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DAVI DE SÁ CAVALCANTE

AVALIAÇÃO DE ASPECTOS ORAIS, SOCIOECONÔMICOS E CRANIOFACIAIS
EM PACIENTES COM SÍNDROME DE SHEEHAN

FORTALEZA

2018

DAVI DE SÁ CAVALCANTE

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EM PACIENTES COM SÍNDROME DE SHEEHAN**

Dissertação apresentada ao Programa de Pós-Graduação em Odontologia da Faculdade de Farmácia, Odontologia e Enfermagem da Universidade Federal do Ceará, como um dos requisitos para a obtenção do título de Mestre em Odontologia.

Área de Concentração: Clínica Odontológica

Orientador: Prof. Dr. Fábio Wildson Gurgel Costa

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Dissertação submetida à coordenação do Programa de Pós-Graduação em Odontologia da Universidade Federal do Ceará, como requisito parcial para a obtenção do título de Mestre em Odontologia; Área de Concentração: Clínica Odontológica.

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“Comece fazendo o que é necessário,
depois o que é possível, e de repente você estará
fazendo o impossível”.

São Francisco de Assis

RESUMO

O sistema estomatognático é reconhecidamente sede para manifestação de várias doenças do endócrinas. Nesse contexto, a síndrome de Sheehan (SSH) é uma endocrinopatia mais predominante em países subdesenvolvidos, caracterizada pela necrose parcial ou total da glândula hipofisária decorrente de isquemia por choque hipovolêmico durante ou após o parto. Pelo fato da SSH ser uma condição de hipopituitarismo relacionada a alterações osteometabólicas, justifica-se a realização de estudos relacionados a aspectos odontológicos em tais indivíduos. Dessa forma, a presente dissertação é composta por dois capítulos que têm como objetivo, respectivamente: 1) realizar um estudo observacional transversal sobre aspectos orais em pacientes com SSH; 2) realizar um estudo caso-controle sobre aspectos morfológicos craniofaciais em pacientes com SSH. No capítulo 1, foi realizado um estudo observacional transversal com 23 mulheres diagnosticadas com SSH onde foram coletados dados referentes a aspectos sociodemográficos, dentários e fluxo salivar por meio de abordagem clínica e avaliação de radiografias panorâmicas. A média de idade foi de $64 \pm 11,5$ anos, com a amostra constituída principalmente por mulheres casadas (56,5%), classe socioeconômica C2 ou D/E (78,2%) e anos de educação de até 8 anos (69,5%). Presença de perda óssea horizontal ($p < 0,001$) e pneumatização bilateral do seio maxilar ($p = 0,015$) foram dados significantes. O número médio de dentes ausentes considerando-se todos os indivíduos foi de $23,17 \pm 9,7$, sendo estatisticamente significativo ($p < 0,0001$). Em relação à idade, o número médio de dentes ausentes foi superior em indivíduos com mais de 65 anos ($p = 0,048$). Fluxo salivar reduzido foi observado em 78,3% das pacientes. Em uma análise bivariada, considerando-se as variáveis de desfecho “dentes ausentes” e “fluxo salivar reduzido”, observou-se que classe econômica ($p < 0,001$), renda familiar (0,037) e pneumatização do seio maxilar (0,032) foram estatisticamente significantes. No capítulo 2, foi realizado um estudo caso-controle no qual foram analisadas radiografias cefalométricas laterais de 19 mulheres diagnosticadas com SSH e 19 controles sem SSH pareados por sexo e idade. O perfil cefalométrico esquelético incluiu medidas angulares e lineares obtidas através do programa Radiocef Studio 2. Valores médios e desvios padrão (DP) foram obtidos. O nível de significância foi estabelecido em 5%. A média de idade das pacientes foi $65,47 \pm 10,19$. Os dados evidenciaram: posição da maxila em relação à base craniana protusiva em 52,63% (S.N.A $> 82^0$); mandíbula protusiva em 52,63% (S.N.B $> 80^0$); prognatismo mandibular em 73,68% (A.N.B $< 2^0$); padrão de crescimento profundo em 42,1% (SN.GoGn $< 32^0$); aumento do plano mandibular em 36,84%; e altura facial anterior reduzida (N-Me < 114 mm). O grupo SSH comparado aos controles apresentou diferença

estatisticamente significativa em relação ao S.N.B ($p=0,026$), ao N-Me ($p=0,006$), palato mole ($p=0,011$) e Ena-Me ($p<0,001$). Obteve-se EDP anormal em relação ao comprimento maxilar total (Co-A, EDP= $3,5\pm 10,84$) e comprimento mandibular total (Co-Gn, EDP= $5,2\pm 15,38$). Como conclusões de ambos os estudos se destaca que: 1) pacientes com SSH evidenciaram baixos níveis educacional e socioeconômico, fluxo salivar reduzido e severas perdas dentais; 2) indivíduos com SSH apresentaram padrão craniofacial caracterizado por prognatismo maxilar/mandibular, face curta, plano mandibular aumentado e comprimento do palato mole reduzido.

Palavras-chave: hipopituitarismo, radiografia panorâmica, fluxo salivar, análise cefalométrica.

ABSTRACT

The stomatognathic system is admittedly the site for manifestation of various diseases of the endocrine system. In this context, Sheehan syndrome (SSH) is a more predominant endocrinopathy in underdeveloped countries, characterized by partial or total necrosis of the pituitary gland due to hypovolemic shock ischemia during or after delivery. By the fact SSH is a condition of chronic hypopituitarism related to osteometabolic alterations, it is justified to carry out studies related to odontological aspects in such individuals. Thus, the present dissertation is composed of two chapters that have as objective, respectively: 1) to conduct a cross-sectional observational study on oral aspects in patients with SSH; 2) to carry out a case-control study on craniofacial morphological aspects in patients with SSH. In Chapter 1, a cross-sectional observational study was performed with 23 women diagnosed with SSH in which data on sociodemographic, dental and salivary flow aspects were collected through a clinical approach and panoramic radiographs evaluation. The mean age was 64 ± 11.5 years, with the sample consisting mainly of married women (56.5%), socioeconomic class C2 or D / E (78.2%) and years of education up to 8 years (69,5%). Presence of horizontal bone loss ($p < 0.001$) and bilateral pneumatization of the maxillary sinus ($p = 0.015$) were significant. The mean number of teeth absent considering all subjects was 23.17 ± 9.7 , being statistically significant ($p < 0.0001$). In relation to age, the mean number of missing teeth was higher in individuals over 65 ($p = 0.048$). Reduced salivary flow was observed in 78.3% of the patients. In a bivariate analysis, considering the "missing teeth" and "reduced salivary flow" outcome variables, it was observed that economic class ($p < 0.001$), family income (0.037) and maxillary sinus pneumatization (0.032) were statistically signifiers. In Chapter 2, a case-control study was performed in which lateral cephalometric radiographs of 19 adult women diagnosed with SSH and 19 non-SSH controls matched by sex and age were analyzed. The skeletal cephalometric profile included angular and linear measurements obtained through the Radiocef Studio 2 program. Mean values and standard deviations (SD) were obtained. The level of significance was set at 5%. The mean age of the patients was 65.47 ± 10.19 . The data showed: position of the maxilla in relation to the protusive cranial base in 52.63% ($S.N.A > 82^0$); protusive mandible in 52.63% ($S.N.B > 80^0$); mandibular prognathism in 73.68% ($A.N.B < 2^0$); deep growth pattern at 42.1% ($SN.GoGn < 32^0$); mandibular plane increase in 36.84%; and reduced anterior facial height ($N-Me < 114mm$). The SSH group compared to controls had a statistically significant difference in relation to S.N.B ($p = 0.026$), N-Me ($p = 0.006$), soft palate ($p = 0.011$) and ANS-Me ($p < 0.001$). Abnormal EDP was obtained in relation to total maxillary length (Co-A, EDP

= 3.5 ± 10.84) and total mandibular length (Co-Gn, EDP = 5.2 ± 15.38). As conclusions of both studies it is highlighted that: 1) patients with SSH evidenced low educational and socioeconomic levels, reduced salivary flow and severe dental losses; 2) individuals with SSH presented a craniofacial pattern characterized by maxillary / mandibular prognathism, short face, increased mandibular plane and reduced soft palate length.

Key words: hypopituitarism, panoramic radiography, salivary flow, cephalometric analysis.

LISTA DE ABREVIATURAS E SIGLAS

ACTH	Hormônio adrenocorticotrófico
CCI	Coeficiente de correlação intraclasse
DP	Desvio Padrão
GH	Hormônio do crescimento
FSH	Hormônio folículo-estimulante
LH	Hormônio luteinizante
PRL	Prolactina
SDS	Standard Deviation Score
SPSS	<i>Statistical package for the social sciences</i>
SSH	Síndrome de Sheehan
STROBE	Strengthening the Reporting of Observational studies in Epidemiology
TSH	Hormônio estimulante da tireoide
TIFF	Tagget Image File Format

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Introdução

1. INTRODUÇÃO

O sistema endócrino tem como atribuição coordenar e regular as diversas funções do organismo como, por exemplo, a reprodução, o metabolismo orgânico e o balanço energético, de modo que a distribuição de nutrientes e outros elementos ocorram em quantidades suficientes às necessidades dos diversos órgãos e tecidos (DIAMANTI-KANDARAKIS et al., 2017)

Os hormônios regulam praticamente todas as funções orgânicas, e, portanto, as alterações hormonais podem provocar doenças das mais variadas, envolvendo o organismo como um todo. Nesse contexto, incluem-se as alterações osteometabólicas (CHERIAN et al., 2017).

Algumas doenças endócrinas se manifestam alterando o padrão ósseo da região maxilomandibular (BRAS, 1982; BENSON, 1991; KAUFMAN, 1992; DE BOER, 1994; AY, 2015). O hiperparatireoidismo, ocasionado pelo aumento do hormônio da paratireoide circulante, causa um desequilíbrio da atividade osteoblástica e osteoclástica, alterando a morfologia do trabeculado normal e revela maxilares com densidade óssea reduzida (ERGÜN et al., 2009; KHALEKAR et al., 2016; BRABYN et al., 2017; PALLA et al., 2017). A osteoporose, por sua vez, é uma doença osteometabólica onde ocorre a redução generalizada da massa óssea cujo aspecto histológico do osso é normal (BRAS et al., 1982; BENSON et al., 1991; KLEMETTI et al., 1993; TAGUCHI et al., 1995). Mas, em contrapartida, resulta numa redução generalizada da densidade óssea. A lâmina dura pode parecer mais fina que o normal. Em outras regiões da mandíbula a redução do número de trabéculas é evidente (TAGUCHI et al., 1995; LEDGERTON et al., 1999; HORNER, 2002). O hipopituitarismo resulta da secreção reduzida dos hormônios hipofisários, os quais regulam uma grande parte de glândulas e órgãos

importantes no controle das mais variadas funções no organismo. Casos são relatado de pacientes com nanismo hipofisário, anomalias dentárias múltiplas, variação na morfologia facial. (MANOVSAK et al., 2015; FERRANTE et al., 2017). Já o desequilíbrio hormonal da adeno-hipófise é mais preocupante, uma vez que, na região anterior da hipófise, são produzidos e secretados hormônios indispensáveis a homeostasia como: hormônio do crescimento (GH), prolactina, hormônio folículo-estimulante (FSH), hormônio luteinizante (LH), hormônio estimulante da tireoide (TSH), hormônio adrenocorticotrófico (ACTH) e endorfinas.

Entre as endocrinopatias que podem acometer a glândula hipofisária, destaca-se a síndrome de Sheehan (SSH) onde ocorre à diminuição da secreção de hormônios adeno-hipofisários. Também conhecida como necrose pituitária pós-parto, é uma condição rara que foi relatada pela primeira vez em 1937, por Sheehan e colaboradores, os quais descreveram um caso de necrose e insuficiência pituitárias após o parto (KARACA et al., 2016). SSH é uma insuficiência adeno-pituitária decorrente de hipovolemia secundária a uma perda excessiva de sangue durante ou mesmo após o parto, pelo fato de a glândula hipófise hiperplasiar durante a gestação, em virtude de uma maior produção de hormônios gestacionais (GOKALP et al., 2009). Nessa situação, a referida glândula torna-se mais vulnerável a uma necrose (total ou parcial) por isquemia ocasionada por um choque hipovolêmico, uma vez que a deficitária irrigação sanguínea da região anterior da hipófise compromete a sua função em consequência de uma possível isquemia durante ou após o parto (GOKALP et al., 2009; KARACA et al., 2016)

A perda da função da glândula diminui, com o tempo, a secreção dos hormônios como, FSH, LH, TSH, ACTH, cortisol, estradiol, prolactina (PRL). Tais hormônios podem alterar o padrão trabeculado ósseo, podendo causar osteopenia, bem como quadros de osteoporose (BOLANOWSKI et al., 2015). Os níveis séricos de LH, FSH e estradiol são consideravelmente diminuídos em pacientes com SSH, portanto, o hipogonadismo pode ser um

dos possíveis mecanismos de osteoporose nesses pacientes. A redução dos níveis de GH tem um efeito significativo no metabolismo ósseo e desempenha um papel crucial na manutenção da massa óssea em adultos, regulando a remodelação óssea (GOKALP et al., 2009). O hipotireoidismo apresenta alteração das taxas dos hormônio TSH em pacientes com SSH, pacientes com essa deficiência hormonal possuem uma maior dificuldade de cicatrização e redução do fluxo salivar (GEI-GUARDIA et al., 2011; GUPTA et al., 2014). Além disso, pacientes com SSH são mais susceptíveis às doenças cardiovasculares, visto que, à medida que os níveis de estrogênio diminuem, as lesões arterioscleróticas se desenvolvem na região da bifurcação carotídea e tem sido implicada como a causa precipitante na maioria dos eventos associados a essa condição (BOHDANOWICZ-PAWLAK et al., 2006; SAVANELLI et al., 2016).

A razão da pesquisa para a avaliação de parâmetros radiográficos craniofaciais é relevante. Presume-se que, pela diminuição da secreção hormonal em pacientes com SSH, entre eles hormônios que regulam o mecanismo osteometabólico, que o complexo maxilomandibular possa apresentar osteopenia ou osteoporose. Portanto, o objetivo do presente estudo será realizar uma análise radiográfica craniofacial em indivíduos com SSH.

Objetivos

2. OBJETIVOS

2.1 Objetivo geral

Avaliar aspectos orais, socioeconômicos e craniofaciais em pacientes com SSH.

2.2 Objetivos específicos

1. Avaliar o status dentário, aspectos socioeconômicos e fluxo salivar de pacientes com SSH;
2. Comparar os aspectos morfológicos craniofaciais observados em cefalométrias laterais de pacientes com SSH versus os de indivíduos controle sem diagnóstico de SSH e pareados por sexo e idade.

PROPOSIÇÃO

A presente dissertação será apresentada por meio dos seguintes capítulos:

Capítulo 1: Dental status, salivary flow, and sociodemographic aspects in Sheehan Syndrome patients.

Capítulo 2: Avaliação da morfologia craniofacial de indivíduos brasileiros com Síndrome de Sheehan: um estudo caso-controle.

3. CAPÍTULOS

A presente dissertação será baseada no Artigo 46 do Regimento Interno do Programa de Pós-Graduação em Odontologia da Universidade Federal do Ceará que regulamenta o formato alternativo para dissertações de Mestrado e teses de Doutorado e permite a inserção de artigos científicos de autoria ou coautoria do candidato (Anexo I). Por se tratar, em parte, de pesquisa envolvendo seres humanos, o projeto de pesquisa referente ao trabalho desenvolvido nos Capítulos 1 e 2 foram submetidos à apreciação do Comitê de Ética em Pesquisa da Universidade Federal do Ceará, tendo sido aprovado sob o número do parecer 983.022, em 05/03/2015 e emenda número 1.457.233 (CAAE 39632714.1.0000.5054) (Anexo II). Desta forma, a dissertação é composta por dois capítulos, conforme descrito abaixo:

Capítulo 1: Dental status, salivary flow, and sociodemographic aspects in Sheehan Syndrome patients.

O presente artigo foi publicado na revista “*Medicina oral, patologia oral y cirugia bucal,*” (Print version ISSN 1698-4447; On-line version ISSN 1698-6946; Fator de impacto 1.671; Qualis CAPES B1) (Anexo III).

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Capítulo 2: Avaliação da morfologia craniofacial de indivíduos brasileiros com Síndrome de Sheehan: um estudo caso-controle.

O presente artigo será submetido à publicação na revista “*Journal Of American Geriatrics Society*” (Print version ISSN 0002-8614; On-line version ISSN 1532-5415; Fator de impacto 4.155; Qualis CAPES A1) (Anexo IV).

3.1 CAPÍTULO 1

Dental status, sociodemographic aspects, and salivary flow in ageing Sheehan Syndrome patients

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Statement of relevance:

We certify that this work is novel. Sheehan Syndrome (SS) is considered a rare disease in developed countries in which oral findings have not been discussed. We observed a severe tooth loss which could be associated with a decline in the functional capacity of ageing women affected by this disorder.

BACKGROUND/OBJECTIVES: Sheehan syndrome (SS) is one of the leading causes of hypopituitarism in developing countries, and it is considered a significant public health problem. This study aimed to perform an analysis on oral aspects in ageing patients with SS.

DESIGN: It was performed a cross-sectional study.

SETTING: Division of Endocrinology and Diabetology of the Walter Cantídio University Hospital (Fortaleza, Ceará, Brazil)

PARTICIPANTS: 23 women diagnosed with SS.

MEASUREMENTS: Data on dental status, sociodemographic data, and salivary aspects were collected. The mean age was 64 ± 11.5 years old, with the sample consisting mainly of married women (56.5%), socioeconomic class C2 or D/E (78.2%), and low education level (69.5% up to 8 years of schooling). The presence of horizontal bone loss ($p < 0.001$) and bilateral pneumatization of the maxillary sinus ($p = 0.015$) were significant data. The mean number of missing teeth considering all subjects was 23.17 ± 9.7 , being statistically significant ($p < 0.0001$). The mean number of missing teeth was higher in individuals over 65 years old ($p = 0.048$). The reduced salivary flow was observed in 78.3% of the patients. In a bivariate analysis, considering the outcome variables "missing teeth" and "reduced salivary flow," it was observed that economic class ($p < 0.001$), family income ($p = 0.037$), and maxillary sinus pneumatization ($p = 0.032$) were statistically significant.

CONCLUSION: In this context, patients with SS showed low educational and socioeconomic levels, reduced salivary flow, and severe teeth missing, which could be associated with a decline in the functional capacity of women affected by SS.

Keywords: Sheehan Syndrome, hypopituitarism, tooth loss, salivary flow.

INTRODUCTION

The stomatognathic system has been considered a region for the manifestation of endocrine system disorders.¹ Sheehan syndrome (SS), also known as postpartum pituitary necrosis, is an uncommon condition that was reported by Sheehan et al. (1937) and is characterized by partial or total necrosis of the pituitary gland. The pituitary gland becomes hyperplastic during gestation by higher production of gestational hormones, and the anterior pituitary region becomes more vulnerable to ischemic necrosis caused by hypovolemic shock, once short irrigation of the anterior area of the gland impairs its function as a result of severe bleeding or hypovolemic collapse during or after childbirth.^{2,3} The diagnosis of SS remains reasonably late. History of bleeding during or after delivery and the subsequent onset of hypopituitarism constitute the primary basis for clinical suspicion.⁴

Due to the loss of function of the pituitary gland, a gradual decrease in the secretion of hormones essential for the functioning of the organism occurs. The involvement of the somatotrophic axis leading to GH deficiency and prolactin production deficit is the most observed. Some clinical findings related to the presence of hypopituitarism in SSH such as agalactia due to prolactin deficiency, amenorrhea or menstrual irregularity due to gonadal axis failure, asthenia, hypoglycemia, hypotension and hydroelectrolytic disorders due to adrenal insufficiency, besides cold intolerance, gain of weight and constipation resulting from thyroid axis involvement. The presence of multiple hormonal deficiencies leads to impairment of bone microarchitecture, which can cause osteopenia and even osteoporosis,^{4,5} and a high risk for the development of cardiovascular events.⁶

Although there are no studies on the oral aspects specifically involved in SS, studies on the local effect of deficiency of certain pituitary hormones on bone and dental tissues can be found. Reduction of estrogen levels may adversely affect oral cavity epithelium, salivary gland function, and propensity for inflammatory processes related to periodontal tissues.⁷⁻⁹ Also, patients who produce a lower amount of thyroid hormone tend to have a higher difficulty in

healing. Thus, the onset of inflammation in the oral cavity, such as gingivitis, has a higher chance of worsening, progressing to periodontitis, and causing tooth loss.⁶ In this context, it has been observed that dental absences have been associated with a more significant decline in functional capacity, as well as physical imbalance, altered cognitive function, and impairment in the performance of communicative social skills,¹⁰ which reinforces the importance of studies evaluating the status in patients with hypopituitarism.

Decreased skeletal bone mineral density has been found in patients with SS,^{4,5} and hypothetically may be related to changes in the oral cavity, although not yet described in the literature. It is possible that there may be an interrelation between the deleterious manifestations that the multiple hormonal deficiencies cause in the organism,³ and the tissues of the oral cavity. Also, depending on the severity of the hypopituitarism present in SS, one can expect a more considerable difficulty in the tissue healing process,⁶ as well as a decrease in salivary flow.¹¹

In this context, this study aimed to conduct a new investigation about tooth loss, sociodemographic data, and salivary data in Brazilian SS patients. To date, there are no published studies focusing on the oral health of SS.

MATERIALS AND METHODS

An observational, cross-sectional and analytical study was performed with patients diagnosed with SS from the Endocrinology and Diabetology Department of the Walter Cantídio University Hospital (Fortaleza, Ceará, Brazil), who had been in clinical follow-up for more than ten years. The research protocol was evaluated by the Human Research Ethics Committee of the Federal University of Ceará (approval number # 983,022). The diagnosis of SS was based on the presence of classic obstetric history and presence of hormonal deficiency. Imaging exams of sella turcica were performed when there was suspicion of a pituitary tumor or other etiologies such as autoimmune hypophysitis.

SS is considered a rare disease, with an incidence of 0.2 to 2.8 cases per 100,000 women in developed countries.¹² Thus, the sample adopted for the present study was of convenience. Patients with a previously confirmed diagnosis of SS, in any age group, under periodic medical follow-up, and those that agreed to participate in this study after reading and signing an informed consent form were included. Patients who met the eligibility criteria were submitted to an anamnesis, as well as digital panoramic radiography and salivary flow assessment. The data collected in the present study were: sociodemographic aspects, dental functional status, and salivary flow measurement. Also, data from SS patients medical records included: age and time of diagnosis, age of last childbirth, presence/absence of agalactia, amenorrhea, and obstetric history of postpartum hemorrhage, and presence/absence of 2 or more hormonal deficiencies.

Regarding sociodemographic variables, age was recorded in years and grouped into two categories (up to 65 and over 65 years). Marital status was categorized as follows: married, single, divorced, and widowed. Data on family income were collected to outline the socioeconomic profile according to the Brazilian Economic Classification Criteria (<http://www.abep.org/criterio-brasil>). It considers a score of 0 to 5 for the schooling of the head of the family. In addition, the remaining points are attributed to the quantity of durable household goods (automobile, color television, radio, fridge, freezer, washing machine, etc.), number of domiciliary rooms (with emphasis on the number of bathrooms), and number of monthly home-based employees who work in the household. At the end, the number of points obtained stratifies the individual into classes, from "A1" (most favored) to "E" (the least favored). Socioeconomic status was categorized according to Noce et al.¹³: low (8 or less years of education or monthly family income less than 2 minimum wages), average (9-11 years of education or family income between 3- 9 minimum wages, or 9-11 years of education and

monthly family income less than 9 minimum wages), and 12 or more years of education or monthly family income exceeding 10 minimum wages.

The dental functional status was considered through the evaluation of the number of teeth in digital panoramic radiographs, which were classified according to Sato et al 2016 as absence (edentulism) and presence (≥ 20 , 10-19, 1-9) of teeth.¹⁰ In order to obtain the images, the patients were referred to the Dental Radiology service of the Dentistry course of the Federal University of Ceará. The Kodak K9000 3D equipment (Kodak Dental Systems, Carestream Health, Rochester, NY, USA) was used with a 14-bit grayscale (16384 tons), exposure time of 13.9 seconds and kilovoltage and milliamperage adjusted according to each patient. Other imaging parameters evaluated for the present study were presence/absence of horizontal bone loss, maxillary sinus pneumatization, degenerative condylar alterations and styloid process elongation.

Before obtaining the panoramic radiograph, a saliva sample was collected for each participant between 8:00 and 11:00 am in order to minimize possible circadian contributions after a minimum of three hours of fasting. It was required that routine oral cavity sanitization procedures be performed one hour before collection. Each volunteer remained in rest for 30 minutes, and after that the saliva was collected in a millimeter cup, the patient with the head tilted towards the beaker, allowing the saliva to flow freely into the vessel for 5 minutes. The salivary flow was then measured in mL/min.

The data collected were tabulated using Microsoft Excel® software version 2010. For the statistical analysis, the Statistical Package for the Social Sciences (SPSS), version 17.0 for Windows® software was used. Descriptive statistics (mean, median and standard deviation) and frequency of the data were used. Chi-square or Fisher's exact test (parametric data) and Mann-Whitney test (non-parametric data) were used, adopting a significance level of 5%.

RESULTS

A total of 23 patients diagnosed with SS were evaluated in this study, exhibiting a mean age of 64 ± 11.5 years (47-79 years). Concerning the data collected in the medical records, the mean age at the time the diagnosis was 40.38 ± 10.53 (28-66 years of age), while the mean time of disease diagnosis delay was 10.92 ± 8.22 (1-31 years). The mean age at the time of the last childbirth was 29.53 ± 6.61 (19-38 years). The clinical manifestations related to the hormonal deficits were observed at the time of diagnosis: agalactia (46.15%), amenorrhea (53,84%) and adynamia in (61,54%). During a 10-year clinical follow-up, 92.31% were diagnosed with hypothyroidism, and 100% had glucocorticoid replacement. Therefore, all patients had more than 1 hormone deficiency. No patient had a replacement of the somatotropic axis, due to the following factors: socioeconomic status, medication unavailability at the time of diagnosis in the public service, and no indication of replacement for patients ≥ 60 years or older according to the Brazilian Ministry of Health protocol. MRI or CT scan was performed in 38.51%. These imaging exams were conducted in specific cases with diagnostic doubt to rule out the possibility of tumor causes, with the presence of empty sella turcica or the presence of pituitary hypoplasia.

According to Table 1, at the time of dental evaluation approximately half were 65 years of age and 48.2% were over 65 years of age ($p=1.000$). There was no statistically significant difference regarding marital status although the majority of the sample consisted of married patients (56.5%). Low socioeconomic status was observed among SS patients. Approximately three-quarters of the sample belonged to class C2 or D/E (78.2%; $p=0.115$), about 70% of the patients had up to 8 years of schooling ($p=0.237$), and the most cited family income ($p=0.552$) was in the range of 1 to 1.9 minimum wages (43.5%) followed by 2 to 2,9 minimum wages (39.1%). The horizontal alveolar bone loss was observed in all patients ($p<0.001$), the most prevalent pneumatization of the maxillary sinus was bilateral (69.6%, $p=0.015$), the absence of degenerative changes in the mandibular condyle was observed in a significant majority of the

patients (73%, $p=0.017$), as well as the absence of elongation of the styloid process (91.3%, $p=0.003$) was highlighted in the sample.

Regarding tooth status, 47% of the patients were partially dentate, while 39.1% of the sample were edentulous individuals (Table 1). The mean number of teeth absent considering all individuals was 23.17 ± 9.7 (5-32), which was a statistically significant variable ($p<0.0001$; Figure 1). According to table 2, the maxilla concentrated 53.45% of teeth absences, while mandible had a value of 46.55%. In jaws, the anatomic region that presented significant missing teeth was the posterior mandible (34.3%), followed by posterior maxilla (33.53%), anterior maxilla (19.92%) and anterior mandible (12.26%).

Figure 2 shows that the mean number of missing teeth was statistically higher ($p=0.048$) in individuals over 65 years (26.75 ± 7.84) compared to the group of individuals up to 65 years (19.27 ± 10.37). In individuals up to 65 years (Table 2), tooth loss was more prevalent in the maxilla (24.71%). The posterior mandible region (17.82%) was the most affected anatomic region, followed by posterior maxilla (15.71%), anterior maxilla (9%), and anterior mandible (4.21%). In SS individuals aged over 65 years, the maxilla (28.74%) was also the most affected anatomic location. These patients showed a higher prevalence of tooth loss in the posterior maxilla (17.82%), followed by posterior mandible (16.48%), anterior maxilla (10.92%), and anterior mandible (8.05%).

The mean salivary flow value was 0.14 ± 0.16 in individuals over 65 years of age and 0.2 ± 0.31 in individuals aged up to 65 years. In 18 patients (78.3%), reduced salivary flow values were found, while five patients (21.7%) presented normal values for salivary flow. Regarding reduced salivary flow, 72.22% ($n=13$) presented very low values and 27.78% ($n=5$) presented low values.

In a bivariate analysis considering the outcome variables "missing teeth" and "reduced salivary flow" (Table 3), it was observed that economic status ($p < 0.001$), family income (0.037), and maxillary sinus pneumatization (0.032) were statistically significant variables.

DISCUSSION

The study of systemic diseases, especially hypopituitarism, can be considered a valuable field of research, with a close interface between Medicine and Dentistry since many endocrine disorders exhibit manifestations in the maxillomandibular complex, which may raise its presence and assist, in a certain way, its diagnosis. In this context, SS stands out because it is an endocrinopathy still observed in developing countries such as Brazil, but there are no published studies on oral aspects of such patients to date.

The present study investigated the relationship between dental losses, sociodemographic variables, and salivary flow in a group of women with SS, which were more prevalent in the sixth decade of life. This data corroborates with the study by Diri et al. (2014),¹⁴ which reported patients aged 63.2 ± 12.5 years, as well as the research conducted by Dökmetaş et al. (2006) who reported an average age of 60.1 years in a sample of 20 patients.¹⁵ However, a study of 28 patients diagnosed with SS in the period between 1982 and 2002 in Turkey showed individuals aged between 30 and 70 years and mean of 48.2 ± 10.5 years.¹⁶

The presence of permanent teeth is considered a reliable indicator of oral as well as systemic health,¹⁷ and some authors have observed that longevity/life expectancy may be affected by the number of teeth present and that tooth loss is a predictive factor shortening of longevity.¹⁸ A dentition with various dental absences attenuates masticatory efficiency and causes a subsequent high limiting food selection with a diet low in fruits, vegetables and other foods containing essential nutrients.^{19,20} Such aspects reinforce the importance of the present study when analyzing the dental status in a group of patients with endocrinopathy still present

in developing countries. It was observed that the individuals affected by SS had a high number of dental losses, with the majority having 20 or more missing teeth. In this context, in a study investigating the relationship between the number and position of teeth with satisfaction with the oral cavity, it was found that at least 20 natural teeth are required to obtain satisfactory aesthetic function and function.²¹ Hiroto et al. (2015) observed in a 5-year longitudinal study that individuals with 20 or more teeth had a lower mortality rate (2.5%) than individuals with up to 19 teeth (6.1%), which was statistically significant.²² Hayasaka et al. (2013) showed an inverse dose-response relationship between the number of remaining teeth and mortality, and individuals with 10 to 19 teeth presented a relative risk of 1.16 compared to individuals with 20 or more teeth.²³

Over the last few years, sociodemographic variables have been considered important factors contributing to tooth loss,²⁴ with emphasis on educational and socioeconomic levels.¹⁷ According to Rozier et al. (2017), low socioeconomic status was pointed out as the most consistent predictive factor of missing teeth in his study, which discussed trends in dental caries, periodontal disease, and tooth loss for the US population.²⁵

In Brazil, a longitudinal study that used the Gini Index to measure socioeconomic inequality showed that the increase in this index was associated with a higher prevalence of severe tooth loss and loss of functional dentition, being considered when there were at least 20 natural teeth.²⁶ For the present study, patients with SS were classified according to the Economic Classification Criteria Brazil and a higher percentage of individuals with low socioeconomic status, represented by classes C2, D and E (about 78%) were observed. The data found in the present sample of SS patients were distributed like that of Silva et al. (2017) that used the Economic Classification Criteria Brazil.²⁷ The authors observed a significant association between socioeconomic classes and the number of natural teeth present in the oral cavity, evidencing that individuals with high socioeconomic status had a higher number of

permanent teeth when compared to lower socioeconomic status. Also, the data found in the present study corroborate the socioeconomic profile of patients with SS already described in the literature. Famuyiwa et al. (1992) identified 11 patients with SS over a 5-year period from an endocrinology department of a university hospital in Nigeria and observed that about 64% of the sample belonged to a low socioeconomic class.²⁸

The impairment of salivary function is associated with dental losses due to a high risk of caries and periodontal disease.²⁹ In the present study, it was observed that patients with SS had low salivary flow in the majority, representing about 80% of the analyzed sample. In this specific group of patients, the majority had significant low values of salivary flow. These findings corroborate the high percentage of missing teeth, which was a statistically significant result. Marques et al. (2017) investigated predictive factors of dental loss among Brazilian adults and found that the low salivary flow represented an independent outcome variable.³⁰ In a logistic regression model controlling matrimonial status, race, and socioeconomic status performed by Caplan, Hunt (1996) among 818 patients aged at least 65 years, a statistically significant association was observed between low salivary flow and dental loss.²⁹

Gokalp et al. (2008) reinforced the importance of hypogonadotropic hypogonadism in the development of osteoporosis in SS patients. These authors conclude that growth hormone has a significant effect on bone metabolism and plays a crucial role in maintaining bone mass in adults by regulating bone remodeling.⁵ In this context, such systemic findings reinforce the data found in the present study, especially the severe dental loss observed, which also reflected a significant prevalence of horizontal bone loss and maxillary sinus pneumatization. It is noteworthy that in our research there was no adequate replacement of the gonadal axis nor of the somatotrophic axis by previously reported factors, being patients that due to delayed diagnosis was submitted to many years of hypoestrogenism. Chihaoui et al. (2016) in a study of 60 patients diagnosed with SS concluded that reduced bone mineral density was a finding

frequently observed in such individuals.³¹ Such result inserted in the context of the present study is important because of the existence of an association between low bone mineral density and tooth loss and maxillomandibular alveolar bone loss.^{32,33}

CONCLUSION

In summary, the present study evidenced oral cavity-related findings reflecting the chronic hypopituitarism related to SS. It was observed a sample represented by adult women, mainly in the sixth decade of life, who presented low educational and socioeconomic levels, reduced salivary flow, and severe teeth missing, which could be associated with a decline in functional capacity of women affected by SS.

Conflict of Interest: none.

Author Contributions: FWGC, ARPQ, and MRAM prepared the draft. DSC and AMPLC collected the data. ASWA, PGBS and RFC completed the manuscript.

Sponsor's Role: none.

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FIGURE LEGENDS

Figure 1. Mean number of missing teeth considering all individuals in the sample studied.

Asterisk (*) indicates statistical significance (Mann-Whitney test).

Figure 2. Mean number of missing teeth considering individuals up to 65 years of age and those older than 65 years. Asterisk (*) indicates statistical significance (Mann-Whitney test).

Fig. 1: Mean number of missing teeth in SS sample. Asterisk (*) indicates statistical significance (Mann-Whitney test)

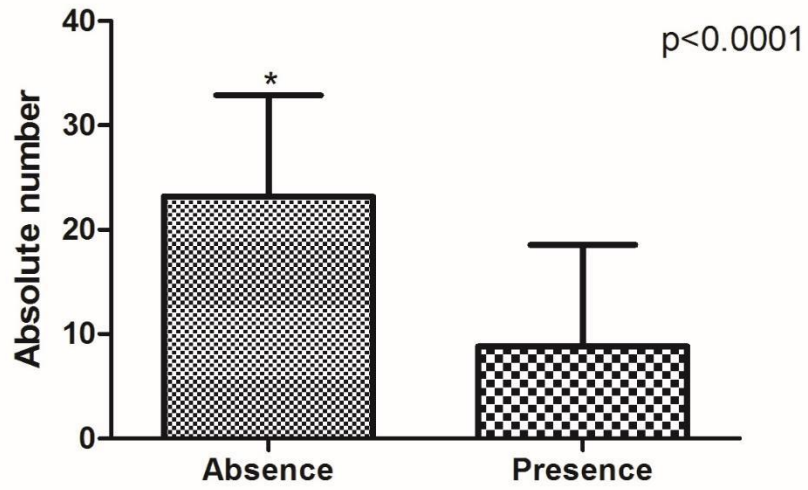


Fig. 2: Mean number of missing teeth considering individuals ≤ 65 years versus >65 years. Asterisk (*) indicates statistical significance (Mann-Whitney test).

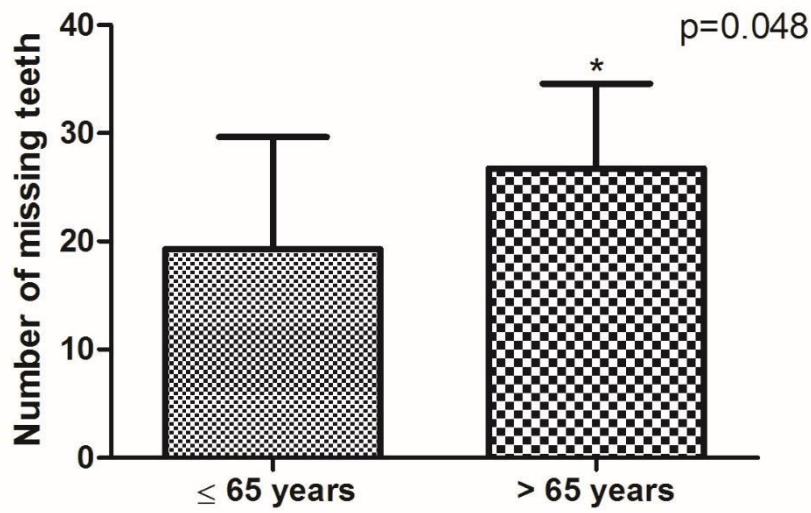


Table 1. Sample characterization regarding sociodemographic data and imaging variables.

	n	%	p-value
Age (years)			
Up to 65	12	51.8	1.000
> 65	11	48.2	
Marital status			
Married	13	56.5	0.237
Single	3	13	
Divorced	1	4.3	
Widow	6	26.1	
Socioeconomic class			
B1	1	4.3	0.115
B2	2	8.7	
C1	2	8.7	
C2	11	47.8	
D/E	7	30.4	
Schooling (years)			
≤ 8	16	69.5	0.237
9-11	3	13	
≥ 12	4	17.5	
Family income (MW)			
<1	1	4.3	0.552
1-1.9	10	43.5	
2-2.9	9	39.1	
3-5	2	8.7	
>6	1	4.3	
Edentulism			
No	14	60.9	0.453
Yes	9	39.1	
Partially toothed			
No	12	52.2	1.000
Yes	11	47.8	
Horizontal alveolar bone loss			
No	0	0	<0.001
Yes	23*	100	
Maxillary sinus pneumatization			
No	6	26.1	0.015
Unilateral	1	4.3	
Bilateral	16*	69.6	
Condyle with signs of degenerative change			
No	17*	73.9	0.017
Unilateral	4	17.4	
Bilateral	2	8.7	
Styloid process elongation			
No	21	91.3	0.003
Yes	2	8.7	

*p<0.05, chi-square or Fisher's exact test; MW, minimum wage.

Table 2. Teeth loss in patients with maxillary sinus pneumatization.

Maxillary sinus pneumatization				
	No	Yes	OR (95% CI)	P- Value
Missing teeth	14.5±10.5	27.3±5.8	-	0.001^a
0-9	3 (50.0%)	0 (0.0%)	1.0	0.006^b
10-19	1 (16.7%)	2 (11.8%)	11.7 (0.3 - 422.5)	
≥ 20	2 (33.3%)	15 (88.2%)	43.4 (1.7 - 1121.0)	

^aStudent t test; ^bChi-square test; OR = Odds Ratio; 95% CI = Confidence Interval

Table 3. Anatomical distribution of missing teeth (n = 522) according to age.

	≤ 65 years		> 65 years		Total	
	n	%	n	%	n	%
Jaws:						
Maxilla	129	24.71	150	28.74	279	53.45
Mandible	115	22.03	128	24.52	243	46.55
Anatomical region:						
Anterior maxilla	47	9	57	10.92	104	19.92
Posterior maxilla	82	15.71	93	17.82	175	33.53
Anterior mandible	22	4.21	42	8.05	64	12.26
Posterior mandible	93	17.82	86	16.48	179	34.3

Table 4. Influence of the outcome variables "missing teeth" and "reduced salivary flow" on study variables.

	Total	Missing teeth			p	Reduced salivary flow		p
		0-9	10-19	≥20		No	Yes	
Marital status								
Married	16 69.6%	3 100%	3 100%	10 58.8%	0.169	3 60%	13 72.2%	0.621
Not married	7 30.4%	0 0%	0 0%	7 41.2%		2 40%	5 27.8%	
Age (years)								
Up to 65	12 52.2%	3 100%	1 33.3%	8 47.1%	0.187	2 40%	10 55.6%	0.640
> 65	11 47.8%	0 0%	2 66.7%	9 52.9%		3 60%	8 44.4%	
Socioeconomic class								
B1	1 4.3%	1* 33.3%	0 0%	0 0%	<0.00 1	0 0%	1 5.6%	0.886
B2	3 13%	0 0%	0 0%	3 17.6%		1 20%	2 11.1%	
C1/2	3 13%	0 0%	3* 100%	6 35.3%		2 40%	9 50%	
D/E	8 34.8%	0 0%	0 0%	8* 47.1%		2 40%	6 33.3%	
Schooling								
Until complete elementary school	16 69.6%	2 66.7%	2 66.7%	12 70.6%	0.984	5 100%	11 61.1%	0.272
>complete elementary school	7 30.4%	1 33.3%	1 33.3%	5 29.4%		0 0%	7 38.9%	
Family income (MW)								
<2	11 47.8%	0 0%	2 66.7%	9 52.9%	0.187	0 0%	11* 61.1%	0.037
≥2	12 52.2%	3 100%	1 33.3%	8 47.1%		5* 100%	7 38.9%	
Horizontal alveolar bone loss	23 100%	3 100%	3 100%	17 100%	1.000	4 80%	10 55.6%	0.611
Maxillary sinus pneumatization								
No	6 26.1%	3* 100%	1 33.3%	2 11.8%	0.032	1 20%	5 27.8%	0.791
Unilateral	1 4.3%	0 0%	0 0%	1 5.9%		0 0%	1 5.6%	
Bilateral	16 69.6%	0 0%	2* 66.7%	14* 82.4%		4 80,0%	12 66.7%	
Condyle with signs of degenerative change	6 26.1%	1 33.3%	0 0%	5 29.4%	0,538	1 20 %	5 27.8%	1.000
Styloid process elongation	2 8.7%	0 0%	0 0%	2 11.8%	0.679	0 0%	2 11.1%	1.000

*p<0.05, chi-square or Fisher's exact test; MW, minimum wage.

3.2 CAPÍTULO 2

Avaliação da morfologia craniofacial de indivíduos brasileiros com Síndrome de Sheehan: um estudo caso-controle

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OBJETIVOS: Este estudo teve como objetivo realizar uma avaliação cefalométrica da morfologia craniofacial em pacientes brasileiros portadores da Síndrome de Sheehan (SSH), que é uma forma adquirida de hipopituitarismo ainda considerado um importante problema de saúde pública em países em desenvolvimento.

DESENHO DO ESTUDO: estudo observacional, caso-controle,

LOCAL: Divisão de Endocrinologia e Diabetologia (Hospital Universitário Walter Cantídio, Fortaleza, Brasil).

PARTICIPANTES: 19 mulheres adultas com diagnóstico de SSH e 19 pacientes controles pareados por sexo e idade.

MENSURAÇÕES: Radiografias cefalométricas laterais foram obtidas, mensurando o perfil cefalométrico esquelético, onde incluiu 30 medidas angulares e lineares traçadas em telerradiografias digitais utilizando o software Radiocef Studio 2. Valores médios e desvios padrão (DP) foram obtidos. O nível de significância foi estabelecido em 5%.

RESULTADOS: A média de idade das pacientes foi $65,47 \pm 10,19$. Os dados evidenciaram: posição da maxila em relação à base craniana protusiva em 52,63% (S.N.A $>82^0$); mandíbula protusiva em 52,63% (S.N.B $> 80^0$); prognatismo mandibular em 73,68% (A.N.B $<2^0$); padrão de crescimento profundo em 42,1% (SN.GoGn $<32^0$); aumento do plano mandibular em 36,84%; e altura facial anterior reduzida (N-Me $<114\text{mm}$). O grupo SS comparado aos controles apresentou diferença estatisticamente significativa em relação ao S.N.B ($p=0,026$), ao N-Me ($p=0,006$), palato mole ($p =0,011$) e Ena-Me ($p <0,001$). Obteve-se EDP anormal em relação ao comprimento maxilar total (Co-A, EDP= $3,5 \pm 10,84$) e comprimento mandibular total (Co-Gn, EDP= $5,2 \pm 15,38$).

CONCLUSÃO: Portanto, indivíduos com SSH apresentaram padrão craniofacial caracterizado por prognatismo maxilar/mandibular, face curta, plano mandibular aumentado e comprimento do palato mole reduzido. Assim, este estudo abordou aspectos importantes em relação aos achados craniofaciais em SS não publicados até o momento.

Palavras-chave: Síndrome de Sheehan, hipopituitarismo, análise cefalométrica.

INTRODUÇÃO

A Síndrome de Sheehan (SSH), também denominada de necrose pituitária pós-parto, é uma condição rara que foi descrita pela primeira vez por Sheehan em 1937, onde foi relatada necrose da região da adeno-hipófise em mulheres que sofreram grave hemorragia durante ou após o parto. É um importante problema de saúde pública que ainda é diagnosticado em países subdesenvolvidos, onde são observados pouca assistência obstétrica e precária assistência à saúde.¹⁻³

A ocorrência da SSH apresenta intrínseca relação com o período gestacional. Durante essa fase, a hipófise praticamente duplica o seu volume, sobretudo pela hiperplasia de células secretoras de prolactina encontradas na região anterior da glândula. Por esse fato, a adeno-hipófise fica mais susceptível a algum dano por isquemia, pois apresenta uma deficitária microirrigação arterial, com predominância de microvascularização venosa. A queda repentina do fluxo sanguíneo normal pode ocasionar isquemia na região, provocando uma necrose parcial ou total da adeno-hipófise.^{2,4} Nessa região são secretados diversos hormônios que regulam o metabolismo e controlam as mais diversas funções no organismo, destacando-se o hormônio do crescimento (GH), prolactina (PRL), hormônio folículo-estimulante (FSH), hormônio luteinizante (LH), hormônio estimulante da tireoide (TSH), hormônio adrenocorticotrófico (ACTH) e endorfinas.²

O hipopituitarismo adquirido causado por essa perda gradual dos hormônios adeno-hipofisários provocam significantes alterações no trabeculado ósseo, ocasionando osteopenia, e até mesmo, osteoporose. Além dessas alterações osteometabólicas, os pacientes diagnosticados com SSH apresentam aumento do risco cardiovascular, hipogonadismo e redução da força muscular.^{3,5}

Diversos estudos têm avaliado alterações osteometabólicas, bem como a redução da massa muscular em pacientes com SSH, onde é possível observar redução significativa do metabolismo ósseo mineral em consequência da redução de estrogênio, PRL, LH e FSH do hormônio do crescimento (GH).⁵⁻⁷ Nesse contexto, observa-se que a deficiência hormonal tem se mostrado com um fator preponderante nas características craniofaciais dos indivíduos. O desequilíbrio hormonal, principalmente relacionado aos hormônios produzidos na adeno-hipófise, demonstram que variações esqueléticas dos ossos gnáticos decorrentes de alterações hormonais podem interferir no padrão craniofacial desses pacientes, e de certa forma, causar algum dano para esses indivíduos.^{8,9,10}

Estudos envolvendo aspectos odontológicos em indivíduos com SSH são escassos, visto que apenas uma pesquisa avaliando o status dental e parâmetros salivares em um grupo de pacientes com SSH foi recentemente descrito na literatura, a qual foi conduzida por partes dos autores do presente artigo.¹¹ Em adição, aparentemente não existem estudos publicados que tenham analisado o padrão craniofacial de indivíduos acometidos por hipoptuitarismo crônico ocasionado por necrose pituitária pós-parto até a presente data. Portanto, o objetivo do presente estudo inédito foi realizar uma avaliação imaginológica sobre a morfologia craniofacial de pacientes diagnosticados com SSH oriundos do Brasil.

METÓDOS

Desenho do estudo

Foi realizado um estudo observacional, caso-controle, com pacientes previamente diagnosticados com SSH pareados por sexo e idade com indivíduos não afetados por essa condição. Em adição, o presente desenho metodológico seguiu as diretrizes indicadas pelo STROBE (STrengthening the Reporting of Observational studies in Epidemiology) para estudos observacionais (<https://www.strobe-statement.org/>).

Contexto

Os voluntários com SSH foram provenientes do Serviço de Endocrinologia e Diabetologia do Hospital Universitário Walter Cantídio (Fortaleza, Ceará, Brasil), que estavam em acompanhamento clínico há mais de 10 anos. Nesse serviço hospitalar, o qual é referência em Endocrinologia no Nordeste brasileiro, os pacientes foram encaminhados para que fossem realizados os exames de imagem no serviço de Imaginologia Odontológica da Faculdade de Farmácia, Odontologia e Enfermagem da Universidade Federal do Ceará (UFC). Todos os participantes da pesquisa assinaram um termo de consentimento livre e esclarecido, e o estudo foi conduzido segundo protocolo de pesquisa aprovado pelo Comitê de Ética em Pesquisa em Seres Humanos da Universidade Federal do Ceará (número de aprovação # 983.022).

Participantes

A população de indivíduos com SSH consistiu de 66 pacientes registrados no ambulatório de Endocrinologia e Diabetologia do Hospital Universitário Walter Cantídio (Brasil), cujo diagnóstico foi baseado na presença de história obstétrica clássica para a SSH (presença de hemorragia pós-parto ou por complicações obstétricas) e presença de deficiência

hormonal em reposição. Após a fase de recrutamento que ocorreu durante os atendimentos ambulatoriais, foram excluídos 37 pacientes pelos seguintes motivos: não comparecimento às consultas médicas rotineiras durante a fase de recrutamento desta pesquisa (n=22) e não retorno aos telefonemas (n=15). Após essa fase, 29 voluntários com SSH foram submetidos a uma anamnese e encaminhados para realização de teleradiografia lateral digital no serviço de imaginologia odontológica da Faculdade de Farmácia, Odontologia e Enfermagem da Universidade Federal do Ceará objetivando realizar posterior análise cefalométrica. Desse total, uma paciente veio a óbito, uma paciente apresentava incapacidade física que não a permitia a participação do estudo e 8 pacientes não realizaram o exame imaginológico odontológico necessário para a condução da presente investigação. Portanto, a amostra final foi composta por 19 indivíduos com SSH e para cada caso um voluntário não portador de SSH ou alterações sistêmicas que pudessem interferir no metabolismo ósseo foi pareado por sexo e idade. Dessa forma, 38 voluntários foram analisados de acordo com as variáveis cefalométricas adotadas para a presente pesquisa (Figura 1).

Variáveis

As variáveis analisadas no presente estudo foram idade, características clínico-laboratoriais relativas à SSH, medidas cefalométricas lineares e angulares, além do valor do escore de desvio padrão (SDS) dessas medidas. As medidas cefalométricas foram baseadas nos seguintes pontos craniométricos: Ponto Sela (S) - ponto localizado no centro geométrico da sela túrcica; Ponto Basio (Ba) - ponto localizado na porção mais inferior na margem anterior do forame Magno; Ponto Nasio (N) - ponto mais anterior da sutura fronto-nasal; Ponto Pório (Po) - ponto mais superior do meato acústico externo; Ponto Orbital (Or) - ponto mais inferior no contorno inferior da órbita; Ponto Pterigóideo (Pt) - ponto mais superior e posterior da fossa pterigomaxilar; Ponto A - ponto localizado na maior concavidade da porção anterior da maxila; Ponto Espinha Nasal Anterior (ENA) - ponto localizado na porção mais anterior da espinha nasal anterior; Ponto P' - ponto localizado na intersecção da imagem radiográfica do soalho nasal com a linha NA; Ponto Espinha Nasal Posterior (ENP) - ponto localizado na porção mais posterior da maxila óssea; Ponto B - ponto localizado na maior concavidade da porção anterior da sínfise mentoniana; Ponto Pogônio (Pg) - ponto mais anterior do contorno anterior da sínfise mentoniana; Ponto E - ponto mais anterior da sínfise mentoniana, tomando como base uma perpendicular ao plano mandibular (Go-Me); Ponto Gnátio (Gn) - ponto mais anterior e inferior da sínfise mentoniana; Ponto Mentoniano (Me) - ponto mais inferior da sínfise mentoniana;

Ponto Gônio (Go) - ponto mais inferior e posterior da mandíbula; Ponto Condílio (Co) - ponto mais superior e posterior do côndilo mandibular; Ponto Pró-nasal (Pn) - ponto mais anterior do nariz; Ponto Columela (Cm) - ponto mais anterior e inferior do nariz; Ponto Subnasal (Sn) - ponto de união entre o nariz e o lábio superior; Ponto Lábio Superior (Ls) - ponto mais anterior do lábio superior; Lábio inferior (Li) – ponto mais anterior do vermelhão do lábio inferior; Incisal do incisivo superior (iis) – ponto mais inferior da coroa do incisivo central superior; Incisal do incisivo inferior (iii)– ponto mais superior da coroa do incisivo central inferior; Ápice do incisivo inferior (aii) – ponto mais inferior do ápice radicular do incisivo central inferior; Ponto Stomion Superior (Sts) - ponto mais inferior do lábio superior; Ponto Pogônio Mole (Pg') - ponto mais anterior do queixo; Ponto Palato Mole (pm) - ponto situado no meio da parede posterior do palato mole; Ponto Adenóide (ad) - ponto situado na parede posterior da faringe no nível do ponto palato mole (pm); Ponto bl - ponto situado na parede posterior da língua onde esta cruza com a borda inferior da mandíbula; Ponto bf - ponto situado na parede posterior da faringe na altura do ponto bl; Ponto C3 - Ponto mais antero-inferior da 3ª vértebra cervical; Ponto H - Ponto anterior, mais superior, do osso hióide;

Fontes de dados/ Mensuração

As telerradiografias laterais digitais foram obtidas através do equipamento Kodak K9000 3D (Kodak Dental Systems, Carestream Health, Rochester, NY, EUA) do curso de Odontologia da UFC, com uma escala de cinza de 14 bits (16384 tons), kilovoltagem e miliamperagem ajustadas de acordo com o tamanho de cada paciente. Os pacientes ficaram de pé com suas cabeças posicionadas corretamente no cefalostato e orientadas horizontalmente no plano de Frankfurt, com os dentes em máxima oclusão. As telerradiografias foram exportadas em formato TIFF (Tagget Image File Format) sem compressão e importadas para o software Radiocef Studio 2 (Radiomemory, Belo Horizonte-MG), onde foram calibrada em 300 dpi. Para cada paciente SSH e controle, o diagnóstico das cefalométrias foram avaliadas pela análise pré-determinada de acordo com Mcnamara,¹² bem como uma análise designada no presente estudo como “Sheehan” e customizada por meio da ferramenta Mixcef do software, a qual permite criar traçados individualizados. No total, foram avaliados 30 fatores considerando as duas análises cefalométricas. A análise “Sheehan” utilizou 11 medidas lineares/angulares (S-Go, N-me, Altura Facial Posterior/Anterior, EAPS, EAP, Ba-Ena, Palato Mole, SPW, MP-H, C3-H, Rgn-H) e 6 medidas angulares (S.N.A, S.N.B, A.N.B, Ba.SN, SN.GoGn, PoOr.GoMe).

Na análise Mcnamara os fatores avaliados foram 9 medidas lineares/angulares (A-N Perpendicular, Co-Gn, Co-A, Diferença maxilar/mandibular, Ena-Me, Iii-A.Pog, Nfa-Nfp, Pog-N Perpendicular, Bfa-Bfp) e 3 medidas angulares ((PmSn.Ls), (PoOr. GoMe), (BaN.PtmGn)). A figura 2 evidencia os fatores utilizados, bem como a demarcação dos pontos de referência descritos.

Viés

Para evitar/minimizar a ocorrência de viés de seleção, foram recrutados pacientes independentemente da severidade de alterações osteometabólicas que os mesmos pudessem apresentar, tendo sido realizados esforços no sentido de recrutar todas as pacientes em atendimento rotineiro no ambulatório médico, bem como foi realizado cálculo amostral prévio. Para evitar/minimizar a ocorrência de viés de informação, foi realizada uma anamnese detalhada e análise aprofundada dos prontuários médicos a fim de se obterem dados consistentes. Para evitar/minimizar a ocorrência de viés de medição, foi realizada análise de confiabilidade antes da realização da medição dos desfechos determinados para a presente investigação, bem como a utilização das imagens originais sem compressão no formato TIFF.

Tamanho do estudo

Em virtude da SSH ser considerada uma doença rara, com incidência de 0,2 a 2,8 casos por 100.000 mulheres em países desenvolvidos realizou-se um cálculo amostral para o presente estudo.¹³ Baseado no estudo de FUNATSU et al (2006) que observou que os participantes não tratados com hormonoterapia apresentavam menos medida de Pog-Go que os pacientes controle ($70,5 \pm 4,3$ versus $74,7 \pm 4,2$) estima-se necessário avaliar 19 pacientes por grupo de estudo a fim de obter uma amostra que represente com 80% de poder e 95% de confiança a hipótese alternativa deste estudo.⁹

Variáveis quantitativas

Todas as 30 medidas foram mensuradas em milímetros (medidas lineares) ou graus (medidas angulares), conforme cada análise adotada. As mensurações e os traçado cefalométricos predictivos foram realizados automaticamente pelo software RadioCef 2.

Confiabilidade

Foi realizada uma análise cefalométrica de 38 teleradiografias laterais digitais em um intervalo de 30 dias, para garantir a confiabilidade e concordância das medições. Para avaliar erros de reprodutibilidade, foram realizadas as seguintes análises: (1) coeficiente de correlação intraclass (CCI) para avaliar erros sistemáticos referentes aos dados numéricos, (2) fórmula de Dahlberg para avaliar erros casuais das medições realizadas. Em relação ao CCI, foi utilizado o modelo CCI de efeitos aleatórios bidirecional e com intervalo de confiança de 95%, considerando-se satisfatórios os valores com $p < 0,05$. Para avaliar os possíveis erros técnicos de método, foi utilizada a fórmula de Dahlberg, a qual é representada pela seguinte equação: $erro\ de\ método = \sqrt{\frac{\sum d^2}{2n}}$. Portanto, o valor do erro representa a raiz quadrada do somatório dos valores ao quadrado das diferenças ($\sum d^2$) entre as medições (valor da segunda medição subtraído do valor da primeira medição) dividido pelo número de medições (n) multiplicado por dois.

Métodos estatísticos

Os dados cefalométricos foram expressos em forma de média e erro-padrão, submetidos ao teste de normalidade de Kolmogorov-Smirnov e comparados por meio do teste t de Student (dados paramétricos) e o teste ANOVA-2-way seguido do pós-teste de Bonferroni foi utilizado para avaliar a influência das variáveis clínicas na variação das medidas cefalométricas nos dois grupos. Os dados categóricos foram expressos em forma de frequência absoluta e percentual e comparados por meio dos testes exato de Fisher ou Qui-quadrado de Pearson (SPSS 20,0, $p < 0,05$). A comparação dos dados cefalométricos entre os indivíduos com SSH e os controles foi baseada no SDS (standard deviation score) é um escore calculado com base na intensidade da diferença de cada medida em relação à média do seu grupo ajustado ao desvio-padrão do mesmo. Assim, o SDS foi calculado através da diferença de cada valor de medida obtido pela média do seu grupo e, esta subtração foi dividida pelo desvio-padrão do mesmo grupo ($SDS = (X - Mean) / SD$, onde X é a medida, mean é a média do grupo e SD é o desvio-padrão do grupo), o qual é utilizado para verificar a homogeneidade ou a heterogeneidade dos valores do grupo em estudo, onde os valores menores que -2 ou maiores 2 são definidos como anormal.¹⁴

RESULTADOS

Características gerais do grupo SSH

A idade nesse grupo variou entre 49 a 86 anos, como média de $65,47 \pm 10,19$ anos. Em relação à distribuição dos casos por décadas de vida, foi observado uma paciente na faixa etária de 40 a 49 anos e as demais pacientes encontraram-se distribuídas similarmente entre as demais faixas etárias, havendo 6 indivíduos em cada uma dessas faixas (50 a 59, 60 a 69, e maior ou igual a 70 anos de idade). A idade das pacientes na época do diagnóstico da SSH variou entre 31 e 61 anos de idade, com média de $40,4 \pm 7,78$ anos. A idade das pacientes referente ao seu último parto, quando os eventos obstétricos característicos da SSH ocorreram, variou entre 23 e 40 anos, com média de $29,87 \pm 5,52$. O atraso no diagnóstico dessa condição, representado pelo tempo decorrido entre o último parto e a idade na qual o diagnóstico foi realizado variou entre 1 e 31 anos, exibindo média de $10,79 \pm 9,07$ anos. Em relação aos achados clínicos e/ou laboratoriais associados à SSH, foi observado no diagnóstico: agalactia (53,33%), alterações no ciclo menstrual (53,33%), hipotireoidismo (100%), adinamia (60%), deficiência de prolactina (33,33%), deficiência de FSH/LH (73,33%), deficiência de cortisol (86,66%), e deficiência do hormônio do crescimento (93,33%). O valor médio de glicemia em jejum foi de $88,67 \pm 11,54$ mg/dL, não sendo observado diabetes mellitus nas pacientes do estudo. Em relação a determinadas características do parto, 50% das pacientes referiram parto em domicílio e em 86,67% dos casos foi constatada algum tipo de complicação obstétrica. As pacientes encontravam-se em reposição para déficit do eixo tireidiano e adrenal, sem relato de uso do hormônio do crescimento.

Reprodutibilidade do método

Em relação às medições realizadas, observou-se uma reprodutibilidade e confiabilidade do método significativa para todas as medidas (Tabela 3), variando de satisfatório ($r=0,611$) a muito satisfatório ($r=0,988$). Em adição, a avaliação quanto ao erro técnico das medições, os valores do coeficiente de Dalberg foram satisfatórios, variando de 1,01 a 2,97.

Traçados diagnósticos no grupo SSH

A análise estatística descritiva dos dados das pacientes com SSH está expressa nas tabelas 4 e 5, onde são apresentados: média, desvio padrão médio, erro padrão médio, intervalo de confiança em 95%, valor mínimo, quartis e valor máximo.

A posição da maxila relacionada a base do crânio foi normal em 17,78% (S.N.A = 82^0), retroposicionada em 31,57% (S.N.A < 82^0), e posicionada em 52,63% (S.N.A > 82^0). A mandíbula estava adequadamente posicionada em 10,52% (S.N.B = 80^0), retroposicionada em 36,84% (S.N.B < 80^0), e posicionada em 52,63% (S.N.B > 80^0). Biprotusão maxilo-mandibular foi encontrada em 52,63%. A relação intermaxilar (ângulo A.N.B) foi normal em 15,78% ($2^0 < \text{A.N.B} < 4^0$), enquanto que a mandíbula estava retroposicionada em 10,52% (A.N.B > 4^0) e o prognatismo mandibular estava presente em 73,68% dos casos ($2^0 < \text{A.N.B}$).

Análise das características verticais (SN.GoGn) apresentou uma angulação do plano mandibular normal em 15,78% (SN.GoGn = 32^0), “face longa” ou padrão de crescimento aberto em 42,10% (SN.GoGn > 32^0), e padrão de crescimento “profundo” ou “face curta” em 42,10% (SN.GoGn < 32^0).

A relação do plano mandibular com a base do crânio (SN.GoGn) e com o plano de Frankfurt (PoOr.GoMe) apresentaram valores de normalidade em 36,84% (SN.GoGn = $31,50 \pm 4,60$; PoOr.GoMe = $22,70 \pm 4,30$), diminuído em 26,31% (SN.GoGn < $31,50 \pm 4,60$; PoOr.GoMe < $22,70 \pm 4,30$) e aumentado em 36,84% (SN.GoGn > $31,50 \pm 4,60$; PoOr.GoMe > $22,70 \pm 4,30$) dos pacientes.

O comprimento anterior da face encontrou-se diminuído em 89,47% (N-Me < 114 mm) e aumentado em 10,52% dos pacientes (N-Me > 114 mm). Foi observado, ainda, que o comprimento anterior da face (N-Me) foi menor nos pacientes com SSH quando comparado ao número controle (p=0,006).

Comparação das características esqueléticas entre os grupos SSH e controle

Os achados da análise cefalométrica do grupo SSH customizada pelo software para o presente estudo demonstraram que nesses indivíduos a média±EPM da medida S.N.B foi estatisticamente superior à do controle (p=0,026), e as medidas N-Me (p=0,006) e palato mole (p=0,011) foram significativamente inferiores quando comparadas ao grupo controle. Com relação aos achados obtidos por meio do SDS, as medidas S.N.B (p<0,001), A.N.B (p=0,001), SN.GoGn (p=0,005), PoOr.GoMe (p=0,034), S-Go (p<0,001), N-Me (p<0,001), EAPS (p=0,028), EAP (p=0,010) e palato mole (p<0,001) foram estatisticamente diferentes entre os grupos.

Por sua vez, a análise de McNamara evidenciou que a medida cefalométrica EnaMe foi estatisticamente inferior no grupo SSH quando comparada com o grupo controle (p<0,001). Em relação à avaliação por meio do SDS, foi observado que os grupos diferiram

estatisticamente em relação aos seguintes parâmetros: PmSnLs ($p=0,010$), Pog-N perpendicular ($p<0,001$), Nfa-Nfs ($p=0,040$), Bfa-Bfb ($p=0,011$), Ena-Me ($p<0,001$) e PoOr.GoMe ($p=0,039$). A comparação das características esqueléticas entre os grupos SSH e controle podem ser visualizadas na Tabela 6 e Tabela 7 e na figura 3 e figura 4.

DISCUSSÃO

O hipopituitarismo anterior é caracterizado como uma alteração metabólica frequentemente investigado em pesquisas científicas, principalmente na área da Endocrinologia,¹⁵ e sua relação com a Odontologia ainda é considerado um campo fértil, mas pouco explorado. A necessidade de se desenvolverem constantes pesquisas nessa área é de extrema importância, uma vez que diversas endocrinopatias revelam intrínsecas manifestações no complexo craniofacial tais como hipopituitarismo,¹⁶ acromegalia.¹⁷ A SSH é um exemplo de endocrinopatia com possíveis manifestações estomatognáticas que devem ser investigadas, sendo que apenas um estudo com interface odontológica foi publicado até o presente momento,¹¹ tendo sido realizado pelo grupo de pesquisadores envolvidos neste artigo.

O hipopituitarismo adquirido manifestado no espectro da SSH é observado em países subdesenvolvidos tais como na Turquia com 114 casos,¹⁸ Índia (18 casos),¹⁹ Arábia Saudita (30 casos),²⁰ Costa Rica (60 casos).²¹ Entretanto, mesmo o Brasil sendo considerado um país em desenvolvimento, de economia emergente, alguns autores têm reportado a ocorrência da SSH em indivíduos brasileiros, mas com número reduzido de casos publicados.^{11,22} O presente trabalho, quando comparado a estudos em outros países ou mesmo brasileiros, descreve a análise de um número significativo de indivíduos com SSH, o que reforça a importância dos resultados encontrados.

Alterações metabólicas são distúrbios comumente encontrados nos pacientes com SSH e estudos têm relatado uma íntima relação entre a deficiência de hormônios hipofisários e o seu efeito sobre o metabolismo ósseo e muscular.^{3,23} Embora os exames por imagem sejam ferramentas extensivamente utilizadas para se analisar o efeito de diferentes alterações hormonais sobre os ossos gnáticos e conseqüentemente no padrão morfológico maxilomandibular.^{9,16,17} Ainda não há estudos na literatura que tenham avaliado as características morfológicas craniofaciais de pacientes SSH, o que torna a nossa pesquisa inédita para esse tipo de análise. A análise cefalométrica conduzida no presente estudo, embora possa apresentar certa limitação por não haver pesquisas similares que permitam confrontar os dados obtidos, gerou resultados interessantes ainda não explorados na SSH.

Neste estudo foram observados dados estatisticamente significantes em relação a medidas lineares e angulares dos fatores cefalométricos estudados. Traçando-se um paralelo, diferenças significantes também foram encontradas quando o padrão craniofacial de pacientes com outras síndromes e deficiências hormonais relacionadas à adeno-hipófise foram avaliadas por meio de telerradiografias digitais.^{10,14}

A presente investigação utilizou determinadas análises cefalométricas angulares relacionadas ao ponto craniométrico “S” (S.N.A, S.N.B e A.N.B), o qual se refere à sela Túrctica. Anatomicamente, tal estrutura contém em seu interior a glândula hipófise,²⁴ desempenhando papel chave na fisiopatologia da SSH visto que tem sido reportado alterações morfológicas da hipófise decorrentes da necrose tais como sela Túrctica vazia ou parcialmente preenchida.^{1,18,25} Analisando a posição anteroposterior mandibular do arco dentário em relação à base do crânio, aferida por meio do ângulo S.N.B,²⁶ foi observado um prognatismo mandibular em mais de 50% (S.N.B > 80⁰) dos indivíduos pertencentes ao grupo SSH, assim como um prognatismo maxilar (S.N.A > 82⁰). Tais achados resultaram, portanto, em uma relação de biprotrusão maxilo/mandibular dos arcos dentários. A análise por meio de SDS também sugeriu uma maior discrepância entre os ossos gnátios e um maior prognatismo mandibular considerando-se os valores de normalidade do ângulo A.N.B.²⁷ Além disso, a rotação no sentido anti-horário do plano mandibular (SN.GoGn < 32⁰) foi presente em 42,1% dos pacientes com SSH, o que pode ser justificado pela prevalência acentuada de ausências dentárias já descrita previamente pelo nosso grupo em tais pacientes,¹¹ o que caracteriza um padrão de crescimento profundo ou face curta.²⁸

Valores referentes ao comprimento do palato mole se encontraram diminuídos nos indivíduos com SSH, considerando-se um valor normal de 12mm¹² como sendo a distância do aspecto posterior do palato mole para a parede posterior da faringe, o que é importante para se avaliar a via aérea posterior. O palato mole não se apresentou com a característica de adelgaçamento nos pacientes avaliados, porém, foi encontrado redução da via aérea posterior no grupo SSH. Mesmo tendo sido observada uma tendência de protusão bi maxilar nesses indivíduos, o palato mole pode ter se apresentando diminuído em decorrência de ptose da porção posterior da faringe.

Em relação ao comprimento facial, o grupo SSH apresentou altura da face anterior diminuída (N-Me < 114mm) na grande maioria dos indivíduos, caracterizando uma face mesio ou braquicefálica. Tal aspecto não ocorreu com os valores médios da altura facial posterior (S-Go) entre esses pacientes. De fato, essa diferença em relação à medida N-Me pode ser atribuída

às perdas dentárias encontradas em pacientes com SSH conforme estudo prévio, e, assim, a face anterior se torna diminuída.^{11,18} Embora a angulação do plano mandibular esteja aumentada em mais de 30% dos pacientes com SSH (SN.GoGn > 31,50 ± 4,60), tal fato pode ser explicado pelo aumento da medida Co-Gn que faz com que o ângulo do plano mandibular também aumente.³⁰ Considerando que o aumento do valor do ângulo goníaco que pode ser um reflexo do status dos músculos da mastigação, possíveis fatores relacionados a pacientes com SSH tais como possível redução de massa muscular, deficiência de GH podem contribuir para uma progressiva perda de rigidez dessa musculatura facial, somado-se a severas perdas dentais, e assim, como importância clínica, observa-se dificuldade de mastigação e déficit nutricional.^{11,31,32}

O desequilíbrio na produção de hormônios da adenohipófise, de uma forma geral, altera o metabolismo óssea e muscular, podendo tornar o complexo maxilomandibular vulnerável a modificações esqueléticas. A deficiência de GH é uma das mais comuns alterações hormonais em mulheres com SSH.³ Diversos estudos atribuem a deficiência de GH a ocorrência de mudanças no metabolismo ósseo maxilomandibular, sendo a maxila mais susceptível a alterações metabólicas por ser prevalente mais trabécular, enquanto mais corticalizada na mandíbula.¹⁴ Os pacientes do presente estudo são indivíduos que cursaram com hipopituitarismo por um longo período e não receberam tratamento de reposição de GH conforme mencionado em estudo prévio,¹¹ portanto, susceptíveis a significativas alterações esqueléticas decorrentes dos níveis alterados desse hormônio. Tal achado pode ter contribuído para uma diminuição linear do comprimento facial anterior e alteração no padrão craniofacial dos indivíduos com SSH avaliados. Outra hipótese que justifique em parte os resultados encontrado neste estudo é que a deficiência crônica dos hormônios hipofisários FSH e LH alteram substancialmente o padrão do trabeculado ósseo.⁶ Em um trabalho experimental que avaliou o papel de receptores de hormônios gonadais em ratos foi observado que os hormônios sexuais estavam intimamente relacionados ao crescimento craniofacial.³³ Portanto, tais estudos reforçam o fato de que a deficiência hormonal isolada ou múltipla impactam negativamente no equilíbrio metabólico ósseo, podendo repercutir no padrão craniofacial, como observado no presente estudo.

CONCLUSÃO

Nesse contexto, a partir dos resultados encontrados no presente estudo, conclui-se que os indivíduos com SSH analisados se caracterizavam por apresentar prognatismo maxilo/mandibular, comprimento do palato mole reduzido, plano mandibular aumentado e

padrão de face curta. Portanto, no contexto das endocrinopatias, o presente estudo destaca a importância de estudos que avaliem a morfologia craniofacial em desordens osteometabólicas como a SSH, embora esta seja ainda pouco estudada no campo da Odontologia. Estudos futuros que avaliem o padrão da arquitetura óssea maxilomandibular podem adicionar informações importantes no contexto da SSH que ainda é prevalente em países subdesenvolvidos, mas também pode ser encontrada em países em desenvolvimento, o que reforça a necessidade de mais investigações científicas no campo dessa endocrinopatia.

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Tabela 1. Descrição das variáveis cefalométricas segundo McNamara.

Parâmetro	Medida	Definição
Maxila em relação à base do crânio	A-N Perpendicular	Distância em milímetros do ponto A à uma linha que passa em N e perpendicular ao plano horizontal de Frankfurt (PoOr).
Mandíbula em relação à maxila	Co-Gn	Distância do ponto Co ao Gn
	Co-A	Distância do ponto Co ao ponto A
	Diferença Mx-Md	Diferença maxilomandibular
	Ena-Me	Distância entre a Ena ao Me
	PoOr.GoMe	Ângulo formado pelo plano horizontal de Frankfurt e pelo plano mandibular
	BaN.PtmGn	Ângulo entre as linhas Ba-N e Ptm-Gn
Mandíbula em relação à base do crânio	Pog-N Perpendicular	Distância em milímetros do ponto Pog à uma linha que passa em N, perpendicular ao plano horizontal de Frankfurt (PoOr).
	Iii A-Pog	Distância do Incisivo inferior a linha A-Po
	Nfa-Nfp	Distância linear entre Nfa e Nfp
	Bfa-Bfp	Distância linear entre Bfa e Bfp

Tabela 2. Descrição das variáveis cefalométricas adotadas para a análise customizada realizada no presente estudo.

Parâmetro	Medida	Definição
Relação maxilar	S.N.A	Ângulo formado pelas linhas S-N e N-A
Relação mandibular	S.N.B	Ângulo formado pelas linhas S-N e N-B
Relação maxilomandibular	A.N.B	Diferença dos ângulos S.N.A e S.N.B
	Ba.SN	Ângulo formado pela intersecção das linhas S-N e S-Ba
	SN.GoGn	Ângulo formado pela intersecção das linhas S-N e Go-Gn
	PoOr.GoMe	Ângulo formado pelo plano horizontal de Frankfurt e pelo plano mandibular
	S-Go	Distância entre os pontos S e Go
	N-Me	Distância entre os pontos N e Me.
	Altura Fac Post Ant	Relação entre S-Go / Nme
Espaço aéreo faríngeo	EAPS	Largura do espaço aéreo posteriormente ao palato mole ao longo de uma linha paralela à linha Go-B, que passa pelo ponto médio do comprimento efetivo do palato mole
	EAP	Distância linear entre um ponto sobre a base da língua e outro ponto sobre a parede posterior da faringe
	Ba-ENP	Distância entre os pontos Ba e o ângulo ENA
Palato mole	Palato mole	Comprimento do palato mole
	SPW	Largura do palato mole
Ossó hióide	MP-H	Distância entre o plano mandibular e o osso hióide
	C3-H	Distância entre C3 e o osso hióide
	Rgn-H	Distância entre o ponto de retrognatão mais protuso e o osso hióide

Tabela 3. Análise do método de erro empregada na presente pesquisa.

	Coefficient		
	e de Dalberg	Coefficiente de correlação intraclass	
		p-Valor	r
Medida			
S.N.A	2,06	<0,001	0,978*
S.N.B	1,86	<0,001	0,988*
A.N.B	1,27	<0,001	0,992*
Ba-SN	2,43	<0,001	0,921*
SN,GoGn	2,00	<0,001	0,991*
PoOr,GoMe	1,74	<0,001	0,989*
S-Go	2,97	<0,001	0,985*
N-Me	1,60	<0,001	0,995*
Altura Fac Post/Ant	0,02	<0,001	0,978*
EAPS	1,29	<0,001	0,957*
EAP	1,01	<0,001	0,971*
Ba-Ena	1,81	<0,001	0,941*
Palato Mole	2,60	<0,001	0,963*
SPW	1,10	0,005	0,611*
MP-H	2,53	<0,001	0,975*
C3-H	1,32	<0,001	0,973*
Rgn-H	2,18	<0,001	0,986*

*p<0,05 (correlação de Pearson).

Tabela 4: Valores descritivos da análise cefalométrica “Sheehan”

	Média	Std. Desvio	Std. Erro	95% Confiança Intervalo da média		Mínimo	Q1	Q2	Q3	Máximo
Controle										
S.N.A	82,62	4,58	1,05	80,41	84,82	73,95	79,84	82,73	85,86	91,45
S.N.B	79,12	4,59	1,05	76,91	81,33	71,67	76,68	78,82	82,34	89,57
A.N.B	3,50	3,06	0,70	2,02	4,97	-3,26	1,88	4,14	5,70	8,49
Ba.SN	132,76	5,16	1,18	130,27	135,24	123,30	129,93	131,91	136,43	143,54
SN.GoGn	35,06	6,66	1,53	31,86	38,27	24,28	28,59	35,55	41,21	47,83
PoOr.GoMe	27,39	6,28	1,44	24,36	30,41	16,98	22,88	29,20	30,58	40,41
S-Go	69,72	4,60	1,06	67,50	71,94	62,10	66,83	69,02	73,03	77,61
N-Me	110,85	5,10	1,17	108,39	113,31	102,82	105,35	112,02	114,33	119,60
Altura Fac Post Ant	0,63	0,05	0,01	0,61	0,65	0,56	0,59	0,62	0,68	0,72
EAPS	11,38	3,00	,69	9,93	12,82	6,32	9,04	11,83	13,94	17,95
EAP	11,03	3,36	,77	9,42	12,65	5,31	9,41	11,16	12,83	19,06
Ba-Ena	42,89	3,54	,81	41,19	44,60	37,39	40,18	42,81	45,14	50,25
Palato mole	32,46	4,26	,98	30,40	34,51	23,27	29,34	33,21	36,30	39,24
SPW	8,04	1,02	,23	7,55	8,53	5,84	7,15	7,96	8,80	9,82
MP-H	15,24	5,08	1,17	12,79	17,69	8,31	10,47	14,62	19,13	28,41
C3-H	72,00	3,35	,77	70,38	73,61	64,18	70,45	71,99	73,93	78,22
Rgn-H	36,72	4,13	,95	34,73	38,71	30,64	33,18	35,18	40,80	44,85

Sheehan

S.N.A	83,85	4,51	1,04	81,67	86,02	75,14	80,89	83,41	86,72	91,71
S.N.B	82,57	4,55	1,04	80,38	84,77	76,03	78,45	81,73	86,33	90,14
A.N.B	1,27	3,87	,89	-,59	3,14	-3,60	-1,44	,90	3,22	10,25
Ba.SN	132,36	4,50	1,03	130,19	134,53	123,29	128,67	133,25	136,19	138,58
SN.GoGn	31,27	8,27	1,90	27,29	35,26	14,88	23,73	32,57	36,20	46,29
PoOr.GoMe	24,82	7,70	1,77	21,11	28,52	9,27	17,24	25,71	30,25	38,81
S-Go	66,83	5,44	1,25	64,21	69,46	58,28	62,74	66,96	68,93	81,29
N-Me	104,55	8,00	1,83	100,70	108,41	90,19	96,79	104,96	109,00	120,78
Altura Fac Post Ant	0,64	0,06	0,01	0,61	0,67	0,55	0,60	0,64	0,70	0,77
EAPS	12,43	2,41	,55	11,27	13,59	7,11	11,02	12,25	13,28	16,92
EAP	13,03	4,77	1,09	10,73	15,32	6,33	8,77	12,66	14,87	23,81
Ba-Ena	43,25	3,56	,82	41,53	44,96	36,53	41,03	43,46	45,45	49,05
Palato mole	28,80	4,13	,95	26,81	30,80	19,32	26,47	29,07	30,80	35,96
SPW	8,01	1,71	,39	7,18	8,83	4,72	7,42	8,07	9,40	10,69
MP-H	16,25	4,38	1,01	14,14	18,36	7,74	15,14	16,42	18,98	25,17
C3-H	70,48	6,18	1,42	67,50	73,46	58,91	65,83	70,15	72,31	88,39
Rgn-H	39,33	8,91	2,04	35,04	43,62	24,52	33,93	39,00	44,54	67,04

Tabela 5. Valores descritivos da análise cefalométrica de McNamara

	Média	Std. Desvio	Std. Erro	95% Confiança		Mínimo	Q1	Q2	Q3	Máximo
				Intervalo da média						
Controle										
AN Perpendicular	2,03	3,19	0,73	0,49	3,57	-4,89	-0,87	1,85	5,56	7,04
PmSn Ls	91,78	13,85	3,18	85,11	98,46	72,46	79,80	89,46	101,77	120,88
Co-Gn	106,75	5,93	1,36	103,90	109,61	95,22	102,45	107,08	110,87	117,68
Co-A	80,61	4,53	1,04	78,43	82,79	74,23	76,56	80,19	84,46	89,09
Diferença Mx Md	26,14	4,47	1,03	23,99	28,30	19,07	23,59	25,94	29,43	33,55
Ena-Me	65,37	4,96	1,14	62,98	67,76	58,44	61,18	64,19	68,56	77,92
PoOr.GoMe	27,39	6,28	1,44	24,36	30,41	16,98	22,88	29,20	30,58	40,41
BaN.PtmGn	-1,23	5,01	1,15	-3,65	1,18	-8,86	-5,78	-2,75	3,51	5,84
Pog-N Perpendicular	-,77	6,57	1,51	-3,94	2,40	-14,75	-6,66	-1,38	4,95	11,94
Iii APog	3,98	2,78	0,64	2,64	5,32	-1,12	2,16	3,35	5,91	10,07
Nfa-Nfp	11,38	3,00	0,69	9,93	12,82	6,32	9,04	11,83	13,94	17,95
Bfa-Bfp	11,03	3,36	0,77	9,42	12,65	5,31	9,41	11,16	12,83	19,06
Sheehan										
AN Perpendicular	3,01	2,96	0,94	0,89	5,13	-1,32	0,23	3,36	5,51	7,00
PmSn Ls	94,48	15,67	4,96	83,26	105,69	70,35	82,52	91,57	109,58	115,85
Co-Gn	127,51	64,31	20,34	81,50	173,51	101,57	103,44	108,30	111,20	310,25
Co-A	104,17	69,65	22,03	54,34	153,99	78,57	80,16	82,22	85,95	302,25
Diferença Mx Md	23,34	6,49	2,05	18,69	27,98	7,99	21,77	23,29	27,83	32,44
Ena-Me	59,07	7,48	2,37	53,72	64,42	48,04	52,64	59,80	65,12	70,57

PoOr.GoMe	24,65	5,92	1,87	20,41	28,89	15,69	20,64	24,60	28,05	34,72
BaN.PtmGn	-1,21	19,86	6,28	-15,41	12,99	-54,00	-4,82	2,99	10,77	15,41
Pog-N Perpendicular	2,90	6,41	2,03	-1,68	7,49	-7,61	-2,64	4,92	7,65	11,33
Iii APog	3,29	3,88	1,23	,52	6,07	-4,65	0,78	3,08	6,73	7,93
Nfa-Nfp	12,42	2,68	0,85	10,50	14,34	7,11	11,31	12,59	13,68	16,92
Bfa-Bfp	13,80	5,56	1,76	9,82	17,78	6,33	8,57	13,53	18,38	23,81

Tabela 6. Valor médio das medidas cefalométricas e do escore de desvio padrão (SDS) segundo a análise personalizada de “Sheehan”

	Grupos		p-Valor
	Controle	Sheehan	
Medidas cefalométricas			
S.N.A	82,62±1,05	83,85±1,04	0,410
S.N.B	79,12±1,05	82,57±1,04	*0,026
A.N.B	3,50±0,70	1,27±0,89	0,057
Ba.SN	132,76±1,18	132,36±1,03	0,802
SN.GoGn	35,06±1,53	31,27±1,90	0,128
PoOr.GoMe	27,39±1,44	24,82±1,77	0,267
S-Go	69,72±1,06	66,83±1,25	0,086
N-Me	110,85±1,17	104,55±1,83	*0,006
Altura Fac Post Ant	0,63±0,01	0,64±0,01	0,518
EAPS	11,38±0,69	12,43±0,55	0,242
EAP	11,03±0,77	13,03±1,09	0,145
Ba-Ena	42,89±0,81	43,25±0,82	0,761
Palato mole	32,46±0,98	28,80±0,95	*0,011
SPW	8,04±0,23	8,01±0,39	0,948
MP-H	15,24±1,17	16,25±1,01	0,515
C3-H	72,00±0,77	70,48±1,42	0,354
Rgn-H	36,72±0,95	39,33±2,04	0,254
SDS			
S.N.A	0,273±0,233	0,269±0,226	0,104
S.N.B	0,758±0,231	0,752±0,227	*<0,001
A.N.B	0,574±0,181	0,726±0,290	*0,001
Ba.SN	0,088±0,263	0,077±0,200	0,620
SN.GoGn	0,459±0,185	0,570±0,285	*0,005
PoOr.GoMe	0,334±0,187	0,410±0,281	*0,034
S-Go	0,531±0,194	14,529±0,27	*<0,001
N-Me	0,787±0,146	1,236±0,360	*<0,001
Altura Fac Post Ant	0,190±0,180	0,243±0,293	0,217
EAPS	0,436±0,286	0,350±0,184	*0,028
EAP	0,418±0,162	0,593±0,325	*0,010

Ba-Ena	0,099±0,228	0,100±0,231	0,543
Palato mole	0,884±0,236	0,858±0,223	*<0,001
SPW	0,018±0,137	0,029±0,384	0,909
MP-H	0,231±0,266	0,199±0,198	0,203
C3-H	0,245±0,125	0,451±0,423	0,129
Rgn-H	0,293±0,106	0,632±0,495	0,083

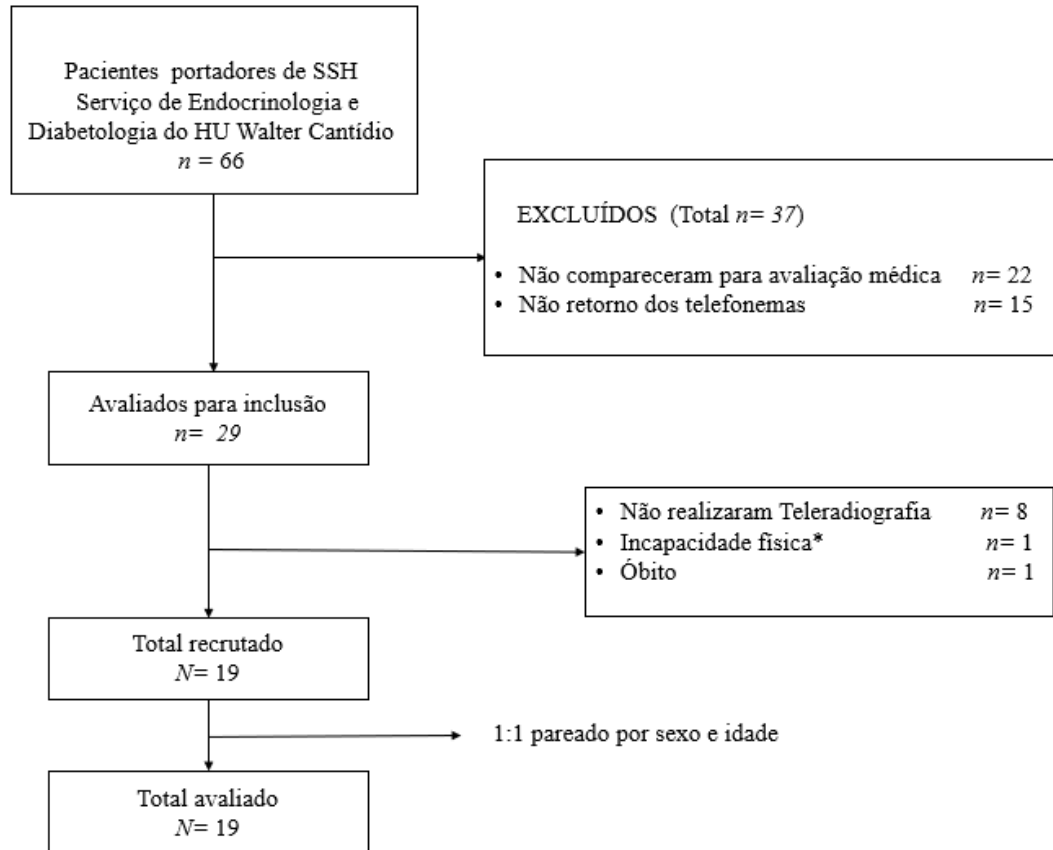
*p<0,05, teste t de Student (média±EPM).

Tabela 7. Valor médio das medidas cefalométricas e do escore de desvio padrão (SDS) segundo a análise de McNamara

	Grupos		p-Valor
	Controle	Sheehan	
Cefalometria			
AN Perpendicular	2,03±0,73	3,01±0,94	0,863
PmSn Ls	91,78±3,18	94,48±4,96	0,147
Co-Gn	106,75±1,36	127,51±20,3	0,340
Co-A	80,61±1,04	104,17±22,0	0,308
Diferença Mx Md	26,14±1,03	23,34±2,05	0,350
Ena-Me	65,37±1,14	59,07±2,37	*<0,001
PoOr.GoMe	27,39±1,44	24,65±1,87	0,280
BaN.PtmGn	-1,23±1,15	-1,21±6,28	0,478
Pog-N Perpendicular	-0,77±1,51	2,90±2,03	0,053
Iii APog	3,98±0,64	3,29±1,23	0,588
Nfa-Nfp	11,38±0,69	12,42±0,85	0,281
Bfa-Bfp	11,03±0,77	13,80±1,76	0,150
Situação dentária			
Total de dentes ausentes	14,16±1,57	23,95±2,17	*0,001
Dentes com sugestão de cáries	2,47±0,52	1,68±0,47	0,266
Dentes material restaurador	7,79±0,96	3,37±1,25	*0,008
CPO-D	24,42±1,16	29,00±0,99	*0,005
SDS			
AN Perpendicular	0,055±0,220	0,058±0,240	0,731
PmSn Ls	0,418±0,164	0,584±0,321	*0,010
Co-Gn	0,223±0,029	1,769±1,816	0,287
Co-A	0,238±0,020	2,680±2,583	0,273
Diferença Mx Md	0,269±0,167	0,369±0,315	0,084
Ena-Me	1,094±0,149	1,685±0,353	*<0,001
PoOr.GoMe	0,324±0,186	0,399±0,282	*0,039
BaN.PtmGn	0,173±0,076	0,524±0,693	0,330
Pog-N Perpendicular	0,649±0,230	0,647±0,229	*<0,001
Iii APog	0,176±0,164	0,246±0,441	0,388
Nfa-Nfp	0,392±0,275	0,327±0,191	*0,040

Bfa-Bfp	0,412±0,161	0,587±0,327	*0,011
---------	-------------	-------------	---------------

*p<0,05, teste t de Student (média±EPM).

Figura 1. Fluxograma da população avaliada do estudo

* Paciente apresentava incapacidade física que não a permitia a participação do estudo

Figura 2. Janela do software Radiocef Studio 2 onde está demonstrada a demarcação dos pontos cefalométricos utilizados para a presente pesquisa.

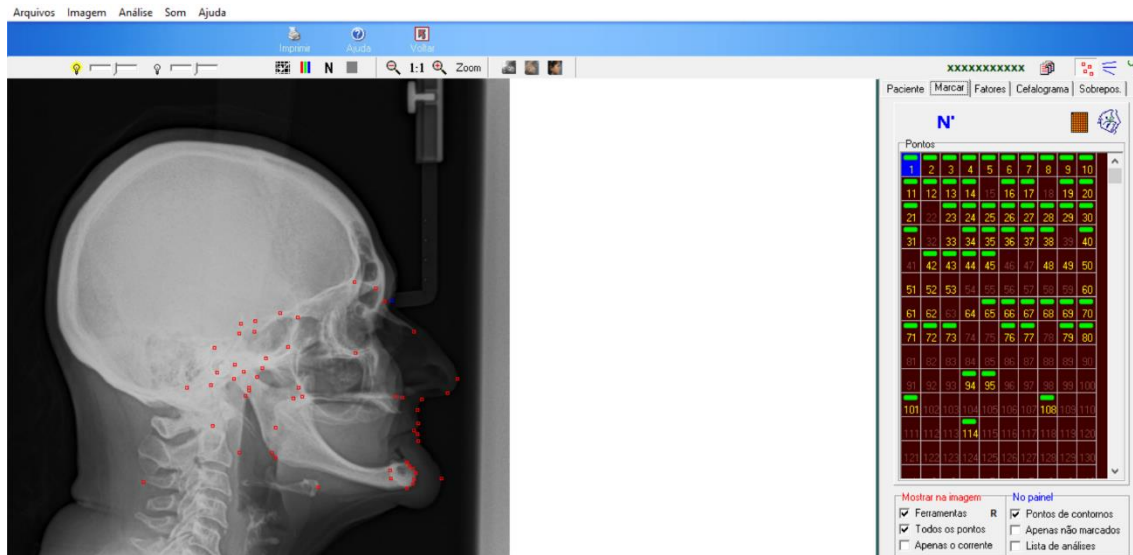


Figura 3. Gráfico do tipo boxplot com os valores de SDS segundo a análise cefalométrica de McNamara.

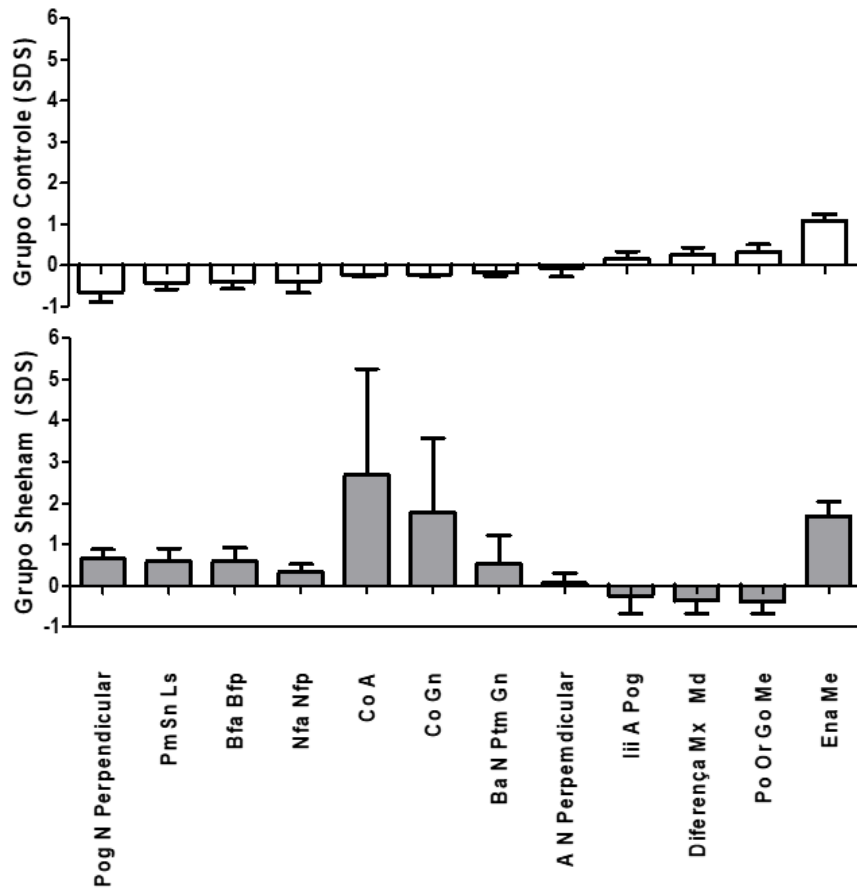
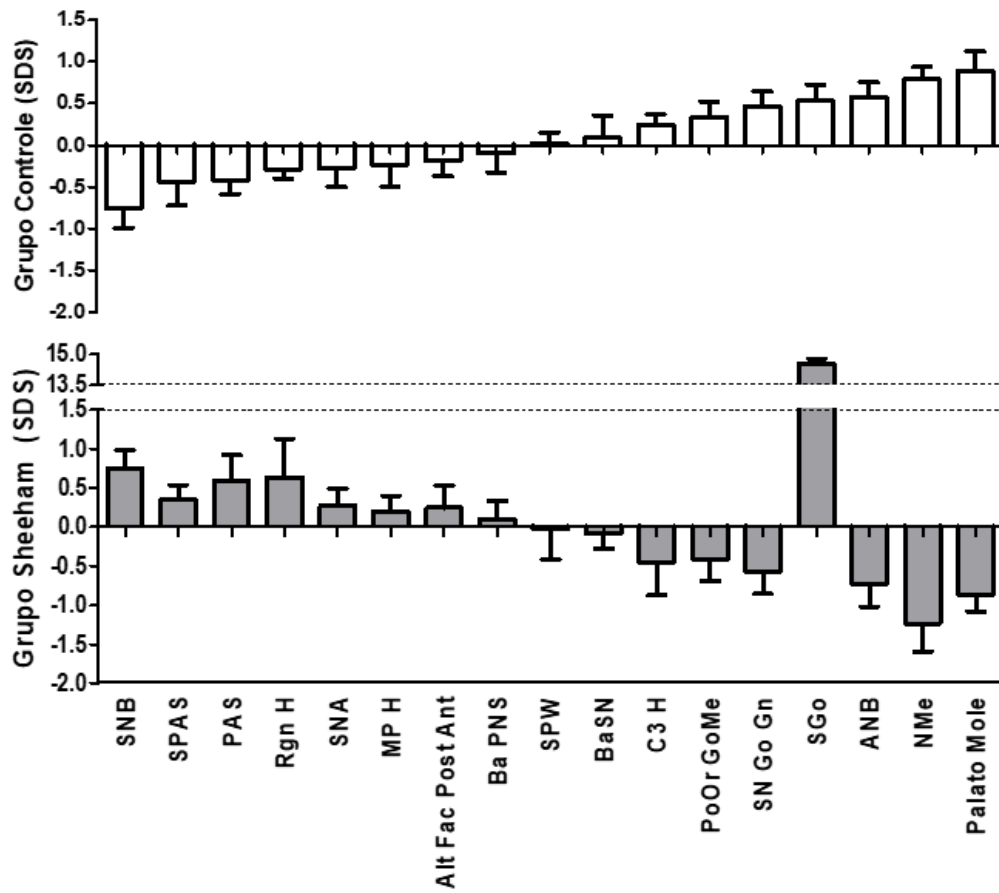


Figura 4. Gráfico do tipo boxplot com os valores de SDS segundo a análise cefalométrica customizada para o presente estudo.



4. CONCLUSÃO GERAL

As conclusões do presente estudo podem ser sumarizadas da seguinte maneira:

- 1) pacientes com SSH evidenciaram baixos níveis educacional e socioeconômico, fluxo salivar reduzido e severas perdas dentais.
- 2) indivíduos com SSH apresentaram padrão craniofacial caracterizado por prognatismo maxilar/mandibular, face curta, plano mandibular aumentado e comprimento do palato mole reduzido quando comparados a indivíduos sem SSH e pareados por sexo e idade.

5. REFERÊNCIAS (INTRODUÇÃO GERAL)

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ANEXO

ANEXO I. SEGUIMENTO DO REGIMENTO INTERNO

Art. 46 – As dissertações e as teses apresentadas ao Programa de Pós-Graduação em Odontologia da Universidade Federal do Ceará poderão ser produzidas em formato alternativo ou tradicional. O formato

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alternativo estabelece: a critério do orientador e com a aprovação da Coordenação do Programa, que os capítulos poderão conter cópias de artigos e/ou relatórios de patentes de autoria ou coautoria do candidato, publicados ou submetidos para publicação em revistas científicas, escritos no idioma exigido pelo veículo de divulgação.

§1º - O orientador e o candidato deverão verificar junto às editoras a possibilidade de inclusão dos artigos na dissertação ou tese, em atendimento à legislação que rege o direito autoral, obtendo, se necessária, a competente autorização, deverão assinar declaração de que não estão infringindo o direito autoral transferido à editora.

§2º - A dissertação e a tese em formatos tradicionais ou formatos alternativos deverão seguir as normas preconizadas pelo Guia para Normalização de Trabalhos Acadêmicos da Biblioteca Universitária disponível no sítio <http://www.biblioteca.ufc.br>. As partes específicas do formato alternativo deverão ser feitas em concordância com o *Manual de Normalização para Defesa de dissertação de Mestrado e tese de Doutorado no formato Alternativo do PPGO*, disponível no sítio <http://www.ppgo.ufc.br>.

§3º - As dissertações defendidas no formato alternativo deverão constar de, no mínimo, 01(um) capítulo, enquanto que as teses no mesmo formato deverão constar de, no mínimo, 02 (dois) capítulos.

§4º - Admite-se que a dissertação ou a tese sejam escritas e/ou defendidas em língua estrangeira seguindo as diretrizes definidas no regimento interno do Programa;

ANEXO II. PARECER CONSUBSTANCIAL DO COMITÊ DE ÉTICA

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PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: AVALIAÇÃO DE PARÂMETROS RADIOGRÁFICOS MAXILOMANDIBULARES E PERFIL DE PROTEÍNAS E PEPTÍDEOS SALIVARES EM PACIENTES COM SÍNDROME DE SHEEHAN

Pesquisador: Fábio Wildson Gurgel Costa

Área Temática:

Versão: 2

CAAE: 39632714.1.0000.5054

Instituição Proponente: UNIVERSIDADE FEDERAL DO CEARÁ

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 983.022

Data da Relatoria: 05/03/2015

Apresentação do Projeto:

Projeto de pesquisa do Prof. Fabio Wildson Gurgel Costa sobre as possíveis alterações nos ossos maxilomandibulares e no perfil de proteínas e peptídeos salivares em pacientes portadores da Síndrome de Sheehan. Será realizado um estudo observacional, caso-controle, transversal e analítico com os pacientes previamente diagnosticados e provenientes do Serviço de Endocrinologia do Hospital Universitário Walter Cantídio. Para cada caso será selecionado um controle de mesmo sexo e idade, não-sindrômico, e que seja paciente do curso de Odontologia da Faculdade de Farmácia, Odontologia e Enfermagem da Universidade Federal do Ceará. Todos os pacientes realizarão radiografia panorâmica digital e coleta de saliva. A ultrassonografia Doppler colorido de artérias carótidas somente será realizada nos pacientes síndrômicos. A presença de placas calcificadas ateromatosas e índices radiomorfométricos quantitativos e qualitativos serão avaliados nas tomadas panorâmicas. Através do exame ultrassonográfico será estimado o grau de estenose dessas artérias conforme metodologia descrita por Erthas et al. (2005). Quanto a saliva, serão estudados o fluxo salivar, pH e concentração de proteínas totais. Os dados coletados serão tabulados no software Microsoft Excel® versão 2010 e submetidos a análise estatística através do Statistical Package for the Social Sciences (SPSS), versão 17.0 para Windows®, sendo considerado com significância estatística p de 0,05.

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UF: CE **Município:** FORTALEZA

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Continuação do Parecer: 983.022

Objetivo da Pesquisa:

Objetivo Primario:

Avaliar parametros radiograficos maxilomandibulares e perfil de proteinas e peptideos salivares em pacientes com síndrome de Sheehan.

Objetivos Secundarios:

1. Avaliar a prevalencia de placas ateromatosas calcificadas em radiografias panoramicas e ultrassonografias de Doppler colorido de arterias carotidas de pacientes com síndrome de Sheehan.
2. Determinar a acuracia, sensibilidade e especificidade de radiografias panoramicas na deteccao de placas ateromatosas calcificadas observadas em ultrassonografias de Doppler colorido de arterias carotidas de pacientes com síndrome de Sheehan.
3. Correlacionar a presenca de placas ateromatosas calcificadas e fatores de risco cardiovasculares como presenca de hipertensao arterial sistemica, idade, perfil lipidico, presenca de diabetes ou intolerancia a glicose, aumento da circunferencia abdominal, antecedentes de eventos cardiovasculares e tabagismo em pacientes com síndrome de Sheehan.
4. Avaliar indices radiomorfometricos em radiografias panoramicas de pacientes com síndrome de Sheehan.
5. Avaliar o perfil de proteinas e peptideos salivares em pacientes com síndrome de Sheehan.

Avaliação dos Riscos e Beneficios:

A pesquisa apresenta baixo risco visto que a coleta de saliva constitui-se um procedimento nao-invasivo. Alem disso, as radiografias panoramicas e ultrassonografia doppler constituem-se exames imaginologicos bem estabelecidos com baixas doses de radiacao ionizante.

Quanto aos beneficios, apesar da raridade da Síndrome de Sheehan, faz-se necessario o conhecimento das alteracoes osseas maxilomandibulares e salivares que possam estar presentes nestes pacientes. A qualidade do osso mandibular e maxilar determina o planejamento da reabilitacao protetica, impactando nos tratamentos odontologicos. Acrescenta-se, ainda, que a radiografia panoramica, um exame de rotina em Odontologia, possa ser utilizado como um instrumento adequado para visualizar placas ateromatosas calcificadas consideradas fatores de risco cardiovasculares.

Comentários e Considerações sobre a Pesquisa:

A pesquisa tem merito cientifico e esta bem delineada sob o ponto de vista metodologico.

Considerações sobre os Termos de apresentação obrigatória:

O pesquisador apresentou a este comite: projeto, folha de rosto devidamente preenchida e

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Continuação do Parecer: 963.022

assinada pela chefe do DCO, TCLE, termo de fiel depositario da Clinica de Radiologia do Curso de Odontologia,orcamento, cronograma, declaracao de concordancia dos pesquisadores envolvidos, curriculo lattes, carta de encaminhamento e autorizacoes dos seguintes locais: Clinica de Radiologia do curso de Odontologia, Ambulatorio de Endocrinologia e Laboratorio da Bioquimica-UECE, e do Serviço de Cardiologia do HUWC, onde serão realizadas as ultrassonografias doppler de carótidas.

Recomendações:

Conclusões ou Pendências e Lista de Inadequações:

Não há pendências éticas nem documentais.

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Não

Considerações Finais a critério do CEP:

FORTALEZA, 12 de Março de 2015

Assinado por:
FERNANDO ANTONIO FROTA BEZERRA
(Coordenador)

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UNIVERSIDADE FEDERAL DO
CEARÁ/ PROPESQ



PARECER CONSUBSTANCIADO DO CEP

DADOS DA EMENDA

Título da Pesquisa: AVALIAÇÃO DE PARÂMETROS RADIOGRÁFICOS MAXILOMANDIBULARES E PERFIL DE PROTEÍNAS E PEPTÍDEOS SALIVARES EM PACIENTES COM SÍNDROME DE SHEEHAN

Pesquisador: Fábio Wildson Gurgel Costa

Área Temática:

Versão: 4

CAAE: 39632714.1.0000.5054

Instituição Proponente: UNIVERSIDADE FEDERAL DO CEARÁ

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 1.457.233

Apresentação do Projeto:

Emenda para a inclusão da Telerradiografia se faz necessária para caracterizarmos radiograficamente a sella Túrcica de pacientes com Síndrome de Sheehan, visto que esta condição caracteriza-se como uma forma de hipopituitarismo pós-parto secundário à necrose da glândula hipófise, a qual encontra-se, anatomicamente, na sela Túrcia. Dessa maneira, se faz necessária a Telerradiograia Lateral pois esta irá proporcionar uma avaliação mais criteriosa e fidedigna desse aspecto que é de grande relevância na Síndrome de Sheehan. Ademais, tal exame será realizado na clínica de radiologia odontológica do curso de Odontologia da Universidade Federal do Ceará, conforme documento de autorização anexo. A interpretação/análise de todas as imagens será realizada pelo pesquisador responsável. Em anexo encontra-se a segunda versão do Termo de Consentimento Livre e Esclarecido, o qual foi modificado para permitir a inclusão do referido exame.

Objetivo da Pesquisa:

Emenda para a inclusão da Telerradiografia se faz necessária para caracterizarmos radiograficamente a sella Túrcica de pacientes com Síndrome de Sheehan, visto que esta condição caracteriza-se como uma forma de hipopituitarismo pós-parto secundário à necrose da glândula hipófise, a qual encontra-se, anatomicamente, na sela Túrcia. Dessa maneira, se faz necessária a

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Continuação do Parecer: 1.457.233

Telerradiografia Lateral pois esta irá proporcionar uma avaliação mais criteriosa e fidedigna desse aspecto que é de grande relevância na Síndrome de Sheehan. Ademais, tal exame será realizado na clínica de radiologia odontológica do curso de

Odontologia da Universidade Federal do Ceará, conforme documento de autorização anexo. A interpretação/análise de todas as imagens será realizada pelo pesquisador responsável. Em anexo encontra-se a segunda versão do Termo de Consentimento Livre e Esclarecido, o qual foi modificado para permitir a inclusão do referido exame.

Avaliação dos Riscos e Benefícios:

Emenda para a inclusão da Telerradiografia se faz necessária para caracterizarmos radiograficamente a sela Túrcica de pacientes com Síndrome de Sheehan, visto que esta condição caracteriza-se como uma forma de hipopituitarismo pós-parto secundário à necrose da glândula hipófise, a qual encontra-se, anatomicamente, na sela Túrcica. Dessa maneira, se faz necessária a Telerradiografia Lateral pois esta irá proporcionar uma avaliação mais criteriosa e fidedigna desse aspecto que é de grande relevância na Síndrome de Sheehan. Ademais, tal exame será realizado na clínica de radiologia odontológica do curso de Odontologia da Universidade Federal do Ceará, conforme documento de autorização anexo. A interpretação/análise de todas as imagens será realizada pelo pesquisador responsável. Em anexo encontra-se a segunda versão do Termo de Consentimento Livre e Esclarecido, o qual foi modificado para permitir a inclusão do referido exame.

Comentários e Considerações sobre a Pesquisa:

Emenda para a inclusão da Telerradiografia se faz necessária para caracterizarmos radiograficamente a sela Túrcica de pacientes com Síndrome de Sheehan, visto que esta condição caracteriza-se como uma forma de hipopituitarismo pós-parto secundário à necrose da glândula hipófise, a qual encontra-se, anatomicamente, na sela Túrcica. Dessa maneira, se faz necessária a Telerradiografia Lateral pois esta irá proporcionar uma avaliação mais criteriosa e fidedigna desse aspecto que é de grande relevância na Síndrome de Sheehan. Ademais, tal exame será realizado na clínica de radiologia odontológica do curso de Odontologia da Universidade Federal do Ceará, conforme documento de autorização anexo. A interpretação/análise de todas as imagens será realizada pelo pesquisador responsável. Em anexo encontra-se a segunda versão do Termo de Consentimento Livre e Esclarecido, o qual foi modificado para permitir a inclusão do referido exame.

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Considerações sobre os Termos de apresentação obrigatória:

Emenda para a inclusão da Telerradiografia se faz necessária para caracterizarmos radiograficamente a sela Túrcica de pacientes com Síndrome de Sheehan, visto que esta condição caracteriza-se como uma forma de hipopituitarismo pós-parto secundário à necrose da glândula hipófise, a qual encontra-se, anatomicamente, na sela Túrcica. Dessa maneira, se faz necessária a Telerradiografia Lateral pois esta irá proporcionar uma avaliação mais criteriosa e fidedigna desse aspecto que é de grande relevância na Síndrome de Sheehan. Ademais, tal exame será realizado na clínica de radiologia odontológica do curso de Odontologia da Universidade Federal do Ceará, conforme documento de autorização anexo. A interpretação/análise de todas as imagens será realizada pelo pesquisador responsável. Em anexo encontra-se a segunda versão do Termo de Consentimento Livre e Esclarecido, o qual foi modificado para permitir a inclusão do referido exame.

Recomendações:

Não se aplica.

Conclusões ou Pendências e Lista de Inadequações:

Não se aplica.

Considerações Finais a critério do CEP:

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_612176_E1.pdf	04/03/2016 17:14:17		Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	2a_versao_do_TCLE.pdf	04/03/2016 17:12:21	Fábio Wildson Gurgel Costa	Aceito
Projeto Detalhado / Brochura Investigador	Segunda_versao_projeto_detalhado.pdf	04/11/2015 21:33:11	Fábio Wildson Gurgel Costa	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	Segunda_versao_do_TCLE.pdf	04/11/2015 21:31:06	Fábio Wildson Gurgel Costa	Aceito
Outros	Autorizacao_clinica_radiologia.pdf	19/10/2015 21:03:04	Fábio Wildson Gurgel Costa	Aceito
Outros	solicitacao_adendo.pdf	19/10/2015	Fábio Wildson	Aceito

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Outros	solicitacao_adendo.pdf	21:01:07	Gurgel Costa	Aceito
Projeto Detalhado / Brochura Investigador	Editado_13FEV_FÁBIO WILDSON_PROJETO SHEEHAN.pdf	18/02/2015 18:32:22		Aceito
Outros	Autorização Cardiologia.pdf	18/02/2015 18:29:18		Aceito
Outros	Currículo do Sistema de Currículos Lattes (Fábio Wildson Gurgel Costa).pdf	05/12/2014 21:19:28		Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE_Projeto FábioWildson.pdf	05/12/2014 21:18:40		Aceito
Outros	Autorização_Bioquímica.pdf	02/12/2014 21:43:12		Aceito
Outros	Folha de rosto.pdf	02/12/2014 19:29:06		Aceito
Outros	Fiel depositário.pdf	02/12/2014 19:28:28		Aceito
Outros	Ciência em concordar como pesquisador.pdf	02/12/2014 19:28:09		Aceito
Outros	Carta de encaminhamento.pdf	02/12/2014 19:26:40		Aceito
Outros	Autorização_Endocrinologia.pdf	02/12/2014 19:26:17		Aceito
Outros	Autorização_Clínica de radiologia.pdf	02/12/2014 19:26:00		Aceito
Folha de Rosto	Folha de rosto.jpg	02/12/2014 19:24:25		Aceito

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Não

FORTALEZA, 18 de Março de 2016

Assinado por:
FERNANDO ANTONIO FROTA BEZERRA
(Coordenador)

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ANEXO III. ARTIGO CIENTÍFICO PUBLICADO (CAPÍTULO 1) NO PERIÓDICO *MEDICINA ORAL PATOLOGIA ORAL Y CIRUGIA BUCAL* (pISSN 1698-4447 eISSN: 1698-6946)

Med Oral Patol Oral Cir Bucal. 2018 Jul 1;23 (4):e436-42.

Oral aspects in Sheehan Syndrome

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Publication Types: Research

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Dental status, salivary flow, and sociodemographic aspects in Sheehan Syndrome patients

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<http://dx.doi.org/doi:10.4317/medoral.22377>

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Abstract

Background: Sheehan's syndrome (SS) is one of the leading causes of hypopituitarism in developing countries. It occurs after postpartum necrosis of the pituitary gland, and it is considered a significant public health problem. This paper, apparently unpublished, aimed to perform an analysis on oral aspects in patients with SS.

Material and Methods: A cross-sectional study was performed with 23 women diagnosed with SS at the Division of Endocrinology and Diabetes (Walter Cantídio University Hospital, Fortaleza, Brazil).

Results: Data on sociodemographic, dental and salivary flow aspects were collected through a clinical approach and a panoramic radiograph request. The mean age was 64 ± 11.5 years old, with the sample consisting mainly of married women (56.5%), socioeconomic class C2 or D / E (78.2%) and years of education up to 8 years (69.5%). The presence of horizontal bone loss ($p < 0.001$) and bilateral pneumatization of the maxillary sinus ($p = 0.015$) were significant data. The mean number of absent teeth considering all subjects was 23.17 ± 9.7 , being statistically significant ($p < 0.001$). In relation to age, the mean number of missing teeth was higher in individuals over 65 years old ($p = 0.048$). Reduced salivary flow was observed in 78.3% of the patients. In a bivariate analysis, considering the outcome variables "missing teeth" and "reduced salivary flow", it was observed that economic class ($p < 0.001$), family income (0.037) and maxillary sinus pneumatization (0.032) were statistically significant.

Conclusions: In brief, patients with SS showed severe teeth loss, reduced salivary flow, and low educational status. This study addressed important aspects regarding oral findings in SS and highlighted the importance of researches in oral medicine.

Key words: Sheehan's Syndrome, hypopituitarism, tooth loss, salivary flow.

Introduction

The stomatognathic system has been considered a field for the manifestation of endocrine system disorders (1). Sheehan syndrome (SS), also known as postpartum pituitary necrosis (2), is an uncommon condition characterized by partial or total necrosis of the pituitary gland. Some clinical findings include agalactia, amenorrhea, asthenia, hypoglycemia, hypotension, hydroelectrolytic disorders, gain of weight, and constipation. The presence of multiple hormonal deficiencies leads to impairment of bone microarchitecture, which can cause osteopenia and even osteoporosis (3,4). Although there are no studies on the oral aspects in SS, the local effect of pituitary hormones deficiency on bone and dental tissues has been described. Reduction of estrogen levels may affect oral cavity epithelium, salivary gland function, and propensity for inflammatory processes related to periodontal tissues (5). The onset of inflammation in the oral cavity has a higher probability of further tooth loss (6). Since tooth pathologies have been associated with a more significant decline in functional capacity, physical imbalance, altered cognitive function, and impairment in the performance of communicative social skills (7), it reinforces the importance of studies evaluating oral aspects in patients with chronic hypopituitarism. In this context, this study aimed to evaluate tooth loss, sociodemographic data, and salivary flow in Brazilian SS patients. To date, there are no published studies focusing on the oral health of SS.

Material and Methods

A cross-sectional study was performed with patients diagnosed with SS from the Endocrinology and Diabetes Division at the Walter Cantídio University Hospital (Fortaleza, Ceará, Brazil), who had been in clinical follow-up for more than ten years. The research protocol was evaluated by the Human Research Ethics Committee of the Federal University of Ceará (approval number # 983,022).

SS is considered a rare disease, with an incidence of 0.2 to 2.8 cases per 100,000 women in developed countries (8). Thus, the present sample was of convenience. Patients with a previously confirmed diagnosis of SS, under periodic medical follow-up, and those that agreed to participate in this study after reading and signing an informed consent form were included. Patients who met the eligibility criteria were submitted to an anamnesis,

imaging exam, and salivary flow assessment. Sociodemographic aspects, dental functional status, salivary flow and medical data (age and time of diagnosis, the age of last childbirth, presence/absence of agalactia, amenorrhea, obstetric history of postpartum hemorrhage, and hormonal deficiencies) were evaluated.

Age was grouped into two categories (up to 65 and over 65 years). Marital status was categorized as follows: married, single, divorced, and widowed. Socioeconomic profile followed the Brazilian Economic Classification Criteria (<http://www.abep.org/criterio-brasil>), and the number of obtained points stratified the individual into classes, from A1 (the most favored) to E (the least favored). Socioeconomic status was categorized according to Noce *et al.* (9), which considered the years of education and the monthly family income.

The dental functional status was obtained through the evaluation of the number of teeth in digital panoramic radiographs, which were classified according to Sato *et al.* (9) as edentulism and teeth groups (≥ 20 , 10-19, 1-9). It was used the Kodak K9000 3D equipment (Kodak Dental Systems, Carestream Health, Rochester, NY, USA). Additionally, presence/absence of horizontal bone loss, maxillary sinus pneumatization (sinus wall depression toward maxillary alveolar ridge, rendering an imaging aspect of increased sinus space), degenerative condylar alterations, and styloid process elongation were recorded. Before obtaining the panoramic radiograph, a saliva sample was collected for each participant between 8:00 and 11:00 am during a 5-minute period (salivary flow as mL/min).

The Statistical Package for the Social Sciences software (version 20.0 for Windows®) was used. Descriptive statistics and data frequency were recorded. Also, Chi-square or Fisher's exact and Mann-Whitney tests were used (significance level of 5%).

Results

A sample of 23 patients diagnosed with SS was evaluated in this study, showing a mean age of 64 ± 11.5 years (47-79 years). Concerning the medical data, the mean age at the time the diagnosis was 40.38 ± 10.53 years, while the mean time of disease diagnosis delay was 10.92 ± 8.22 years. The mean age at the time of the last childbirth was 29.53 ± 6.61 years. Also, it was recorded agalactia (46.15%), amenorrhea (53.84%), and adynamia (61.54%). During a 10-year clinical follow-up, 92.31%

were diagnosed with hypothyroidism, and 100% had glucocorticoid replacement. Therefore, all patients had more than 1 hormone deficiency. No patient had a replacement of the somatotrophic axis, due to the following factors: socioeconomic status, medication unavailability at the time of diagnosis in the public service, and no indication of replacement for patients ≥ 60 years or older according to the Brazilian Ministry of Health protocol.

According to Table 1, 51.8% of the patients were up to 65 years at the time of dental evaluation, and the majority of the sample consisted of married subjects (56.5%). Low socioeconomic status was observed among SS patients, since 78.2% belonged to the category C2 or D/E, and about 70% of the patients had up to 8 years of schooling and low family income. The horizontal alveolar bone loss was observed in all patients ($p < 0.001$), the most prevalent pneumatization of the maxillary sinus was bilateral ($p = 0.015$), and the absence of degenerative changes in the mandibular condyle and normal styloid process were commonly observed ($p = 0.017$ and $p = 0.003$, respectively).

Regarding tooth status, 47% of the patients were partially dentate (Table 1). The mean number of absent teeth was 23.17 ± 9.7 , which was statistically significant ($p < 0.0001$; Fig. 1). According to Table 2, the maxilla concentrated 53.45% of teeth loss. In jaws, missing teeth were mainly in the posterior mandible (34.3%), followed by posterior maxilla (33.53%), anterior maxilla (19.92%), and anterior mandible (12.26%). The mean number of missing teeth in patients with maxillary sinus pneumatization (Table 2) was statistically significantly ($p = 0.001$). The prevalence of maxillary sinus pneumatization was statistically significant ($p = 0.006$) in patients with 10-19 (11.7; odds ratio of 0.3-422.5) and ≥ 20 (43.4; odds ratio of 1.7-1121.0) missing teeth.

Figure 2 shows that the mean number of missing teeth was statistically higher ($p = 0.048$) in individuals over 65 years. In subjects up to 65 years (Table 3), tooth loss was more prevalent in the posterior mandible (17.82%) followed by posterior maxilla (15.71%). The patients over 65 years showed a higher prevalence of tooth loss in the posterior maxilla (17.82%), followed by posterior mandible (16.48%).

The mean salivary flow value was 0.14 ± 0.16 in individuals over 65 years of age and 0.2 ± 0.31 in individuals aged up to 65 years. In 78.3% of the sample, reduced salivary flow was found. Regarding reduced salivary flow, 72.22% ($n = 13$) presented very low values and 27.78% ($n = 5$) presented low values. Also, in a bivariate analysis considering the outcome variables "missing teeth" and "reduced salivary flow" (Table 4), it was observed that economic status ($p < 0.001$), family income ($p = 0.037$), and maxillary sinus pneumatization ($p = 0.032$) were statistically significant variables.

Table 1: Sample characterization regarding sociodemographic data and imaging variables.

	n	%	p-value
Age (years)			
Up to 65	12	51.8	1.000
> 65	11	48.2	
Marital status			
Married	13	56.5	0.237
Single	3	13	
Divorced	1	4.3	
Widow	6	26.1	
Socioeconomic class			
B1	1	4.3	0.115
B2	2	8.7	
C1	2	8.7	
C2	11	47.8	
D/E	7	30.4	
Schooling (years)			
≤ 8	16	69.5	0.237
9-11	3	13	
≥ 12	4	17.5	
Family income (MFW)			
<1	1	4.3	0.552
1-1.9	10	43.5	
2-2.9	9	39.1	
3-5	2	8.7	
>6	1	4.3	
Edentulism			
No	14	60.9	0.453
Yes	9	39.1	
Partially toothed			
No	12	52.2	1.000
Yes	11	47.8	
Horizontal alveolar bone loss			
No	0	0	<0.001
Yes	23*	100	
Maxillary sinus pneumatization			
No	6	26.1	0.015
Unilateral	1	4.3	
Bilateral	16*	69.6	
Condyle with signs of degenerative change			
No	17*	73.9	0.017
Unilateral	4	17.4	
Bilateral	2	8.7	
Styloid process elongation			
No	21	91.3	0.003
Yes	2	8.7	

* $p < 0.05$, chi-square or Fisher's exact test; MFW, minimum wage.

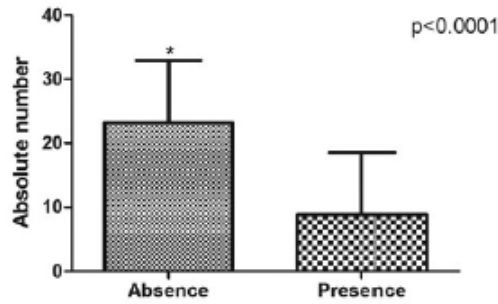


Fig. 1: Mean number of missing teeth in SS sample. Asterisk (*) indicates statistical significance (Mann-Whitney test).

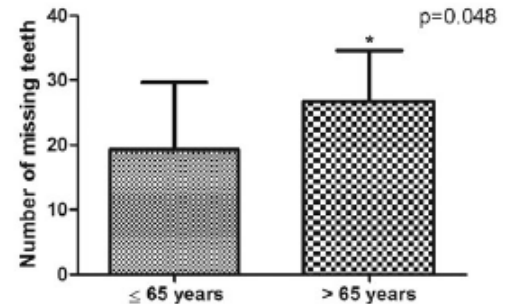


Fig. 2: Mean number of missing teeth considering individuals ≤ 65 years versus > 65 years. Asterisk (*) indicates statistical significance (Mann-Whitney test).

Table 2: Teeth loss in patients with maxillary sinus pneumatization.

	Maxillary sinus pneumatization			
	No	Yes	OR (95% CI)	p-Value
Missing teeth	14.5 \pm 10.5	27.3 \pm 5.8	-	0.001*
0-9	3 (50.0%)	0 (0.0%)	1.0	0.006 ^b
10-19	1 (16.7%)	2 (11.8%)	11.7 (0.3 - 422.5)	
≥ 20	2 (33.3%)	15 (88.2%)	43.4 (1.7 - 1121.0)	

*Student t test; ^bChi-square test; OR = Odds Ratio; 95% CI = Confidence Interval.

Table 3: Anatomical distribution of missing teeth (n=522) according to age.

	≤ 65 years		> 65 years		Total	
	n	%	n	%	n	%
Jaws:						
Maxilla	129	24.71	150	28.74	279	53.45
Mandible	115	22.03	128	24.52	243	46.55
Anatomical region:						
Anterior maxilla	47	9	57	10.92	104	19.92
Posterior maxilla	82	15.71	93	17.82	175	33.53
Anterior mandible	22	4.21	42	8.05	64	12.26
Posterior mandible	93	17.82	86	16.48	179	34.3

Discussion

The study of systemic diseases, especially hypopituitarism, can be considered a valuable field of research in oral medicine. In this context, SS should be investigated because it is an endocrinopathy still observed in developing countries such as Brazil, but there are no published studies on its oral aspects to date.

The present study investigated the relationship between tooth loss, sociodemographic variables, and salivary flow in a sample of SS subjects, which were more prevalent in the sixth decade of life. This data agrees with Diri *et al.* (10), which reported patients with 63.2 \pm 12.5 years, as well as with the study of Dökmetaş *et al.* (11)

that reported an average age of 60.1 years in a sample of 20 patients. However, a study of 28 patients diagnosed with SS in the period between 1982 and 2002 in Turkey showed individuals with a mean age of 48.2 \pm 10.5 years (12).

The presence teeth is considered a reliable indicator of oral and systemic health (13), and some authors have observed that longevity/life expectancy may be affected by the number of teeth present and that tooth loss is a predictive factor shortening of longevity (14). A dentition with various dental absences attenuates masticatory efficiency and causes a subsequent high limiting food selection with a low diet in fruits, vegetables and other

Table 4: Influence of the outcome variables "missing teeth" and "reduced salivary flow" on study variables.

	Total	Missing teeth			p	Reduced salivary flow		p
		0-9	10-19	≥20		No	Yes	
Marital status								
Married	16	3	3	10	0.169	3	13	0.621
	69.6%	100%	100%	58.8%		60%	72.2%	
Not married	7	0	0	7		2	5	
	30.4%	0%	0%	41.2%		40%	27.8%	
Age (years)								
Up to 65	12	3	1	8	0.187	2	10	0.640
	52.2%	100%	33.3%	47.1%		40%	55.6%	
> 65	11	0	2	9		3	8	
	47.8%	0%	66.7%	52.9%		60%	44.4%	
Socioeconomic class								
B1	1	1*	0	0	<0.001	0	1	0.886
	4.3%	33.3%	0%	0%		0%	5.6%	
B2	3	0	0	3		1	2	
	13%	0%	0%	17.6%		20%	11.1%	
C1/2	3	0	3*	6		2	9	
	13%	0%	100%	35.3%		40%	50%	
D/E	8	0	0	8*		2	6	
	34.8%	0%	0%	47.1%		40%	33.3%	
Schooling								
Until complete elementary school	16	2	2	12	0.984	5	11	0.272
	69.6%	66.7%	66.7%	70.6%		100%	61.1%	
>complete elementary school	7	1	1	5		0	7	
	30.4%	33.3%	33.3%	29.4%		0%	38.9%	
Family income (MW)								
<2	11	0	2	9	0.187	0	11*	0.037
	47.8%	0%	66.7%	52.9%		0%	61.1%	
≥2	12	3	1	8		5*	7	
	52.2%	100%	33.3%	47.1%		100%	38.9%	
Horizontal alveolar bone loss	23	3	3	17	1.000	4	10	0.611
	100%	100%	100%	100%		80%	55.6%	
Maxillary sinus pneumatization								
No	6	3*	1	2	0.032	1	5	0.791
	26.1%	100%	33.3%	11.8%		20%	27.8%	
Unilateral	1	0	0	1		0	1	
	4.3%	0%	0%	5.9%		0%	5.6%	
Bilateral	16	0	2*	14*		4	12	
	69.6%	0%	66.7%	82.4%		80,0%	66.7%	
Condyle with signs of degenerative change	6	1	0	5	0,538	1	5	1.000
	26.1%	33.3%	0%	29.4%		20 %	27.8%	
Styloid process elongation	2	0	0	2	0.679	0	2	1.000
	8.7%	0%	0%	11.8%		0%	11.1%	

*p<0.05, chi-square or Fisher's exact test; MW, minimum wage.

essential nutrients (15). Such aspects reinforce the importance of the present study when analyzing the dental status in a group of patients with endocrinopathy still present in developing countries. It was observed that the individuals affected by SS had a high number of dental losses, with the majority having 20 or more missing

teeth. In this context, in a study investigating the relationship between the number and position of teeth with satisfaction with the oral cavity, it was found that at least 20 natural teeth are required to obtain satisfactory aesthetic function and function (16). Hirotomi *et al.* (17) observed in a 5-year longitudinal study that individuals

with 20 or more teeth had a lower mortality rate (2.5%) than individuals with up to 19 teeth (6.1%), which was statistically significant. Hayasaka *et al.* (18) showed an inverse dose-response relationship between the number of remaining teeth and mortality, and individuals with 10 to 19 teeth presented a relative risk of 1.16 compared to individuals with 20 or more teeth.

Over the last few years, sociodemographic variables have been considered important factors are contributing to tooth loss (19), with emphasis on educational and socioeconomic levels (14). According to Rozier *et al.* (20), low socioeconomic status was the most consistent predictive factor of missing teeth in the US population. In Brazil, a longitudinal study that used the Gini Index to measure socioeconomic inequality showed that the increase in this index was associated with a higher prevalence of severe missing teeth and loss of a functional dentition, which is considered when there were at least 20 natural teeth (21). Presently, patients with SS showed low socioeconomic status. This finding was similar to Silva *et al.* (22) study that used the Economic Classification Criteria Brazil. These authors observed a significant association between socioeconomic status and the number remaining natural teeth, evidencing that individuals with high socioeconomic status had a higher number of permanent teeth when compared to lower socioeconomic status. Also, the present data corroborate the socioeconomic profile of patients with SS described in the literature. Famuyiwa *et al.* (23) identified 11 patients with SS over a 5-year period from a university hospital in Nigeria and observed that about 64% of the sample belonged to a low socioeconomic class.

The impairment of salivary function is associated with teeth loss due to a high risk of caries and periodontal disease (24). In the present study, it was observed that patients with SS had low salivary flow in the majority, representing about 80% of the analyzed sample. In this specific group of patients, the majority had significant low values of salivary flow. These findings corroborate the high percentage of missing teeth, which was a statistically significant result. Marques *et al.* (25) investigated predictive factors of tooth loss among Brazilian adults and found that the low salivary flow represented an independent outcome variable. In a logistic regression model controlling marital status, race, and socioeconomic status performed by Caplan, Hunt (24) among 818 patients aged at least 65 years, a statistically significant association was observed between low salivary flow and dental loss.

Gokalp *et al.* (4) highlighted the importance of hypogonadotropic hypogonadism in the development of osteoporosis in SS patients. These authors conclude that growth hormone has a significant effect on bone metabolism and plays a crucial role in maintaining bone mass in adults by regulating bone remodeling. In this

context, such systemic findings reinforce the data found in the present study, especially the severe dental loss observed, which also reflected a significant prevalence of horizontal bone loss and maxillary sinus pneumatization. It is noteworthy that in our research there was no adequate replacement of the gonadal axis nor of the somatotrophic axis by previously reported factors, being patients that due to delayed diagnosis was submitted to many years of hypoestrogenism. Chihaoui *et al.* (26) in a study of 60 patients diagnosed with SS concluded that reduced bone mineral density was a finding frequently observed in such individuals. Such result inserted in the context of the present study is important because of the existence of an association between low bone mineral density and tooth loss and maxillomandibular alveolar bone loss (27).

Conclusions

In summary, the present study evidenced oral cavity-related findings reflecting the chronic hypopituitarism related to SS. It was observed a sample represented by adult women, mainly in the sixth decade of life, who presented low educational and socioeconomic levels, reduced salivary flow, and severe teeth missing, which could be associated with a decline in functional capacity of women affected by SS.

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Conflict of interest

The authors have declared that no conflict of interest exist.

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Terminology: The AMA Manual of Style provides its own guidance on terms NOT to use when describing older people. JAGS and the AGS have modified these recommendations even further (Table 1) for work published in our journal, recognizing that language (even down to specific word choices) has been a significant obstacle to conveying to the general public and policymakers the advances we have made in healthcare and aging services (Table 2 below).

Table 1 below summarizes JAGS modifications to specific guidance in the AMA Manual of Style. In brief: JAGS requires that authors use the term "older adult" when describing individuals aged 65 and older. To align geriatrics research with efforts to promote and highlight age inclusivity, authors also are asked to provide a specific age range (e.g., "older adults aged 75 to 84") and to include additional information on age specificity (average age and median age, where available) when describing their research or making recommendations about patient care or the health of the population.

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<p>Use specific terminology to refer to persons' age. See also 11.10.3, Inclusive Language, Age.</p> <p>[...]</p> <p>Adults are persons aged 18 years and older and</p>	<p>Use specific terminology to refer to persons' age. Whenever possible, include information about the age range, average age, and median age of the study population.</p> <p>Age specificity (including age range, average age, and median age, if possible) is generally</p>



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should be referred to as men or women. Persons 18 to 24 years of age may also be referred to as young adults.	[...]	age, and median age, if possible, is generally preferred on first reference to a study population. On second reference, or when referring to groups generally, adults are persons aged 18 years and older and should be referred to as men or women. Persons 18 to 24 years of age may also be referred to as young adults. Persons 65-years-old and older may also be referred to as older people or older adults.	
Section 2: Style Chapter 11: Correct & Preferred Language 11.10.3—Age			
<p>Discrimination based on age (young or old) is ageism. Because the term elderly connotes a stereotype, avoid using it as a noun. When referring to the entire population of elderly persons, use of the elderly may be appropriate (as in the impact of prescription drug costs on the elderly, for example). Otherwise, terms such as older persons, older people, elderly patients, geriatric patients, older adults, older patients, aging adults, persons 65 years and older, or the older population are preferred.</p> <p>Note: In studies that involve human beings, age should always be given specifically. Researchers in geriatrics may use defined terms for older age groups, eg, young-old (usually defined as 60 or 65 to 70 or so years) and old-old (80 years and older). See also 11.5, Age and Sex Referents.</p> <p>Adultism is a form of ageism in which children and adolescents are discounted.</p>		<p>Discrimination based on age (young or old) is ageism. Because terms like seniors, elderly, the aged, aging dependents, old-old, young-old, and similar "other-ing" terms connote a stereotype, avoid using them. Terms such as older persons, older people, older adults, older patients, older individuals, persons 65 years and older, or the older population are preferred.</p> <p>Note: In studies that involve human beings, age should always be given specifically (e.g., "older people aged 75 to 84," "older adults over age 65").</p> <p>Adultism is a form of ageism in which children and adolescents are discounted.</p>	

Table 2.

Instead of These Words:	Try:
"Tidal wave," "tsunami," and similarly catastrophic terms for the growing population of older adults"	Talking affirmatively about changing demographics: "As Americans live longer and healthier lives ..."
"Choice," "planning," "control," and other individual determinants of aging outcomes"	"Emphasizing how to improve social contexts: "Let's find creative solutions to ensure we can all thrive as we age..."
"Seniors," "elderly," "aging dependents," and similar "other-ing" terms that stoke stereotypes"	"Using more-neutral (older people, Americans) and inclusive ("we" and "us") terms"
"Struggle," "battle," "fight," and similar conflict-oriented words to describe aging experiences"	The Building Momentum metaphor: "Aging is a dynamic process that leads to new abilities and knowledge we can share with our communities ..."
Using the word "ageism" without explanation	Defining ageism: "Ageism is discrimination against older people due to negative and inaccurate stereotypes..."
Making generic appeals to the need to "do something" about aging	Using concrete examples like intergenerational community centers to illustrate inventive solutions
From Gaining Momentum: A FrameWorks Communications Toolkit (2017)	



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Voice: We prefer authors use the first person and active voice. The guidelines for publication conform to those of the International Committee of Medical Journal Editors and the AMA Manual of Style. A Guide for Authors and Editors, 10th Ed. An explication of statistical guidelines is presented in John C. Bailar III and Frederick Mosteller, "Guidelines for Statistical Reporting in Articles for Medical Journals," *Annals of Internal Medicine* (1998;108:266–273).

Unit of Measurement: Although JAGS accepts the use of conventional units of the Système International d'Unités (SI), we do prefer units of measurements most familiar to those working in the United States (e.g., mg/deciliter, cells/microliter instead of mg/liter, cells/liter).

Abbreviations: Abbreviations are acceptable provided they are commonly used or well recognized, but the use of many abbreviations in a single manuscript is discouraged. Abbreviations should be given only if the term is used more than one time. Terms must also be spelled out and followed by the abbreviation in parentheses when first used in the abstract and text. Terms must also be spelled out in tables and figures, with abbreviations provided in parentheses immediately following first use of the term or as footnotes. Abbreviations of units of measurement are not discouraged, but units of time should not be abbreviated except in virgule construction (e.g., 40 mg/d).

P-Values: Decimal places for numerical values of measures other than statistics should be limited to 1 unless it is essential to have 2 for the interpretation. For example, do not use more than one decimal place for basic demographic information such as age, sex, etc. For statistics:

- P-values can be reported with 2 or 3 decimal places, except for $p < .001$, which should include 3 decimal places
- Values for confidence intervals, hazard or risk ratios, etc. should be limited to 2 decimal places
- Provide nonsignificant and significant P-values to no more than three places past the decimal. Use $p < .001$ for "all" "i" "P-values less than .001.

Other Style Notes: Do not use "NS" for nonsignificant values. For percentages use no more than one place past the decimal. In referring to cases with 25 or fewer subjects, state number ("one of four" cases), rather than percentages (25%) in the text. For instruments or scales, indicate normal range in the table (footnote) or figure as well as in the text if reference is made to these in this section.

Drug Names: Generic names should be used whenever possible. Brand names may be included in parentheses after a generic name the first time it is used.

Footnotes: Do not use footnotes in the main running text of the manuscript file. Footnotes should only be used on the title page (for author affiliations) and in tables and figures (for explanatory or clarification remarks). Please use lower case English alphabet starting with a, b, c, etc., in superscript format. Parenthetical statements are more appropriate than footnotes in the text and should be placed in the text within parentheses.

SUPPLEMENTAL INFORMATION

Authors are encouraged to use supplemental material if necessary. Editors and reviewers may ask that primary tables/figures and even some text be moved to supplemental information for space purposes. Authors must include a descriptive title for each individually uploaded supplemental file at the end of the manuscript file. This should not include legends, footnotes, or abbreviations, all of which should be contained within the supplemental file. Cite each file in the main running text. Supplemental files will be available to readers as direct downloads and not included in the print version (though the legends will be listed there). Note that these files will NOT be copyedited or typeset, but published as uploaded. Authors will have a chance to perform a final review of these files after acceptance.

Supplemental files should be titled as *Supplementary Table S1*, *Supplementary Figure S1*, *Supplementary Text S1*, *Supplementary Dataset S1*, etc.

SUBMISSION FORMATS (Types)

To maximize the number of pages that can be published and yet maintain high quality, there are strict limits on the total number of a) text words, b) graphics (tables and figures), and c) references. Authors should carefully read the formatting guidelines below and ensure that their work adheres to the limits of the chosen submission type, including the length and format of the Abstract and main text, as well as the number of graphics and references. JAGS submission types are listed below.

Submission Type	Abstract (words)	Text (words) ^a	References	Tables & Figures (total) ^{a,c}
<i>Clinical Investigation</i> ^b	Structured 300	3,000	50	5
<i>Brief Report</i> ^b	Structured	2,000	30	3



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<i>Health Policy and Economics</i>	Narrative OR Structured*; 250	3,000	30	3	
<i>Special Articles</i>	Narrative OR Structured*; 250	3,000	30	3	
<i>Controversies in Geriatrics and Gerontology</i>	None	1,500	10	2	
<i>Editorials</i>	None	1,500	20	2	
<i>Old Lives Tales</i>	None	1,000	N/A	1	
<i>Letters to the Editor</i>	None	750	10	1	

*These submission types require an "Impact Statement" on the title page.

Abstracts for these submission types should be structured if the paper has original research with quantitative data.

^A note on LENGTH LIMITS: Due to space constraints, JAGS does not allow authors to exceed the word and graphic limits above, even after revisions are requested. Additional text, methods, tables, etc. can always be formatted as Supplemental Material (online only) in order to get around these space limits.

^Papers with at least one figure are preferred over papers that include only tables. Authors are encouraged to provide visual / graphical elements to enhance their work.

***NOTE: Submissions that are systematic reviews, meta-analyses, or major qualitative studies may require a word count greater than the limits shown above. To request an exception, authors must provide justification for the additional words prior to submitting (email jags@jjeditorial.com). Authors submitting systematic reviews or meta-analyses are encouraged to make use of supplemental tables and figures which will be published online..**

Clinical Investigations

These are reports of investigator-initiated research that presents new information. Information that is already available in textbooks or as common knowledge will not be considered for review. The subject matter can be very broad as long as it is relevant to aging conditions in humans.

To improve the quality of reporting randomized, controlled trials (RCTs), it is recommended that authors adhere to the CONSORT (Consolidated Standards of Reporting Trials) statement, which consists of a checklist and flow diagram that authors can use to report RCTs. Authors should refer to the 2001 paper entitled, "The revised CONSORT statement for reporting randomized trials: Explanation and elaboration," in the *Annals of Internal Medicine*.

Brief Reports

These are clinical-investigation or clinical-experience reports whose findings are somewhat preliminary or a clinical study reporting on narrowly focused or limited findings. The journal also welcomes methodological reports on the use of a variety of self-reported, administered, or performance-based measures and scales that assess physical, functional, mood, cognitive, and social domains; the utility of a new method or approach to investigate a clinical or health problem in older people; or an innovative model or design to research issues related to healthcare delivery and service.

Review Articles

Review articles require a complete systematic search of the literature, focusing on, but not necessarily limited to, the last 5 years of published literature. An assessment of quality of the evidence is not required, but is recommended. Formal meta-analyses should be submitted as Clinical Investigations.

Reviews articles should provide critical assessments of the literature pertaining to clinical topics, emphasizing factors such as cause, diagnosis, prognosis, therapy, or prevention. They should address specific questions or issues that are relevant for clinical practice and provide an evidence-based, balanced, patient-oriented review on a focused topic. Following EQUATOR Reporting Guidelines may be helpful.

Education and Training

Papers on models of education and training; research in education, policies related to geriatric training and education, and other issues relevant to teaching.

Ethics

These papers explore and discuss ethical issues that are particularly relevant to the practice of geriatric medicine.



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medicine.

Health Policy and Economics

Papers that explore and discuss the impact of current or new health policy and/or financing on the delivery of health services to older persons.

Models of Geriatric Care, Quality Improvement, and Program Dissemination

These papers disseminate information on effective model programs or services. Descriptive information on the "who, what, and how" of innovative programs with evidence relevant to effectiveness and potential for replication by others is sought. Pure feasibility studies are not appropriate. Review criteria include: (1) *Innovation*: does this model add substantially to existing models of geriatric care? (2) *Model Description*: is the model described in sufficient detail to understand what was done? (3) *Effectiveness*: is there evidence of effectiveness of the model for clinical outcomes? Randomized clinical trials are welcome but not required. (4) *Evidence of feasible implementation and/or dissemination to other settings*. Our goal is to offer a venue for the timely sharing of innovative and effective approaches to important clinical problems in the care of older patients. Authors are encouraged to submit early reports of highly innovative health care payment and service delivery models being developed in response to new payment programs and to the Center for Medicare and Medicaid Innovation.

Special Articles

This section includes papers on history; recommendations for preventive strategies in geriatrics; reports of meetings, task force, or committee activities; guidelines and position statements by the American Geriatrics Society; and other topics relevant to aging but not conforming to any of the *Journal's* existing sections.

Controversies in Geriatrics and Gerontology

For this section, a different format will be implemented. We seek to discuss a topic/issue in geriatrics and gerontology (as well as long-term care) that involve two experts with opposing views on the subject matter. An example might be, "Should we aggressively treat systolic hypertension in the very old?" Each invited expert will submit his/her perspective (1,500 text words/10 references/2 graphics for each expert); as well as a rebuttal to the opposing viewpoint (500 text words/5 references/1 graphic). The assigned associate editor will write a brief (250 words or less) narrative abstract to introduce the topic/issue.

Editorials

Editorials are invited comments on a specific paper published in the *Journal*. Occasionally, opinions or commentary by qualified and respected individuals on a highly relevant topic or controversial issue pertinent to aging will be published in this section at the discretion of the editor in chief.

Old Lives Tales

We invite readers to submit stories, experiences, or incidences which have instructed, saddened or gladdened us as physicians and, above all, taught us something about the care of the older adult. Please note that these pieces are neither editorials nor letters to the editor and are not classically "evidenced-based". Thus there is usually no need for references although the editor may ask you for a citation if you are claiming something that appears unlikely to be supportable from the literature. When describing a particular patient, permission should be received in writing from him/her or the personal details changed sufficiently to conceal the person's identity.

Letters to the Editor

Letters to the Editor should be brief. One type of letter is an objective, constructive, and educational critique of a previously published article in *JAGS* (Comments/Responses); these should be submitted within 3 months after publication of the original paper. The editorial office may submit letters critiquing a paper published in *JAGS* to the authors of the paper, who will be given 1 month to reply to the critique. The letter and the reply will usually be published in tandem. Other letters may discuss matters of general interest to health professionals involved in the care of older patients, interesting clinical findings (not case reports), or brief commentary on any aspect of aging as it relates to humans. Generally, we do not publish letters critiquing papers published in other journals. *JAGS* discourages the submission of Case Reports and limits the number of Research Letters.

POTENTIAL AREAS OF FOCUS

Authors can designate a category for their work at the time of submission, but this is not required. Potential areas of focus include:

<i>Aging and Surgery</i>	High quality research from leaders within the surgical community focusing on geriatric care, including outcomes of surgical procedures with respect to age and in comparison to younger counterparts. Papers focusing on issues of education/training, healthcare delivery and models, and policy focusing on geriatric surgery are also welcomed.
<i>Clinical Management of the</i>	Clinically oriented, with a focus on the diagnosis, treatment, and prevention of clinical problems occurring in older adults. These submissions should include a brief discussion on epidemiology and current concepts on pathogenesis as it applies to aging, with a main

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<i>Older Adult</i>	Current concepts on pathogenesis as it applies to aging, with a major focus on how aging impacts clinical manifestations, diagnostic approach, therapeutic intervention and prevention measures.		
<i>Geriatric Bioscience</i>	Pathophysiology, pathogenesis, or basic scientific information relevant to a geriatric condition or problem. These papers should be written in a style, format and language understandable to our readers, who are predominantly clinicians and not basic scientists; they should not focus on animal studies.		
<i>Dental and Oral Health</i>	Addresses dental care, oral health, and oral disease as they impact the older population.		
<i>Drugs and Pharmacology</i>	Focused on specific drugs or class of drugs, pharmacology, drug prescribing, and related topics as they apply to older adults, as well as current information on drugs from the Food and Drug Administration, and pharmaceutical companies. We discourage papers that appear to be a marketing forum for a specific drug or agent.		
<i>Geriatric Emergency Medicine</i>	Focusing on clinical care, education, research and administration in the older patient in the Emergency Department or Emergency Room.		
<i>Ethnogeriatrics and Special Populations</i>	Focused on issues related to health, disease, disability, healthcare delivery, education, training, research, policies and ethics that are especially unique or relevant to minority and ethnic groups or special populations (e.g., older victims of crime, older prisoners).		
<i>General Geriatrics</i>	Research on clinical topics of interest to JAGS readers that are not covered in other focus areas.		
<i>Health Services Research (other than Models of Care)</i>	Research into the organization and delivery of healthcare.		
<i>International Health Affairs</i>	Current topics on geriatrics and related issues in countries outside the United States. Papers should be focused on models and systems of healthcare delivery for older adults for countries or the country in question. Manuscripts on education/training, economics, politics, policies, and ethics – all related to aging – are also welcomed.		
<i>Nursing</i>	Issues related to nursing research, care, training, education, policies, etc.		
<i>Long-term and Post-acute Care</i>	Research done in or related to care in post-acute care or long-term care settings.		
<i>Palliative Care</i>	Papers in which the topic or issue of palliative care (and/or hospice) intersects with geriatrics. The focus may be a research study, education, clinical care, health policy, etc.		
<i>Literature and Aging</i>	These are invited submissions on narrative articles looking at the human side of the interaction between aging, disease, and health care.		

Supplements

The *Journal* invites a collection of papers to be published as a Supplement. The supplement proposal should be based on symposia or other presentations at national scientific meetings devoted to aging or from projects or initiative with the potential for a national impact on the health care and quality of life of older adults. The following are criteria or requirements for a supplement publication.

1. Articles contained in the supplement must meet the same peer review criteria that are applied to regular issues of the *Journal*.
2. Proposals for supplements that focus on one therapeutic diagnostic agent, product, or strategy to the exclusion or minimization of other options will not be considered.



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1. Articles contained in the supplement must meet the same peer review criteria that are applied to regular issues of the *Journal*.
2. Proposals for supplements that focus on one therapeutic diagnostic agent, product, or strategy to the exclusion or minimization of other options will not be considered.
3. Proposed supplements must have an identified source of support for publishing costs.
4. Authors must provide a statement that the content of the paper represents their work/opinion, and not that of the sponsoring agents, and they verify the accuracy of the content.
5. The editor in chief of the *Journal*, in consultation with the editorial board, is responsible for reviewing and accepting proposals for supplements. In addition, sponsoring agents for the supplement will not be permitted to alter or edit any parts of the manuscript without written permission from the editor in chief.
6. The editor in chief reserves the right to reject one or more papers or the entire supplement if it fails to meet our standards.

MANUSCRIPT PROCESSING

All manuscripts will be initially reviewed by the editor in chief. If further review is deemed appropriate, the paper will be assigned to a deputy editor or possibly an associate or section editor. If the paper is judged to be suitable for review, it will be sent to two or more external referees (reviewers) or, in rare instances, it will receive revision comments directly from the editors.

Authors will be required to provide the names of at least two potential referees who could serve as qualified reviewers of the work; but the editor(s) will make the final choice. Authors will be given 60 days to complete major revisions and 30 days for minor revisions. Extensions can be considered upon request. Do not submit a revision as a new submission.

The guidelines for publication conform to those of the International Committee of Medical Journal Editors "Uniform Requirements for Manuscripts Submitted to Biomedical Journals." The complete document appears in the *Annals of Internal Medicine* (1997;126:36-47) and the *New England Journal of Medicine* (1997;336:309-315). An explication of statistical guidelines is presented in John C. Bailar III and Frederick Mosteller, "Guidelines for Statistical Reporting in Articles for Medical Journals," *Annals of Internal Medicine* (1998;108:266-273), as well as American Medical Association, "AMA Manual of Style. A Guide for Authors and Editors", 10th edition. New York: Oxford University Press, 2007.

The research reported in submitted manuscripts must comply with the ethical rules for human experimentation that are stated in the Declaration of Helsinki (JAMA 1997;277:925-926), including approval of an institutional review board – or human experimentation committee – and informed consent. Authors must disclose this compliance in the Methods section of the manuscript.

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For printed issue, press releases will be sent out to reporters on the last day of the preceding month, with an embargo date of the 9th of the month printed at the top. Authors must contact the JAGS editorial office before they do a press release.

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Authors interested in arranging a press release and/or interested in embargoing the publication of their accepted JAGS paper should contact the Editorial Office. We ask that authors provide Twitter handles for themselves or their co-authors, as available. JAGS encourages its authors, reviewers, editors and readers to engage with the journal through the following mediums:

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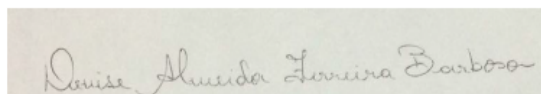
ANEXO V. DECLARAÇÃO DE CORREÇÃO DE PORTUGUÊS

DECLARAÇÃO DE CORREÇÃO DE PORTUGUÊS

Declaro, para os devidos fins, que eu **DENISE ALMEIDA FERREIRA BARBOSA**, realizei a revisão da dissertação **AVALIAÇÃO DE ASPECTOS ORAIS, SOCIOECONÔMICOS E CRANIOFACIAIS EM PACIENTES COM SÍNDROME DE SHEEHAN** de **DAVI DE SÁ CAVALCANTE**, consistindo em correção gramatical, adequação do vocabulário e inteligibilidade do texto.

Fortaleza, 06 de Setembro de 2018.

Atenciosamente,



Professora Denise Almeida Ferreira Barbosa,
Graduada em Letras Língua Inglesa e Literaturas pela UERN