriptively assess symptoms of menopause associated with osteoporosis, as well as the quality of life of these patients. This population was assisted at the Women's Health Reference Center located in the municipality of Boa Vista, in the state of Roraima. The present study found a loss in quality of life, in which 32% reported being very dissatisfied/dissatisfied with their health status. In addition, they mentioned the fact that physical pain causes a functional hindrance in relation to activities of daily living, with 38% being very dissatisfied/dissatisfied. In relation to the aforementioned scenario, it appears that the quality of life and health of the individual must be treated in this group of patients.

KEYWORDS: climacteric, menopause, osteoporosis and quality of life.

RESUMO: O climatério é um processo biológico associado a sintomas que reduzem o bem-estar e quadro clínico compatível com alterações hormonais importantes. Concomitante a isso há um declínio da rigidez óssea com posterior fragilidade do tecido ósseo e predisposição a fraturas devido à osteoporose adjacente. Assim, trata-se de um estudo transversal, exploratório e descritivo desenhado para avaliar do ponto de vista descritivo sintomas do climatério associada à osteoporose, bem como a qualidade de vida desses pacientes. Essa população foi atendida no Centro de Referência da Saúde da Mulher que se encontra localizado no município de Boa Vista,

no estado de Roraima. O presente trabalho verificou prejuízo na qualidade de vida, no qual 32% relataram estarem muito insatisfeita/insatisfeita com o estado de saúde. Além disso, fizeram menção ao fato de a dor física causar um empecilho funcional em relação às atividades de vida diária, com 38% de muito insatisfeita/insatisfeita. Em relação ao cenário citado, verifica-se que a qualidade de vida e a saúde do indivíduo deve ser tratada nesse grupo de pacientes.

PALAVRAS-CHAVE: climatério, menopausa, osteoporose e qualidade de vida.

1. INTRODUCTION

Osteoporosis is a disease that has a strong relationship with the advancement of age, currently recognized as an important public health issue. Postmenopausal women represent a risk group due to rapid bone loss caused by reduced ovarian estrogen production, presenting an annual bone loss rate of 3 to 5% for 5 to 10 years (WHO, 2003).

Lack of estrogen affects all bone cells directly by regulating cell differentiation, activity, and apoptosis or indirectly through altered expression of estrogen-responsive target genes. The result is a resorption exceeding formation, leading to bone degeneration characterized by reduced Bone Mineral Density (BMD) and altered bone structure by thinning and increased cortex porosity and decreased trabeculae connectivity. As a consequence, the structure becomes more fragile in these patients, increasing the probability of fractures occurring, a characteristic feature of what is defined as postmenopausal osteoporosis (FONTES; ARAÚJO; SOARES, 2012).

Prevention of osteoporosis can usually be achieved by different mechanisms. For example, minimize bone loss related to menopause and age. In addition to measures affecting BMD, care to avoid fractures while reducing the risk of falls should be followed. Very restrictive nutritional interventions should be avoided, regular physical activity, moderation of alcohol intake, prevention of falls and smoking cessation are important in preventing osteoporosis and osteoporotic fractures (Ibid).

Currently, the incidence of osteoporosis has been increasing due to the greater longevity achieved by the female population worldwide, affecting up to 70% of women over 80 years of age (WHO, 2003). The earlier the diagnosis is made and possible treatment and care interventions start, the lower the chances of possible fractures.

The present study aimed to determine sociodemographic, clinical and epidemiological aspects of the urogenital syndrome of the climacteric in patients of the Women's Health Reference Center by means of two standardized questionnaires. (WHO, 2003), (ZERBINI, Cristiano Augusto de Freitas, 2019) and (Kanis JA et al., 2008).

2. METHOD

The methodology seeks to follow the instructions of Strengthening the Reporting of Observational Studies in Epidemiology - STROBE.

2.1 DESIGN OF THE STUDY

This is a cross-sectional, exploratory and descriptive study designed to evaluate the urogenital syndrome of the climacteric associated with osteoporosis, as well as the quality of life of these patients. This population was attended to at the Women's Health Reference Center that is located in the municipality of Boa Vista, in the state of Roraima. This study was conducted from February to December 2021 and was approved with the Ethics Review Submission Certificate 30541220.4.0000.5302 and Number of Opinion: 4.054.328.

2.2 SAMPLE SIZE

The sample used in this study was of convenience, corresponding to 36 patients.

2.3 SEARCH PROCEDURES

Each week, it was verified whether there were in the system of the secretariat of the Women's Health Reference Center elective consultations scheduled for patients with urogenital syndrome of the climacteric, the treatment of which occurred five times a week (Monday to Friday) in the sector of medical specialty of gynecology and obstetrics. On the day of the visit, after a completed medical consultation, the patient was invited to participate in the research after clarifying the objetives and methods. After she accepted, she was taken to a private room. And after signing the informed consent form, a face-to-face questionnaire was answered to determine the prevalence of urogenital syndrome of the climacteric, for a period of 30 minutes.

The research instrument was three questionnaires that evaluated sociodemographic and clinical data (Annex A), quality of life (WHO) and osteoporosis

(Frax scale). The patient's secrecy and confidentiality were strictly maintained. Both questionnaires were not published by name.

Annex A seeks to fill in sociodemographic data and clinical variables of the patient, being termed "Sociodemographic Data and Clinical Comorbidities". This consists of 40 questions. The purpose of this Annex is to address sociodemographic data and clinical comorbidities (diseases associated with the clinical picture of urogenital climacteric syndrome).

2.4 INCLUSION AND EXCLUSION CRITERIA

The inclusion criteria included patients with urogenital syndrome of climacteric that are more than 40 years old (adults) of the female sex, who are not indigenous, of different socioeconomic levels, with cognitive capacity to answer the questionnaire and who agreed to participate in the study.

The exclusion criteria were those under 40 years of age, indigenous people, foreigners and those who did not understand or did not wish to participate in the survey.

2.5 RISKS AND BENEFITS

The present study followed strictly the guidelines established by Resolution 466/12 of the National Health Council (CNS). One sees as risks for this research bad memories when remembering about his illness, embarrassment in the act of the interview and loss of confidentiality of the data. And the benefits consist in knowing better the epidemiological panorama of patients with the urogenital syndrome of the climacteric and thus to have an overview of the real situation, since the evaluation of the urogenital complaints of these patients can help the taking of public health measures whose actions increase the quality of life of these patients.

3. RESULTS

In the evaluation of the sociodemographic data of the 50 participants, the mean age of 50.9 years was identified, where the majority corresponded to the age group of

40 to 50 years (52%), followed by 38% with the age of 50 to 60 years and 10% from 60 to 70 years.

In relation to the breed, it was observed a higher percentage of whites and mulattoes and equivalence between the two with 26% of each. There was no significant difference between black and yellow, since both corresponded to 24%. In relation to marital status, 38% reported being unmarried, followed by 26% married, 16% divorced, 16% stable and 4% widowed.

The naturalness of the majority of the interviewees was of the state of Roraima (36%), followed by Maranhão (26%), Amazonas (10%), Ceará (6%), Paraná and Piauí (4% each) followed by the states of Rio Grande do Sul, Minas Gerais, Pará, Mato Grosso and Rio Grande do Norte, all corresponding to 2%. As for schooling, 50% reported having completed high school, 16% reported incomplete elementary school, 12% complete higher education and in equal proportion illiterate, postgraduate and with incomplete high school with 4% of each, and in a smaller proportion, incomplete higher with 2% of those interviewed.

In relation to per capita income, 40% of women responded that they receive from 1 to 2 minimum wages. The number of people who have an income below a minimum wage and income of 3 to 4 wages was identical, with 20% of both, and similarly 18% of women have an income of 2 to 3 minimum wages.

The World Health Organization (WHO) Quality of Life Assessment tool was applied, the epidemiological data course is summarized in table 1.

Table 1. World Health Organization (WHO) Quality of Life Assessment questionnaire

1. How would you evaluate your quality of life? There were reports of very good/good, neither bad nor good and bad/very bad, corresponding to 77.8%, 13.9% and 8.3% respectively.
2. How satisfied are you with your health? 41.7% of respondents responded very satisfied/satisfied, 22.2% neither satisfied nor dissatisfied, and 36.1% very dissatisfied/dissatisfied.
3. To what extent do you think your physical pain prevents you from doing what you need? 38.9% of the interviewees answered nothing/very little, 25% more or less and 36.1% quite/extremely.
4. How much do you need some treatment to take your daily life? 22.2% of the interviewees answered nothing/very little, 11.1% more or less and 66.7% quite/extremely.
5. How much do you enjoy life? 8.4% of the interviewees answered nothing/very little, 33.3% more or less and 58.3% quite/extremely
6. To what extent do you think your life has meaning? 2.8% of the interviewees answered nothing/very little, 13.9% more or less and 83.3% quite/extremely.
7. How much can you concentrate? 8.4% of the interviewees answered nothing/very little, 38.9% more or less and 52.8% quite/extremely.
8. How safe do you feel in your daily life? 5.6% of the interviewees answered nothing/very little, 22.2% more or less and 72.2% quite/extremely.
9. How healthy is your physical environment (climate, noise, pollution, attractiveness)? 2.8% of the interviewees answered nothing/very little, 19.4% more or less and 77.8% quite/extremely.

10. Do you have enough energy for your day-to-day life? 63.9% of respondents responded very/completely, 25% average and 11.1% nothing/very little
11. Are you able to accept your physical appearance? 61.1% of respondents responded very/completely, 33.3% average and 5.6% nothing/very little.
12. Do you have enough money to meet your needs? 30.6% of respondents responded very/completely, 38.9% average and 30.6% nothing/very little.
13. How available are the information you need in your day-to-day life? 58.4% of respondents responded very/completely, 30.6% average and 11.1% nothing/very little.
14. To what extent do you have leisure activity opportunities? 55.5% of respondents responded very/completely, 27.8% average and 16.7 nothing/very little.
15. How well are you able to get around? 80.6% of respondents responded very/completely, 13.9% average and 5.6% nothing/very little.
16. How satisfied are you with your sleep? 55.6% of respondents responded good/satisfied very good/very satisfied, 27.8% neither bad nor good/neither satisfied nor dissatisfied, and 16.7% very bad/very dissatisfied bad/dissatisfied.
17. How satisfied are you with your ability to perform day-to-day activities? 66.7% of respondents responded good/satisfied very good/very satisfied, 22.2% neither bad nor good/neither satisfied nor dissatisfied, and 11.1% very bad/very dissatisfied bad/dissatisfied.
18. How satisfied are you with your ability to work? 66.6% of respondents responded good/satisfied very good/very satisfied, 16.7% neither bad nor good/neither satisfied nor dissatisfied, and 16.7% very bad/very dissatisfied poor/dissatisfied.
19. How satisfied are you with yourself? 68.6% of respondents responded good/satisfied very good/very satisfied, 22.9% neither bad nor good/neither satisfied nor dissatisfied, and 8.6% very bad/very dissatisfied bad/dissatisfied.
20. How satisfied are you with your personal relationships? 80.6% of respondents responded good/satisfied very good/very satisfied, 16.7% neither bad nor good/neither satisfied nor dissatisfied, and 2.8% very bad/very dissatisfied bad/dissatisfied.
21. How satisfied are you with your sex life? 55.5% of respondents responded good/satisfied very good/very satisfied, 16.7% neither bad nor good/neither satisfied nor dissatisfied, and 27.8% very bad/very dissatisfied bad/dissatisfied.
22. How satisfied are you with the support you receive from your friends? 75% of respondents responded good/satisfied very good/very satisfied, 19.4% neither bad nor good/neither satisfied nor dissatisfied, and 5.6% very bad/very dissatisfied poor/dissatisfied.
23. How satisfied are you with the conditions of the place where you live? 91.7% of respondents responded good/satisfied very good/very satisfied, 5.6% neither bad nor good/neither satisfied nor dissatisfied, and 2.8% very bad/very dissatisfied bad/dissatisfied.
24. How satisfied are you with your access to health services? 33.4% of respondents responded good/satisfied very good/very satisfied, 33.3% neither bad nor good/neither satisfied nor dissatisfied, and 33.4% very bad/very dissatisfied poor/dissatisfied.
25. How satisfied are you with your means of transport? 61.1% of respondents responded good/satisfied very good/very satisfied, 19.4% neither bad nor good/neither satisfied nor dissatisfied, and 19.5% very bad/very dissatisfied poor/dissatisfied.
26. How often do you have negative feelings such as: bad mood, despair, anxiety and depression? 19.5% of respondents responded always/very frequently, 22.2% frequently and 58.3% never/sometimes.

Source: Organização Mundial da Saúde – OMS. Prevenção e gestão da osteoporose: relatório de um grupo científico da OMS. Grupo Científico sobre Prevenção, Gestão da Osteoporose, Organização Mundial da Saúde, 2003.

The application of the Fracture Risk Assessment Tool (FRA) scale was used, for which the epidemiological data are summarized in Table 2.

Table 2. Fracture Risk Assessment Tool - Adapted

01. Age?	≤45 years, 14.4% of respondents; 46-50 years, 31.4% of respondents; 51-55 years, 34.4% of respondents and ≥ 56 years, 20.3% of respondents	
02. Gender?	100% Female	
	YES	NO
03. Have you fractured any bones recently?	8.3% of respondents responded	91.7% of respondents responded
04. Does anyone in your family, a first-degree relative, have a history of osteoporosis?	47.2% of respondents responded	52.8% of respondents responded
05. Does anyone in your family, a first-degree relative, have a history of a femur fracture?	8.3% of respondents responded	91.7% of respondents responded
06. Are you a smoker/smoker?	11.1% of respondents responded	88.9% of respondents responded
07. Do you currently use corticosteroids?	8.3% of respondents responded	91.7% of respondents responded
08. Are you a carrier of Rheumatoid Arthritis?	2.8% of respondents responded	97.2% of respondents responded
09. Are you a carrier of Secondary Osteoporosis, that is, Osteoporosis due to some underlying disease?	11.1% of respondents responded	88.9% of respondents responded
10. Do you use alcohol?	25% of respondents responded	75% of respondents responded

Source: Kanis JA, Johnell O, Oden A, Johansson H, McCloskey E. FRAX e a avaliação da probabilidade de fratura em homens e mulheres do Reino Unido. Osteoporosis Int. 2008; v. 19, n.4. p. 385-397.

4. DISCUSSIONS

Bone is a complex and adaptable tissue with specific functions in mobility, protection of vital organs and emergency availability of calcium, so they grow in specific size, shape and structure. There are two main types of bones - spongy and cortical. Calcium stored in spongy bone is essential to catalyze cardiac, nerve, brain, and muscle functions. Dense external cortical bone of limbs and others is required for structure and strength (BOSE; ROY; BANDYOPADHYAY, 2014; DEMPSTER; LIAN; GOLDRING, 2006).

Bone tissue is renewed through bone remodeling, which is a process in which osteoclasts and osteoblasts work sequentially with the stages of: activation when osteoclasts are recruited; reabsorption when osteoclasts reabsorb bone; reverse stage, in which osteoclasts undergo apoptosis and osteoblasts are recruited; formation phase,

in which osteoblasts establish a new organic bone matrix that subsequently mineralizes sequentially in the same bone remodeling unit (CASIMIRO; SAM; BRADY, 2019).

After reaching peak bone mass, bone remodeling is balanced and bone mass remains stable for one or two decades until age-related bone loss begins, in this phase there is an increase in resorptive activity and reduction in bone formation (DEMPSTER and LINDSAY, 1993). Healthy bone tissue is defined by a well mineralized and strong skeleton that characterizes bone mineral density (BMD).

Thus, more physical activity, less sedentary time, more calcium and vitamin D3 intake, and avoidance of intense dietary restrictions are variables that are associated with higher BMD peaks, in addition to genetics and age at menarche. There is growing evidence that combined hormonal contraception (CHC) use during adolescence and young adulthood may interfere with the ideal peak of BMD accumulation, perhaps suppressing the required bone turnover (SOURCES; ARAÚJO; SOARES, 2012).

Estradiol (E2, 'female hormone') is an essential hormone for the development of BMD in adolescence and physiologic levels prevent rapid bone resorption that causes increased BMD loss in adults. However, the decrease in E2 levels triggers bone resorption/loss. Progesterone (P4) is the physiological partner of E2, collaborating with E2 in all cells and tissues; its role in bone tissue is to increase slow P4 receptor-mediated osteoblastic bone formation. When menstrual cycles are normal and usually ovulatory, E2 and P4 are balanced and BMD is stable (KRASSAS and PAPADOPOULOU, 2001; MANOLAGAS, 2000).

Thus, women in the climacteric and post-menopausal phases represent a risk group to develop osteoporosis, since alterations in the production of sex hormones are initiated and these are essential for the formation and maintenance of healthy bone structure.

The climacteric and menopause are constantly terms that can be confused, but it is worth pointing out that the former refers to a relatively indefinite period, being variable for each woman, while the second is considered a physiological phenomenon with absence of activity of the ovarian follicles followed by the progressive fall of the secretion of estradiol, culminating with the definitive interruption of menstrual cycles (BRASIL, 2008; VIEIRA et al., 2007).

The depletion of the follicular reserve with the consequent loss of follicular maturation is the most important physiological element during climacteric, which is

accompanied by changes in the hormonal pattern of women, which includes increase of gonadotrophins (FSH and LH), with decrease in estradiol and practically absence of progesterone (BOTELL, 2013). The diagnosis of climacteric can be made by the clinical picture, since confirmation of the diagnosis requires laboratory tests to check the levels of follicle stimulating hormone, luteinizing hormone, which are high, and estradiol, which is decreased.

The deleterious skeletal effect of loss of ovarian function at menopause has been known for a long time, followed by massive bone loss. Sex hormones are essential for optimal skeletal development and maintenance of healthy bone remodeling during adult life (BILEZIKIAN, 2002; MELTON III et al., 1997).

The presence or absence of sex hormones reflects in bone mass, since it has already been described that hormonal deficiency leads to progressive bone loss (MELTON III et al., 1999). A good example is the high rate of osteoporosis in postmenopausal women, which is the result of a state of estrogen deficiency associated with unbalanced bone remodeling, with a high proportion of bone resorption in relation to bone formation and which can be in parts reversed or softened by estrogen replacement (GENNARI et al., 2002).

Estrogen acts through estrogen receptor (ERα) binding and activation. ERα in osteoblasts and osteoclasts mediates the protective effects of estrogen in cortical and spongy bones, respectively. Thus, estrogen deficiency, in addition to directly increasing bone resorption, can result in a negative calcium balance due to impaired absorption of calcium from the intestine and increased renal excretion of this ion (ALMEIDA et al., 2012). Therefore, the absence of this hormone regulates the bone balance in a negative way, favoring the development of osteoporosis.

The decline in bone health is one of the major concerns of menopausal women. Osteoporosis can be defined as a systemic skeletal disorder characterized by increased bone fragility due to deterioration of bone tissue and low bone mass and favoring susceptibility to fracture (PINTO NETO et al., 2002). The most frequent osteoporotic fractures are hip, wrist, and spine.

Osteoporosis increases the risk of fractures that occur most frequently in the spine, hip, and wrist in postmenopausal women with osteoporosis and can lead to long-term disability (MANOLAGAS; O'BRIEN.; ALMEIDA, 2013; VAN STAA et al., 2001). Although there are minimal changes in BMD during climacteric, BMD decreases

markedly during menopause. Annual rates of bone loss after are estimated to be 1.8 to 2.3% in the spine and 1.0 to 1.4% in the hip (FINKELSTEIN et al., 2008).

Osteoporosis is defined based on the assessment of bone mineral density (BMD). According to WHO criteria, osteoporosis is defined as a BMD that is 2.5 standard deviations or lower than the mean value for young healthy women and (T-score < -2.5 SD) (HERNLUND et al., 2013; WHO, 2004). The most widely validated technique for measuring BMD is dual-energy X-ray absorptiometry (DXA), and diagnostic criteria based on BMD T-score are a recommended entry criteria for the development of pharmaceutical interventions in osteoporosis (SOURCES; ARAÚJO; SOARES, 2012; KANIS, 2002).

Climacteric is a biological process and, although not a disease, is usually associated with several symptoms that reduce well-being and demonstrate a discomfort presenting physical disturbances including heat waves, night sweats, sleep problems, emotional and cognitive symptoms, irritability, anxiety, pruritus and vaginal dryness and urinary symptoms culminating in permanent discontinuation of menstruation and loss of reproductive capacity and the development of osteoporosis (BRAZIL, 2008; VIEIRA et al., 2007).

It is assumed that the quality of life of patients with urogenital climacteric syndrome is affected due to the lack of public policy actions in this population. In this sense, early diagnosis is of extreme importance for initial interventions to avoid fractures (BRASIL, 2008; VIEIRA et al., 2007).

In the present study, in spite of being a descriptive study, patients over 40 years of age with climacteric symptoms presented impairment in quality of life, in which 36.1% reported being very dissatisfied/dissatisfied with the state of health. In addition, they mentioned that physical pain causes a functional impairment in relation to daily life activities, with 36.1% quite/extremely, in this regard.

In relation to the above scenario, it can be seen that the quality of life and the state of health of the patient can have an important impact on daily life activities from a functional point of view. In addition, the fragility of bone tissue with subsequent concomitant clinical picture of osteoporosis should be addressed due to hormonal changes inherent to climacteric.

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CHAPTER 2

PREVALENCE OF THALASSEMIAS AND VARIANT HEMOGLOBINS IN PATIENTS WITH NON-FERTOGENIC ANEMIA

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ABSTRACT: Hereditary anemias, especially thalassemias and variant hemoglobins (Hb), are the most common human genetic alterations; their frequency in the Brazilian population varies greatly, depending on the racial groups that make up each region. Considering that these peoples have genes for abnormal hemoglobins with varying frequencies, it is to be expected that these genetic alterations will be found in our population. The aim of this study was to assess the prevalence of thalassemias and variant hemoglobins. Hereditary anemias, particularly variant hemoglobins and thalassemias, are genetic alterations of hemoglobin resulting from the production of structurally abnormal molecules or from deficient synthesis of normal alpha or beta globin. They are the most common genetic alterations in human populations.

KEYWORDS: thalassemias, hemoglobins, heredity, anemia.

RESUMO: As anemias hereditárias, em especial as talassemias e hemoglobinas (Hb) variantes, são as mais comuns das alterações genéticas humanas; sua frequência na população brasileira é muito variável, dependendo dos grupos raciais formadores de cada região. Considerando que esses povos apresentam genes para as hemoglobinas anormais com freqüências variadas, é esperado que se encontrem essas alterações

genéticas na nossa população. O objetivo deste trabalho foi avaliar a prevalência de talassemias e hemoglobinas variante. As anemias hereditárias, notadamente as hemoglobinas variantes e talassemias, são alterações genéticas da hemoglobina decorrentes da produção de moléculas estruturalmente anormais ou pelas sínteses deficientes de globina alfa ou beta normal. São as alterações genéticas mais frequentes nas populações humanas.

PALAVRAS-CHAVE: talassemias, hemoglobinas, hereditariedade, anemia.

1. INTRODUCTION

Hereditary anemias are among the most common genetic diseases and comprise a group of conditions of variable complexity. In the past, its geographical distribution covered only tropical and subtropical areas of the world, whose explanation is based on the protective effect that sickle-cell and thalassemic heterozygotes had against endemic infections caused by malaria parasites. Due to the increase of migratory movements in several regions, with consequent miscegenation, these variants eventually diffuse in areas previously considered non-endemic, such as in the American Continent and in Northern Europe.

Currently, more than 1,100 mutations involving the genes of the globin chains have been described. In general, hereditary anemia due to hemoglobin defect can be divided into two major groups: (1) hemoglobinopathies, which are characterized by the presence of structurally abnormal hemoglobins, such as hemoglobin S (Hb S), which in the homozygous state is responsible for sickle cell anemia, and (2) thalassemias, characterized by deficient synthesis of one or more polypeptide chains (globins) of normal human hemoglobins. Especially with reference to thalassemias, they can be classified into alpha (a) and beta (b), involving the a and b globin genes, respectively. Alpha-thalassemias are due to partial or complete deficiency of globin a synthesis in the RBCs of affected individuals. The globin chains a are necessary for the synthesis of hemoglobins present in the fetal phase and in the adult phase, playing an important role in maintaining the stability of these hemoglobin molecules. Thus, the defects that interfere with its synthesis have clinical repercussion in both phases, different from the b chains, which are present only in the major adult hemoglobin component, hemoglobin A (Hb A).

2. DEVELOPMENT

In the fetus, deficiency of globins a produces an excess of gamma chains (g), and after 6 months of life, the excess is due to globin b, which becomes free. These free chains form tetramers called Hb Bart's (g4) and Hb H (b4). The pathophysiology of alpha thalassemia is conditioned precisely by the formation of these tetramers, which are unstable and thermolabile.

Alpha thalassemias are mainly due to inherited defects in the expression of the genes encoding globins, affecting one to four of these genes, although synthesis defects can also oc|cur in an acquired form. For this reason, it is possible to classify alpha thalassemias into four categories, according to the level of expression of the a genes: (1) an asymptomatic or silent carrier form, with loss of a single gene (-a / aa); (2) the alpha thalassemic trait, in which there is loss of two alpha genes of a single chromosome (-- / aa) or of a gene a of both chromosomes (-a /-a); (3) hemoglobin H disease, in which only one alpha gene is functional (--/- a) and (4) fetal hydrops, characterized by the absence of the four alpha genes (-/-). Due to the wide variety of possible genetic interactions, generated by processes of deletion, non-deletion and variant hemoglobins, among others, an overlap between the above groups may occur, making their characterization difficult.

The anemia present in alpha thalassemias is due to decreased survival time of RBCs that contain inclusion bodies and are therefore removed by splenic microvasculature. In addition, due to the defect in the synthesis of normal amounts of hemoglobin, erythrocytes are microcytic and hypochromic. These data are of clinical relevance, since these hematological changes are then interpreted as indicators of iron deficiency or characteristics of anemia of chronic diseases.

The Brazilian population is characterized by a great genetic heterogeneity and a significant and progressive level of miscegenation. The distribution of hemoglobinopathies and thalassemias is related to the various racial groups that participated in the formation of the Brazilian population. The IBGE establishes five options for color or race in our population: white, black, yellow, brown and Indian. The data from the 2000 census show the classification of the Brazilian population according to this variable.

Individuals of black or brown color represent 45% of the Brazilian population in the studied group, we identified the presence of 36.8% of cases and 19.1% of controls classified in these categories.

In addition, iron deficiency and anemia of chronic diseases, causes of microcytosis, were excluded through laboratory tests and medical consultations. The frequency of alpha thalassemia among the controls may suggest that they are only silent carriers, since they do not present hematological changes. Our results are

consistent with the observation that many carriers of deletions that reach a single gene have these indices at normal levels.

When we analyze the results obtained by Daudt in 2002 (0.12% of Hb Bart's in newborns at HCPA), we find that this value is much lower than that found in this study. This low rate is justified by the technique used, since the samples were collected on filter paper and were processed, on average, 22 days after collection, which possibly impairs the identification of hemoglobins with faster mobility than Hb A.

With the techniques used in this work, a large number of patients with non-ferropenic microcytic anemia to be clarified can be diagnosed as having some type of hereditary anemia, highlighting alpha and beta thalassemias. The main advantage of the correct identification of these individuals is to avoid unnecessary and deleterious administration of iron, in addition to laboratory tests and medical consultations. However, the presence of patients without anemia, with normal hematimetric indices, classified as silent carriers of alpha thalassemia, stands out.

Although the techniques applied in this study have been able to diagnose approximately two thirds of patients with non-ferropenic anemia, the rest of the patients will only be diagnosed through the use of molecular biology techniques, not yet available for routine use in most clinical laboratories. For alpha thalassemia, the identification of Hb H performed through the techniques employed in this work proved to be useful, relatively simple, reproducible and inexpensive.

According to Weatherall and Clegg (2001), the world prevalence is estimated at 7% of the population and each year occur between 300,000 and 400,000 births of homozygous children with the severe form of these diseases. Variant hemoglobins and thalassemias have a very diverse geographical distribution in Africa, Asia, Europe and the Americas, although originally confined to tropical and subtropical regions.

The dispersion of genes for variant hemoglobins and thalassemias in Brazil is closely related to the ethnic background of the Brazilian population, involving the colonization process. Subsequently, due to the needs of settlement, several peoples of different ethnicities immigrated to Brazil.

Therefore, the population presents diversity in racial origins, with varied and progressive degree of miscegenation, a fact that certainly influenced the prevalence of thalassemias and variant hemoglobins in the various regions of Brazil.

All these population groups were mixed, so that the analysis of the prevalence of hereditary anemia in Brazil caused by thalassemias and variant hemoglobins should take into account the historical processes of ethnic formation of the population under study.

However, it is important to emphasize that the participation of the indigenous in the ethnic composition of the Goiás people was not significant, since the relations between Indians and exploiters of the mines were exclusively warriors and of mutual extermination. In addition, the infectious diseases brought by Europeans and Africans made the Indians susceptible to epidemics (typhus, measles, smallpox etc.).

Genetic alterations with hereditary implications, such as thalassemias and variant hemoglobins, are important in order to obtain knowledge regarding anthropology and migratory movements of populations, as well as contributions to public health and specific preventive methods.

Hereditary anemias are among the most common genetic diseases and comprise a group of conditions of variable complexity. In the past, its geographical distribution covered only tropical and subtropical areas of the world, whose explanation is based on the protective effect that sickle-cell and thalassemic heterozygotes had against endemic infections caused by malaria parasites. Due to the increase of migratory movements in several regions, with consequent miscegenation, these variants eventually diffuse in areas previously considered non-endemic, such as in the American Continent and in Northern Europe.

In general, hereditary anemia due to hemoglobin defect can be divided into two major groups: hemoglobinopathies, which are characterized by the presence of structurally abnormal hemoglobins and thalassemias, characterized by deficient synthesis of one or more polypeptide chains (globins) of normal human hemoglobins. Especially with reference to thalassemias, they can be classified as alpha and beta, involving the alpha and beta globin genes, respectively.

The most common hemoglobinopathy in our setting is sickle cell anemia, caused by a point mutation in the β-globin gene, which leads to abnormal hemoglobin production, with valine instead of glutamic acid at the 6-position globin chain, called hemoglobin S (Hb S). The term sickle cell disease includes the homozygous state for Hb S that is sickle cell anemia and the double heterozygous as the combinations of Hb S and Hb C (hemoglobinopathy SC) or Hb S and thalassemia (Sβ 0 -thalassemia and Sβ + -thalassemia). Sickle cell disease is characterized by chronic hemolytic anemia

with sickle-shaped red blood cells (sickles), polychromasia, stippling basophils, and circulating erythroblasts. Sickle cell trait, which is the combination of Hb A and Hb S (Hb AS), is not considered sickle cell disease.

Because beta thalassemia and variant hemoglobins Hb S, Hb C and Hb E are the most prevalent respectively in European, African and Asian continents, interactions between thalassemias and these variant hemoglobins are not uncommon: Hb S / Tal. Beta; Hb C/ Tal. Beta and Hb E/ Tal. Beta. In Brazil, the presence of interactive thalassemias by Hb S/ Tal is not rare. Beta due to the intense racial miscegenation that occurs among our population.

Despite the variety of possible molecular changes, beta thalassemias can be classified into four major groups:

- **1-β-thalassemia major or major:** uncommon, it is the most severe form and is characterized by severe anemia (Hb 4 to 6g/dL), transfusion dependence, and complications related to iron overload. It is characterized by short stature, pallor, protruding abdomen, mild jaundice, and skeletal abnormalities. Anemia is hypochromic and microcytic, with target cells, stippled basophils, and large numbers of circulating erythroblasts. The percentage of reticulocytes ranges from 5% to 15%. Most of the hemoglobin present is Hb F, with little or no Hb A, associated with variable amounts of Hb A2.
- **2-β-thalassemia intermediata:** characterized by hemolytic anemia of variable severity (Hb 7 to 10g/dL) without transfusion dependence. Its manifestations range from conditions close to β-thalassemia major to the disease with few symptoms. The blood smear exhibits morphological characteristics typical of thalassemias. Hemoglobin electrophoresis is variable with increasing Hb A2 and amounts of Hb F that depend on the degree of synthesis deficiency caused by the mutation present in each case.
- **3-β-thalassemia minor or minor:** associated with erythrocyte abnormalities with microcytosis and hypochromia, many schizocytes, dacryocytes and basophils punctate; with little or no anemia, but with disproportionate values between number of erythrocytes, hemoglobin and hematocrit (erythrocytes: 5 x 1012 - L, Hb: 12g/dL, Ht 36%, VCM: 62 and HCM: 20.6). Hemoglobin electrophoresis shows increased levels of Hb A2 in 95% of cases and in 5% it can present normal values of Hb A2 and elevation of Hb F, with concentration

between 2 and 5%, knowing that the value of Hb F is zero to 1% after the sixth month of age.

- **4-Silent carrier:** form also designated as minimal thalassemia, which is clinically and hematologically undetectable since it presents Hb values between 11 and 16g/dL and slight alteration in erythrocyte morphology.

Due to the defect in the synthesis of normal amounts of hemoglobin, erythrocytes are microcytic and hypochromic. These data are of clinical relevance, since these hematological changes are then interpreted as indicators of iron deficiency or characteristics of anemia of chronic diseases.

The Brazilian population is characterized by a great genetic heterogeneity and a significant and progressive level of miscegenation. The distribution of thalassemias and hemoglobinopathies is related to the various racial groups that participated in the formation of the Brazilian population. The IBGE establishes five options for color or race in our population: white, black, yellow, brown and Indian. The data from the 2000 census show the classification of the Brazilian population according to this variable. Individuals of black or brown color represent 45% of the Brazilian population.

The results presented in this work demonstrate that thalassemias and hemoglobinopathies are infrequent in populations of individuals with non-ferropenic microcytic anemia. Regarding alpha thalassemia, its frequency is not defined, since the technology used is not able to detect carriers.

3. FINAL CONSIDERATIONS

The frequency of thalassemias and hemoglobinopathies identified among patients may be due to the Unilab laboratory being a reference center in the city for the diagnosis of hematological disorders. In addition, iron deficiency and anemia of chronic diseases, causes of microcytosis, were excluded through laboratory tests and medical consultations.

With the techniques used in this work, a large number of patients with non-ferropenic microcytic anemia to be clarified can be diagnosed as having some type of hereditary anemia, highlighting beta thalassemias, sickle cell disease and trait.

The results obtained allow us to conclude that the prevalence of thalassemias and variant hemoglobins in the control group coincides with that described in the

literature. The main advantage of the correct identification of these individuals is to avoid unnecessary administration of iron, in addition to laboratory tests and medical consultations.

However, the presence of 2 patients without anemia, with normal hematimetric indices, classified as silent carriers, stands out. Although the techniques applied in this study have been able to diagnose 9.51% of patients with non-ferropenic anemia, the rest of the patients will only be diagnosed through the use of specific techniques and molecular biology, not yet available for routine use in most clinical laboratories.

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