

# Diffuse idiopathic hyperostosis in human skeletons from a contemporary brazilian collection

# Hiperostose idiopática difusa em esqueletos humanos de uma coleção brasileira contemporânea

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#### ABSTRACT

**Objective:** This work aimed to evaluate the occurrence of diffuse idiopathic skeletal hyperostosis (DISH) in human skeletons of a contemporary Brazilian Identified Skeletal Collection. Materials: A total of 362 skeletons were analyzed macroscopically using two diagnostic methods: Resnick and Niwayama (first analysis) and Rogers and Waldron (second analysis). **Methods:** The frequency, age groups, sex, the vertebral segment most involved with the ossification of the anterior longitudinal ligament, and areas of most significant occurrence of enthesophytes were the variables used in this study. **Results:** In the first analysis, the DISH frequency in the sample was 5.5%, and in the second, 6.6%. The most frequent age group was 61 to 80 years old. The lower thoracic segment was most affected by the ossification of the anterior longitudinal ligament. In this sample, the relationship between DISH and sex was not statistically significant. Conclusions: DISH affected the thoracic vertebrae of individuals of older ages with no relation to sex. **Limitations:** As they are the first data referring to contemporary identified skeletons in Brazil, it was not possible to carry out a comparative analysis. Suggestions for Further **Research:** Other studies aiming to evaluate DISH in other Brazilian collections must be carried out to accomplish the disease profile in this population and subsidize other areas of knowledge, such as Forensic Anthropology since DISH can be precious to contribute to a positive identification.

Keywords: Hyperostosis, Diffuse Idiopathic Skeletal; DISH; Enthesophytes; Spinal manifestations; Extra-spinal manifestations.

### **RESUMO**

Objetivo: Este trabalho teve como objetivo avaliar a ocorrência de hiperostose idiopática difusa do esqueleto (DISH) em esqueletos humanos de uma Coleção de Esqueletos Identificados Brasileira contemporânea. Materiais: Um total de 362 esqueletos foram analisados macroscopicamente usando dois métodos de diagnóstico: Resnick e Niwayama (primeira análise) e Rogers e Waldron (segunda análise). Métodos: A freqüência, grupos etários, sexo, o segmento vertebral mais envolvido com a ossificação do ligamento longitudinal anterior e as áreas de ocorrência mais significativa de entesófitos foram as variáveis utilizadas neste estudo. **Resultados**: Na primeira análise, a frequência DISH na amostra foi de 5,5%, e na segunda, de 6,6%. A faixa etária mais frequente foi de 61 a 80 anos de idade. O segmento torácico inferior foi o mais afetado pela ossificação do ligamento longitudinal anterior. Nesta amostra, a relação entre DISH e sexo não foi estatisticamente significativa. Conclusões: O DISH afetou as vértebras torácicas de indivíduos de idade mais avançada sem relação com o sexo. Limitações: são primeiros dados referentes aos esqueletos contemporaneamente no Brasil, não foi possível realizar uma análise comparativa. Sugestões para pesquisas adicionais: Outros estudos visando avaliar o DISH em outras



coleções brasileiras devem ser realizados para atingir o perfil da doença nesta população e subsidiar outras áreas do conhecimento, como a Antropologia Forense, uma vez que o DISH pode ser precioso para contribuir para uma identificação positiva.

Palavras-chave: Hiperostose, Esqueleto Idiopático Difuso; DISH; Enthesophytes; Manifestações espinhais; Manifestações extra-espinhais.

#### 1 INTRODUCTION

Diffuse Idiopathic Skeletal Hyperostosis (DISH) is a noninflammatory disease characterized by ossification of the anterior longitudinal ligament along the right anterolateral side of the spine and extra-spinal enthesophytes (Resnick et al., 1975). It usually affects individuals over 40 years of age, has a higher frequency in males, and is associated with systemic conditions, such as Diabetes mellitus, osteoarthritis, arterial hypertension, and hyperuricemia (Ribeiro, 2011). Signs and symptoms such as pain, spinal stiffness, weight loss, pharyngeal perforation, airway obstruction, and dysphagia have been described (Oliveira, 2016); however, most patients are asymptomatic.

Several methods for diagnosing DISH have been created since its first description by Forestier and Rotes-Querol in 1950. One of the first was proposed by Resnick and Niwayama (1976), evaluated as a restrictive method for limiting pathology to manifestations in the spine, not considering DISH coexistence with other diseases (Oliveira, 2016). Paleopathology revealed other methods like those proposed by Arlet and Mazières, 1985; Utsinger, 1985; and Rogers and Waldron, 2001. The last two mentioned first accepted that extra-spinal manifestations can simultaneously occur with the ossification of the anterior longitudinal ligament, characterizing the presence of DISH (Holgate, Steyn, 2016).

DISH is easily identified in skeletons due to the gross and characteristic ossification of the anterior longitudinal ligament. In a paleopathological context, the existence of cases reported in the literature goes back to past times, the oldest being a Neolithic individual from Kitoi (6900 BC) found in Siberian Russia (Faccia, 2016).

Information from the study of human skeletal remains can exhibit individualization factors and characteristics common to the population group to which they belonged (Plischuck, 2012). There is a dynamic relationship between Osteology and Forensic Anthropology, in which the identification of bone pathologies and antemortem trauma is relevant regarding the identification and determination of the cause of death (Silva, 2015).



In the present study, we analyzed the frequency of DISH in a contemporary identified skeleton collection from northeastern Brazil, according to two different diagnostic methods. As far as we know, these are the first data on this specific topic for Brazilian collections.

#### 2 MATERIAL AND METHODS

#### Material

This research was carried out at the Center for Studies in Forensic Anthropology, Faculty of Dentistry, University of Pernambuco (CEAF/FOP/UPE), located in the city of Recife, State of Pernambuco, Northeast Brazil, and was approved by the Research Ethics Committee (Opinion No. 2,284,094; CAAE: 72907917.8.0000.5207). All procedures followed the guidelines and rules that regulate research involving human beings in the country.

The studied population consisted of identified human skeletons of both sexes, administratively exhumed after two years of burial (Cunha et al., 2018), from the Santo Amaro Cemetery, located in the central region of the city of Recife. The collection consists of 427 skeletons aged from 0 to 109 years, buried between 2011 and 2016, and exhumed between 2013 and 2018. Data on sex and age at death are available for all skeletons, and there is information on the cause of death for 188 (Carvalho et al., 2020). A fetus, skeletons without a minimum of three contiguous vertebrae, and those without vertebrae were excluded from this study. Thus, the final sample comprised 362 skeletons of adult individuals with at least three contiguous vertebrae.

### Methods

The variables used to carry out the study included ossification of the anterior longitudinal ligament in at least three contiguous vertebrae, categorized as present or absent; sex, categorized as male and female; and age at death, organized into age ranges. After selecting the study sample, 37 skeletons were previously examined to train the examiner for the criteria to be used in the present study. For this, a professional with experience was invited to evaluate the same skeletons to verify the analysis agreement. Inter-examiner and intra-examiner concordances were assessed using the Kappa test, with values of 0.802 and 0.893 being obtained, respectively.



The examination of the skeletons was performed macroscopically, taking into consideration, initially, the ossification of the anterior longitudinal ligament in at least three contiguous vertebrae and, later, the presence of extra-spinal ossifications.

Two diagnostic methods were used: the one developed by Resnick and Niwayama (1976), which is one of the pioneer studies in the definition of criteria for diagnosing DISH, being one of the most used in the literature; and the other, elaborated by Rogers and Waldron (2001), as it is a more recent method and developed by Paleopathology to evaluate the existence or not of differences in the frequency of the disease when different criteria are used.

The criteria developed by Resnick and Niwayama (1976) include A - the presence of calcification and exuberant ossification in the anterolateral side in at least four contiguous vertebral bodies, with or without bone growths in the affected bodies; B preservation of the height of the disc in the affected regions and absence of extensive radiographic alterations of degenerative disc disease; and C - the absence of ankylosis of the apophyseal joints and absence of erosion, sclerosis or bone fusion of the sacroiliac joint.

The factors defined by Rogers and Waldron (2001) are A - hyperostosis of the spine, affecting at least three vertebrae, with or without ankylosis; B - changes confined to the right side of the thoracic vertebrae, except in cases of situs inversus; and C - the evidence of extra-spinal calcifications and ossifications in ligaments and entheses.

The analysis of the results was carried out through statistical tests, using the software IBM<sup>©</sup> Statistical Package for Social Science (IBM SPSS 20.0). Initially, a descriptive analysis was performed to assess the frequency of distribution of the variables, thus seeking to characterize the studied sample. Absolute and percentage distributions were obtained, as well as the statistical measures of mean, median, and standard deviation (descriptive statistics techniques). For categorical variables, the Chi-square association test was used. The confidence level established for the statistical test was 5.0%.

#### 3 RESULTS

Regarding the frequency of DISH in the sample, different values were observed. In the first analysis, using Resnick and Niwayama criteria (1976), the frequency found was 5.5% (20/362). When Rogers and Waldron's criteria (2001) was used, a frequency of 6.6% (24/362) was obtained.



Of the 20 skeletons diagnosed with DISH according to the criteria of Resnick and Niwayama, 11 were male (55.0%) and 9 female (45.0%). Of the 24 diagnosed using the method proposed by Rogers and Waldron, 13 were male (54.2%) and 11 female (45.8%). Despite the higher frequency in male skeletons, the results show that the presence of DISH was not statistically significant between the presence of the pathology and the sex (p = 0.976).

The age group with the highest frequency and number of cases applying the criteria of Resnick and Niwayama (1976) was 61-80 years, in which 15 of the 152 individuals presented the pathology (9.9%). According to Rogers and Waldron's criteria (2001), the age group with the highest frequency and the highest number of cases was also 61-80 years (11.2%), as shown in Table 1.

Table 1 - Distribution of skeletons with DISH using both the Resnick and Niwayama's (1976) and the Rogers and Waldron's criteria (2001).

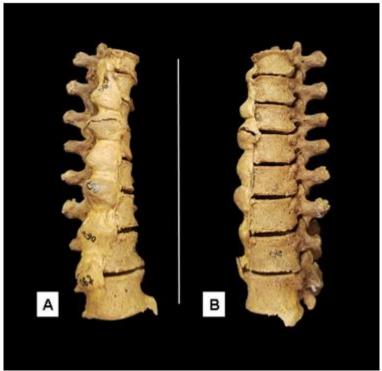
Age group (years)	Total (n/N)	%
Resnick a	nd Niwayama's criteria (1976)	
< 40	0/57	0
41 - 60	2/85	2.4
61 - 80	15/152	9.9
81 - 109	3/68	4.4
Total	20/362	5.5%
Rogers	and Waldron's criteria (2001)	
< 40	0/57	0
41 - 60	2/85	2,4
61 - 80	17/152	11,2
81 - 109	5/68	7,3
Total	24/362	6,6%

The distribution of DISH by age group revealed statistically significant differences ( $X^2 = 11.710$ ; g.l = 3; p = 0.008). The data showed that DISH was more prevalent in individuals belonging to the age group between 61 and 80 years old, whereas individuals under 40 did not present the disease. At CEAF/FOP/UPE, the lowest and highest ages with DISH are 49 and 93 years old, respectively, with a mean of 71 years, a median of 71 years, and a standard deviation of 11.4.



Ossification of the anterior longitudinal ligament on the right side of the spine affecting at least three contiguous vertebrae was the main diagnostic factor (Fig. 1A and B).

Fig. 1 - Skeleton belonging to the CEAF/FOP/UPE collection diagnosed with DISH. A) ossification of the anterior longitudinal ligament on the right side of the spine, affecting the vertebrae T5 to T12; B) observe the maintenance of the intervertebral disc spaces and the absence of ankylosis of the apophyseal joints.



The thoracic vertebrae were the most affected by ossification of the anterior longitudinal ligament. In the first analysis (Resnick and Niwayama's criteria), one skeleton (5.0%) presented ossification of the ligament in the cervical and thoracic regions and the other 19 (95.0%) only in the thoracic segment. In the second analysis (Rogers and Waldron's criteria), only one skeleton (4.2%) presented ossification of the ligament in the cervical and thoracic regions, 22 (91.6%) only in the thoracic segment, and one (4.2%) in thoracic and lumbar vertebrae. The most affected thoracic vertebrae were T7 (95.3%) and T8 (91.6%), followed by T9 (87.5%), T10 (87.5%), and T6 (83.3%).

Enthesophytes (bone projections present in the margins of fibrocartilaginous entheses) were observed on the olecranon of 14 (58.3%) of the 24 skeletons with DISH; as well as ossifications on humeral heads of 7 skeletons (29.2%). Pathological bone growths at the ends of the clavicles in 8 skeletons (33.3%) and hand bones of 4 skeletons (16.6%) were also found.



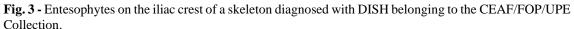
Also, enthesophytes were observed on the tibial tuberosity of 8 skeletons (33.3%), distal epiphysis of the fibula in 10 skeletons (41.6%), and patellas of 16 skeletons (66.6%), where the quadriceps femoris is inserted (Figure 2). Ossifications on the greater trochanter of the femur were found in 10 skeletons (41.6%), on the lesser trochanter in 3 (12.5%), and foot bones in 17 skeletons (70.8%), with the presence of enthesophytes in the calcaneus, at the insertion site of the calcaneus tendon in 16 skeletons (66.6%) (Fig. 2).

**Fig. 2** - Entesophytes on the tibial tuberosity, patella, and calcaneus of skeletons diagnosed with DISH belonging to the CEAF/FOP/UPE Collection. The red arrows indicate the presence of enthesophytes.



Entesophytes were also observed on the iliac crest of 19 skeletons (79.2%); the fusion of the sacroiliac joint in two (8.3%); formation of a bone bridge at the upper edge of the joint, not characterizing a complete fusion in four skeletons (16.6%); ossification of rib cartilage in 13 skeletons (54.2%); the fusion of the 1st rib with the manubrium in two skeletons (8.3%); and osteomas in 6 skulls (25.0%).







# 4 DISCUSSION

According to Carunchio et al. (2020), the study of aging is essential for understanding the difficulties and new demands that arise with it. In this context, DISH presents itself as a pathology of interest.

The DISH frequency varies according to the context, sample, and diagnostic method used. In this study, the frequency of DISH obtained when applying the criteria of Resnick and Niwayama (1976) was 5.5%, the same found by van der Merwe et al. (2012) out of 253 skeletons from two samples from the 16<sup>th</sup> century from Delft, a city located in the province of South Holland, and a modern sample from the dissection room at the University of Leiden Medical Center. The frequency is high compared to that 1.9% of the study performed by Oliveira (2016) and low compared to the frequency of 40.4% found by Verlaan et al. (2007).

The frequency obtained from the criteria of Rogers and Waldron (2001) applied to the CEAF/FOP/UPE sample was 6.6%, similar to that found in the lay cemetery of Wells Cathedral by those researchers (6.5%), higher than the 5.1% found by Oliveira (2016), and lower compared to the frequency of 17.0% obtained by van der Merwe et al. (2012), when using the same diagnostic criteria.

The difference between the two frequencies found in the CEAF/FOP/UPE collection is 1.1%. This difference can be explained by the criteria developed for



confirming the DISH. Resnick and Niwayama (1976) created stricter criteria, which identify the disease in more advanced stages, while Rogers and Waldron (2001) developed a more flexible method. Thus, the results tend to be greater when the skeletons are analyzed using this second method.

As for sex, studies agree that males are most affected. Van der Merwe et al. (2012), using Rogers and Waldron's (2001) method, diagnosed DISH in 26 males and 16 females. In Oliveira's study (2016), DISH was confirmed in 22 skeletons, 17 male and 5 female, with a statistically significant difference (p=0.019). This difference in frequency by sex can be explained by the access to the total number of individuals that happens to be different in each survey (Oliveira, 2016). Besides, the number of male or female skeletons also varied between samples, so the results are diverse. However, differently from what those researchers pointed out, the CEAF/FOP0 UPE skeletal sample, although quantitatively the distribution of the disease has occurred more in male skeletons, there were no statistically significant differences (p = 0.976).

There is a consensus in the literature that the occurrence of DISH is more observed in individuals of older ages. Luo and Varacallo (2020), Mader et al. (2017), and Bateman et al. (2017) state that this pathology occurs more in individuals over 50 years old. Others, such as Ribeiro (2011) and van der Merwe et al. (2012), report that it is uncommon before 40 years old. In the CEAF/FOP/UPE sample, the youngest skeleton with a positive DISH diagnosis was 49 years old, corroborating with the other studies. The age range with the highest frequency and the highest number of cases was 61-80 years.

The thoracic vertebrae were the most affected by ossification of the anterior longitudinal ligament, followed by the lumbar and cervical ones. In the analysis of 416 skeletons from the Bass Donate Collection at the Center for Forensic Anthropology at the University of Tennessee, Milner et al. (2018) observed that the thoracic region was affected in 95.2%, the lumbar region in 41.3%, and the cervical region in 17.5% of the cases. The lower region of the thoracic segment is the most affected, as shown by Kuperus et al. (2018) when analyzing computed CT scans of the chest of patients obtained between the years 2004 and 2011; and also by Navarro and Buckberry (2020), with the T10, T9, and T8 vertebrae most commonly affected by ligament ossification, followed by T7 and T11 vertebrae.

As observed in the literature, in the CEAF/FOP/UPE skeletons, the thoracic segment of the spine was affected in all cases examined. In these cases, the lower thoracic region was particularly affected, especially the T7, T8, T9, and T10 vertebrae, in that



order. The second most affected segment was the lumbar one. Two skeletons showed lumbar vertebrae involvement, corresponding to 4.2% (1/24) of the second analysis. Only one skeleton showed ossification of the ligament on cervical vertebrae.

The appendicular skeleton's manifestations that accompany DISH lesions were first noticed by Sutro et al. (1956) and Harris et al. (1974). The presence of ossifications outside the spine to confirm the diagnosis of DISH is commonly found in criteria created and applied in the context of Archeology. This is possibly due to the fragmented state that archaeological remains are often found and that identifying these ossifications is notably easier in skeletons than in living individuals. Sometimes in Paleopathology, when the vertebrae are not preserved enough to provide a diagnosis, the presence of generalized enthesophytes has been used for this purpose (Navarro, Buckberry, 2020).

The first systematic investigation of extra-spinal ossifications took place in 1975 by Resnick et al. The most affected sites are the triceps brachii muscle's insertion points on the olecranon, the femoral quadriceps on the patella, the patellar ligament on the tibia, and the Achilles tendon on the calcaneus (Oliveira, 2016). However, the pelvis (Terzi, 2014) and other bones of the upper limbs (Resnick et al., 1976; Arlet, Mazières, 1985) and lower limbs (Resnick et al., 1976; Mader, 2003) can also be affected. In CEAF/FOP/UPE skeletons, enthesophytes were more observed on the iliac crest, on the insertion areas of the quadriceps femoris muscle on the patella, of the calcaneus tendon, and the brachial triceps on the olecranon, followed by the greater trochanter of the femur, the area of insertion of the posterior talofibular ligament on the distal epiphysis of the fibula and the patellar ligament in the tibia.

Although the existence of enthesophytes is used as a criterion for the diagnosis of DISH in some methods, the presence of these ossifications alone cannot be considered a pathognomonic sign of the disease, especially since these ossifications do not happen only in patients with DISH. Van der Merwe et al. (2012) found a frequency of 35.0% of enthesophytes formed by the ossification of the yellow ligament and the sternocostal ligament and located on the olecranon of the ulna and the patella as well, in non-related to DISH cases. Thus, it does not seem cautious to diagnose such a condition based solely on these manifestations (Navarro, Buckberry, 2020).

It should be stressed that some pathologies present similar findings to DISH, but a thorough examination can provide important information to obtain the differentiation. In cases like ankylosing spondylitis (AS), vertebrae, ribs, and the sacroiliac joint are commonly affected. However, the bamboo spine is characteristic of individuals with AS



and results from the fusion of the ribs to the thoracic vertebrae. The ankylosis is caused by progressive growth of syndesmophytes that will bridge the intervertebral disc (Østergaard, Lambert, 2012), not observed in DISH. Also, the sacroiliac joints are affected bilaterally, symmetrically, and can be fused, while in DISH the fusion occurs due to calcification of the sacropelvic ligaments. In AS, the spine, pelvis, and ribs can be lifted together, or en bloc, as stated by Waldron (2019). Another difference between DISH and AS is that this affects individuals of puberty and early thirties (Sieper et al., 2002), while DISH is more prevalent in older ages.

Imaging exams are essential for clinical diagnosis of DISH, such as chest or abdomen radiographs, and computed tomography (CT) of the chest and thoracolumbar region, for more reliable results (Kim et al., 2018). Hiyama et al. (2018) performed a study with tomographic images of the entire spine of 1479 patients. They stated that CT provides more detailed images of the ossifications and spaces of the intervertebral discs, being a helpful examination modality for the observation of DISH.

The use of postmortem radiological images is of great value for medico-legal investigations of death (Christensen et al., 2018). Postmortem CT can be compared to antemortem CT scans, which allow the professional to evaluate the individualizing internal morphology when these are available. Since more and more individuals undergo CT during their lifetime, comparing ante and postmortem data provided by this image examination has become a popular means of human identification (Garvin, Stock, 2016)

Lastly, in a Forensic context, macroscopic findings and, eventually, postmortem images can serve as important information for comparison with available antemortem documentation. Thus, the presence of DISH in a skeleton can be precious to contribute to a positive identification.

#### **5 CONCLUSION**

DISH is a pathology that affects older individuals and, differently from what the literature points out, in the CEAF/FOP/UPE sample, it was not related to sex. The most affected vertebral segment was the thoracic, especially the lower region. The bones with the highest occurrence of enthesophytes were the iliac, the patella, the calcaneus, and the ulna.

Other studies aiming to evaluate DISH in other Brazilian collections must be carried out to accomplish the disease profile in this population and also subsidize other



areas of knowledge, such as Forensic Anthropology, since DISH can be precious to contribute to a positive identification.

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