MUSCULOSKELETAL RADIOLOGY



Prevalence and characteristics of diffuse idiopathic skeletal hyperostosis (DISH) in Italy

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Abstract

Purpose Diffuse idiopathic skeletal hyperostosis (DISH) is a benign condition characterized by ossification of the spine and prominent enthesopathies. Highly heterogeneous epidemiological figures have been reported in the literature, while in Italy the largest study has been conducted in 1992. The aim of our research is to contribute updated information about prevalence of DISH in Italy and to describe the clinical and radiographic characteristics associated with the disorder.

Material and methods A retrospective review of lumbosacral spine, thoracic spine and pelvis radiographs was performed. Consecutive patients visiting the emergency department of our Institution over 3 years were enrolled. Presence of DISH was evaluated applying the Resnick and Niwayama criteria. Clinical and radiological features were also assessed.

Results We included 1012 individuals (60.6% women), and DISH was present in 130 cases. The overall prevalence of DISH was 12.8% (95% CI 10.8–15.1), with higher figures in the male sample (16.8%) than in females (10.3%). In binary logistic regression adjusted for age, BMI (OR 1.50, p < 0.001) diabetes (OR 1.85, p = 0.003), hypertension (OR 2.04, p = 0.007) ischiopubic enthesopathy (OR 7.08, p < 0.001), iliac crest enthesopathy (OR 4.63, p < 0.001) and greater trochanter enthesopathy (OR 3.51, p < 0.001), were significantly associated with the condition.

Conclusion The prevalence of DISH observed in our study is consistent with previous literature, and we confirm that the disorder is more frequently retrieved in men and that it is associated with the presence of metabolic disorders and pelvic enthesopathy. Knowledge about the epidemiology and characteristics of DISH is needed to properly identify the condition.

Keywords Diffuse idiopathic skeletal hyperostosis · DISH · Prevalence · Epidemiology · Characteristics · Spondyloarthritis

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Introduction

Diffuse idiopathic skeletal hyperostosis (DISH) is a systemic, non-inflammatory condition characterized by ossification of the anterolateral spine and bone proliferation at the entheses. DISH most commonly occurs in the lower thoracic and thoracolumbar portion of the spine, although it may also affect the peripheral skeleton, with hypertrophic joint changes and prominent enthesopathies [1]. The condition has been initially described in 1950 by Forestier and Rotes-Querol [2], but the most frequently used diagnostic criteria were introduced in 1976 by Resnick and Niwayama [3], who defined DISH on the basis of "flowing" bony bridging of at least four contiguous vertebrae with relative preservation of the intervertebral disc and lack of fusion or erosion of sacroiliac and apophyseal joints.

Extensive ossification of the spinal ligaments can be present in other conditions, and DISH is mentioned in the

"Assessment of Spondyloarthritis international Society" (ASAS) handbook as a differential diagnosis of ankylosing spondylitis (AS) [4]. It is of great importance to distinguish DISH from AS, since the two diseases require different therapeutical approaches. AS is an inflammatory disease that typically presents in the second or third decade of life, associated with HLA-B27 positivity and characterized by paramarginal bony bridges with a less frequent involvement of the anterior longitudinal ligament [5]. However, it should be noted that DISH and AS can be present simultaneously [6].

The etiology of DISH is not clearly understood. The condition is significantly more frequent in older age and in men [7, 8], and it is associated with metabolic syndrome and its components such as obesity, diabetes and hypertension [9, 10]. Due to its commonly asymptomatic presentation, the prevalence of DISH is difficult to estimate. The largest epidemiological research of DISH in Italy was conducted in 1992 on 915 patients. Scutellari et al. described an overall prevalence of 14.1%, with a rate of 17.6% in males and 11.6% in females [11]. In a following study, Pappone et al. found a prevalence of 27.9% in 247 patients and revealed an unusual gender distribution, with a majority of affected women and a male to female ratio of 0.47 [12]. Almost 10 years later, in a small study on 93 women, the same authors reported an estimate of 15.1% [13].

To our knowledge, the prevalence of DISH in the general Italian population has not been re-evaluated since then. Based on this background, the aim of our study is to investigate the epidemiological aspects and the characteristics of DISH patients in Italy.

Materials and methods

Study population

We retrospectively reviewed radiographs of lumbosacral spine, thoracic spine and pelvis obtained from consecutive patients attending the Emergency Department (ED) of IRCCS Rizzoli Orthopaedic Institute, Bologna, Italy. Patients were included in the study if they: (1) were 18 years of age or older; (2) visited the ED between January 1st, 2019, and December 31st, 2021; (3) underwent radiographs of lumbosacral spine, thoracic spine and pelvis. Exclusion criteria were: (1) past diagnosis of axial or peripheral spondyloarthritis (SpA).

Patients visiting the ED repeatedly during the study period were considered only at the time of the first admission. In all patients visiting the ED of our Institution, a comprehensive musculoskeletal assessment is performed with systematic collection of medical history. Comorbidities recorded as dichotomous variables were: hypertension, diabetes, atrial fibrillation, hyperlipidaemia, heart failure, history of stroke, history of acute myocardial infarction (AMI) or coronary artery disease (CAD), history of cancer, chronic kidney disease. Since data about weight and height are not routinely collected in patients visiting the ED, information about body mass index (BMI) was drawn applying a previously published method, based on chest radiographs, when possible [14]. Chest radiographs were performed when deemed necessary in the evaluation of patients admitted for trauma. Briefly, for patients in which chest radiographs were available, transversal body diameter was measured at the T12–L1 intervertebral disc level from standard anterior–posterior or posterior–anterior projections. Applying separate regression models for men and women, BMI was calculated as previously described [14].

Imaging assessment

To evaluate the presence of DISH, two musculoskeletal radiologists (E.B. and G.F., both with > 5 years of experience in musculoskeletal radiology) consecutively and independently scored all anterior–posterior, posterior–anterior and lateral radiographs of thoracic and lumbosacral spine and all anterior–posterior and posterior–anterior radiographs of the pelvis. The presence of DISH was established according to the criteria proposed by Resnick and Niwayama [3]: (1) "flowing" bony bridging of at least four contiguous vertebrae, (2) a relative preservation of the intervertebral disc and (3) lack of fusion or erosion of sacroiliac and apophyseal joints.

Additional radiological features were systematically evaluated. These were: osteitis pubis, osteitis condensans ilii (OCI), pelvic enthesopathy involving the ischiopubic ramus or the iliac crest, enthesopathy of the greater trochanter, hip osteoarthritis (OA), hip replacement, aortic calcification, calcification of interspinous ligament. Disagreements about the main outcome of the study (i.e. presence of DISH) were discussed and resolved by consensus, with the opinion of a third senior investigator (M.M.) if needed. Inter-observer agreement about the presence of DISH was categorized by kappa values as poor (< 0.20), fair (0.20-0.39), moderate (0.40–0.59), good (0.60–0.79) or excellent (>0.80) [15]. Radiological characteristics other than DISH were deemed present only if both observers agreed in the independent scoring. Insertional enthesopathies were assessed according to the definitions proposed by Resnick and Niwayama [16]. OCI was defined as a triangular sclerosis with ossification affecting the iliac portion of the articulation, with spared sacroiliac joint space and no evidence of erosive arthritis [17]. Osteitis pubis was defined as sclerosis, lytic changes or widening of the pubic symphysis [18]. Severity of hip OA was classified according to the Kellgren and Lawrence (K-L) grading system from doubtful (grade 1) to mild (grade 2), moderate (grade 3) and severe (grade 4) [19]. When bilateral hip OA was present, the highest K-L grade of the two coxofemoral joints was reported. In case of disagreement about K–L scoring between the two investigators, the highest grade was kept in the analysis. In patients who underwent unilateral total hip replacement, presence of OA was evaluated at the contralateral side. If a bilateral total hip replacement had been performed, hip OA was not assessed.

Statistical analysis

On the basis of DISH epidemiology data in Italy available from previous literature [11], we hypothesized a prevalence of about 12% in women and 18% in men. Accordingly, we calculated a minimum sample size of 163 female and 227 male patients to estimate such proportion with 5% margin of error and 95% confidence. Data are expressed as mean (standard deviation), median (25th-75th percentile) or number (percentage) as appropriate. Student's t test and Mann–Whitney U test were used, respectively, to compare differences between normally and non-normally distributed continuous variables between two groups. Fisher's exact test was used to compare categorical variables. The Clopper-Pearson "exact" method was used to calculate 95% confidence interval (95% CI) of DISH prevalence based on the beta distribution. Univariate binary logistic regression adjusted for age was used to assess the potential association of DISH with clinical and radiological variables, providing odds ratios (OR) and 95% CI. A p-value < 0.05 was considered statistically significant. All analyses were performed using the Statistical Package for Social Sciences (SPSS) software version 26.0 (IBM, Armonk, NY, USA).

Ethical considerations

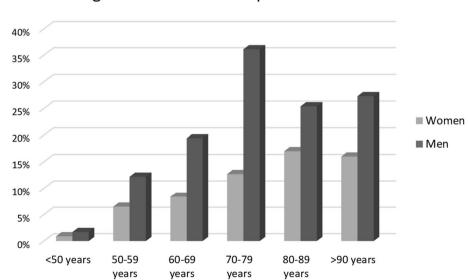
The research was conducted in compliance with the Declaration of Helsinki and its latest amendments [20]. The study was approved by the local Ethics Committee (Comitato Etico Area Vasta Emilia Centrale, Bologna, Italy—approval number: 0008347/2021).

Results

Characteristics of the included population and prevalence of DISH

During the study period, 1020 adult patients underwent radiographs of lumbosacral spine, thoracic spine and pelvis at the ED of our Institution. Of these, 8 were affected by axial or peripheral SpA and were excluded from the study. Median age of the 1012 included patients was 68.1 years (IOR 51.2-79.2) and 613 individuals (60.6%) were females. The overall prevalence of DISH was 12.8% (95% CI 10.8-15.1). Of the 130 patients with DISH, 63 were women and 67 were men, accounting for a prevalence of 10.3% (95% CI 8.0-13.0) in the female sample and of 16.8% (95% CI 13.3–20.8) in the male population. The prevalence rates classified by age groups < 50 years, 50–59 years, 60–69, 70–79, $80-89 \text{ and } \ge 90 \text{ years were, respectively, } 0.9, 6.5, 8.4, 12.7,$ 17.0 and 16.0% in women and 1.7, 12.2, 19.4, 36.1, 25.4 and 27.3% in men (Fig. 1). Comorbidities and associated radiographic characteristics are shown in Table 1. Inter-observer agreement was good, with a Cohen's kappa of 0.74.

Fig. 1 Age distribution of the prevalence of DISH



Age distribution of the prevalence of DISH

 Table 1
 General characteristics

 of patients included in the study

	Women $(n=613)$	Men $(n = 399)$
Age, median (IQR)	71.9 (55.9–80.6)	60.5 (47.0–75.9)
Estimated BMI, mean (SD)	23.8 (4.0)*	25.3 (3.4)*
DISH, n (%)	63 (10.3)	67 (16.8)
DISH level		
Thoracic spine, n (%)	54 (85.7)	59 (88.1)
Thoracolumbar spine, n (%)	9 (14.3)	7 (10.4)
Lumbar spine, n (%)	0	1 (1.5)
Number of involved vertebrae		
4–5, <i>n</i> (%)	34 (54.0)	30 (44.8)
6–7, <i>n</i> (%)	22 (34.9)	26 (38.8)
$\geq 8, n (\%)$	7 (11.1)	11 (16.4)
Additional radiographic characteristics		
Osteitis condensans ilii, n (%)	8 (1.3)	1 (0.3)
Osteitis pubis, n (%)	44 (7.2)	8 (2.0)
Ischiopubic enthesopathy, n (%)	38 (6.2)	34 (8.5)
Iliac crest enthesopathy, n (%)	149 (24.3)	72 (18.1)
Greater trochanter enthesopathy, n (%)	122 (19.9)	42 (10.6)
Aortic calcifications, n (%)	316 (51.5)	132 (33.2)
Calcification of interspinous ligament	16 (2.6)	21 (5.3)
Hip osteoarthrosis K–L grade ≤ 2 , n (%)	312 (50.8)	169 (42.5)
Hip osteoarthrosis K–L grade > 2, n (%)	40 (6.5)	33 (8.3)
Hip replacement, n (%)	72 (11.7)	21 (5.3)
Clinical characteristics		
Diabetes, n (%)	50 (8.1)	44 (11.1)
Hypertension, n (%)	145 (23.6)	99 (24.9)
Atrial fibrillation, <i>n</i> (%)	41 (6.7)	31 (7.8)
Hyperlipidaemia, n (%)	96 (15.6)	66 (16.6)
Heart failure, n (%)	44 (7.2)	30 (7.5)
History of stroke, <i>n</i> (%)	42 (6.8)	25 (6.3)
History of AMI or CAD, n (%)	35 (5.7)	34 (8.5)
History of cancer, n (%)	67 (10.9)	30 (7.5)

AMI acute myocardial infarction; *BMI* body mass index (kg/m²); *CAD* coronary artery disease; *IQR* interquartile range; *K–L* Kellgren & Lawrence; *SD* standard deviation. *BMI has been estimated in 436 women and 270 men

Clinical characteristics of patients with DISH

Clinical characteristics of DISH patients are reported in Table 2. Median age was 76.1 years (IQR 68.4–82.8), and mean BMI was 28.7 (2.8), both higher than in individuals without DISH (p < 0.001). Diabetes (20.0 vs 7.7%, p < 0.001), hypertension (41.5 vs 21.5%, p < 0.001), atrial fibrillation (12.3 vs 4.0%, p = 0.026), hyperlipidaemia (24.6 vs 14.7%, p = 0.007), history of stroke (12.3 vs 5.8%, p = 0.012), history of AMI or CAD (12.3 vs 6.0%, p = 0.014) and chronic kidney disease (13.8 vs 6.3%, p = 0.006) were significantly more frequent in individuals with DISH. In binary logistic regression adjusted for age, only BMI (OR 1.50, 95% CI 1.39–1.62, p < 0.001), diabetes (OR 1.85, 95% CI 1.24–2.76, p = 0.003) and hypertension (OR 2.04, 95% CI 1.22–3.41, p = 0.007) were associated with DISH. Conversely, atrial fibrillation (OR 1.23, 95% CI 0.67–2.27, p = 0.498), hyperlipidaemia (OR 1.31, 95% CI 0.83–2.07, p = 0.247), history of stroke (OR 1.50, 95% CI 0.82–2.77, p = 0.192), history of AMI or CAD (OR 1.47, 95% CI 0.80–2.71, p = 0.219) and chronic kidney disease (OR 1.52, 95% CI 0.85–2.73, p = 0.162) were not predictors of DISH.

Radiographic characteristics of DISH

Radiographic characteristics of DISH patients are reported in Table 2. In men, DISH was located in 88.1% of cases at the thoracic spine level (Fig. 2a) and in 10.4% at the thoracolumbar segment (Fig. 2b), while only one patient had isolated involvement of the lumbar vertebrae (Fig. 2c).

 Table 2
 Differences between

 patients with or without DISH

	Patients with DISH $(N=130)$	Patients without DISH $(N=882)$	P-value
Age, median (IQR)	76.1 (68.4–82.8)	63.6 (49.3–78.6)	< 0.001
Estimated BMI, mean (SD)	28.7 (2.8)*	23.7 (3.5)*	< 0.001
Radiographic characteristics			
Osteitis condensans ilii, n (%)	1 (0.8)	8 (0.9)	1.000
Osteitis pubis, n (%)	15 (11.5)	37 (4.2)	0.002
Ischiopubic enthesopathy, n (%)	37 (28.5)	35 (4.0)	< 0.001
Iliac crest enthesopathy, n (%)	73 (56.2)	148 (16.8)	< 0.001
Greater trochanter enthesopathy, n (%)	54 (41.4)	110 (12.5)	< 0.001
Aortic calcifications, n (%)	83 (63.8)	365 (41.4)	< 0.001
Calcification of interspinous ligament	26 (20)	11 (1.2)	< 0.001
Hip osteoarthrosis K–L grade ≤ 2 , n (%)	90 (69.2)	391 (44.3)	< 0.001
Hip osteoarthrosis K–L grade > 2, n (%)	18 (13.8)	55 (6.2)	0.003
Hip replacement, n (%)	17 (13.1)	76 (8.7)	0.105
Clinical characteristics			
Diabetes, n (%)	26 (20)	68 (7.7)	< 0.001
Hypertension, n (%)	54 (41.5)	190 (21.5)	< 0.001
Atrial fibrillation, n (%)	16 (12.3)	23 (4.0)	0.026
Hyperlipidaemia, n (%)	32 (24.6)	130 (14.7)	0.007
Heart failure, n (%)	15 (11.5)	59 (6.7)	0.068
History of stroke, <i>n</i> (%)	16 (12.3)	51 (5.8)	0.012
History of AMI or CAD, n (%)	16 (12.3)	53 (6.0)	0.014
History of cancer, <i>n</i> (%)	15 (11.3)	83 (9.3)	0.425
Chronic kidney disease, n (%)	18 (13.8)	56 (6.3)	0.006

AMI acute myocardial infarction; *BMI* body mass index (kg/m²); *CAD* coronary artery disease; *IQR* interquartile range; *K–L* Kellgren & Lawrence; *SD* standard deviation. *BMI has been estimated in 436 women and 270 men

In the female sample, DISH affected the thoracic portion in 85.7% of cases and the thoracolumbar spine in 14.3%. Most patients (54% of women and 44.8% of men) had 4 to 5 contiguous vertebrae involved (Fig. 3a), followed by 6 to 7 levels (34.9% of women and 38.8% of men) (Fig. 3b). In 11.1% of women and 16.4% of men, at least 8 vertebrae were interested by DISH (Fig. 3c). In the majority of patients (79.1% of men and 74.6% of women), thick flowing bridging osteophytes (Fig. 4a) were observed, while the remaining cases presented a smoother ossification pattern (Fig. 4b).

The proportion of patients presenting osteitis publs (11.5 vs 4.2%, p = 0.002) (Fig. 5a), ischiopubic enthesopathy (28.5 vs 4.0%, p < 0.001) (Fig. 5b), iliac crest enthesopathy (56.2 vs 16.8%, p < 0.001) (Fig. 5c), greater trochanter enthesopathy (41.4 vs 12.5%, p = 0.477) (Fig. 5b), calcification of interspinous ligament (20 vs 1.2%, p < 0.001) (Fig. 5C), hip OA with K–L grade ≤ 2 (69.2 vs 44.3%, p < 0.001) hip OA with K–L grade ≥ 2 (13.8 vs 6.2%, p = 0.003), aortic calcifications (63.8 vs 41.4%, p < 0.001) (Fig. 5c) was significantly higher in DISH patients. In binary logistic regression adjusted for age, ischiopubic enthesopathy (OR 7.08, 95% CI 4.19–11.94, p < 0.001), iliac crest enthesopathy (OR 4.63, 95% CI 3.09–6.95, p < 0.001), greater trochanter

enthesopathy (OR 3.51, 95% CI 2.31–5.34, p < 0.001), hip OA with K–L grade ≤ 2 (OR 1.94, 95% CI 1.28–2.94, p = 0.002), osteitis pubis (OR 1.95, 95% CI 1.02–3.73, p = 0.043) and calcification of interspinous ligament (OR 18.74, 95% CI 8.81–39.83, p < 0.001) predicted the presence of DISH, while aortic calcifications (OR 0.95, 95% CI 0.57–1.58, p = 0.842) and hip OA with K–L grade > 2 (OR 1.65, 95% CI 0.92–2.96, p = 0.091) were not significantly associated with the condition.

Discussion

Although known to be a common condition, research about the epidemiology of DISH in Italy is limited and largely outdated, with the most relevant study published three decades ago and including less than 1000 patients [11]. Therefore, we decided to provide updated estimates of DISH prevalence reviewing radiographs of lumbosacral spine, thoracic spine and pelvis obtained from 1012 consecutive patients visited during the period 2019–2021 at the ED of our Institution, a tertiary centre for musculoskeletal diseases. According to our data, the overall **Fig. 2** Thoracic, thoracolumbar and lumbar DISH. **a** Anterior– posterior radiograph showing right-sided flowing ossification of the thoracic spine; **b** lateral radiograph showing bone bridges and thick flowing ossification of the anterior lateral ligament of the thoracolumbar portion; **c** lateral radiograph showing large non-marginal ossification involving the lumbar spine segments with calcification of the anterior longitudinal ligament

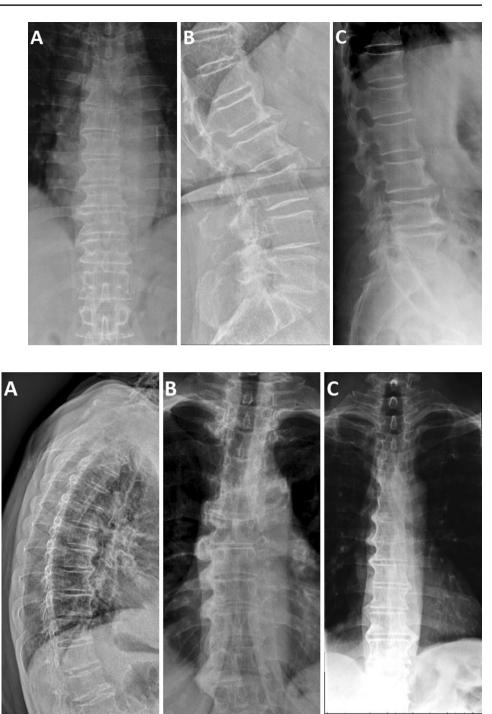


Fig. 3 DISH involving different number of vertebrae. **a** Lateral radiograph showing flowing ossification across 4 vertebral levels; **b** anterior–posterior radiograph showing bone bridges and large ossification of the anterior lateral ligament spanning 6 vertebral segments; **c** anterior–posterior radiograph showing flowing ossification involving 8 contiguous vertebral segments on the right side and 4 non-contiguous vertebrae on the left

prevalence of DISH in Italy is 12.8%. Of the 130 patients with DISH, 63 were women and 67 were men, accounting for a prevalence of 10.3% in women and of 16.8% in men. Our results are consistent with previous literature and prevalence estimates of DISH in Italy appear substantially unchanged [11, 13].

In the last decade, most epidemiological data have been contributed by Asian countries [7, 8, 21–28], with highly variable figures such as 3.8% in China [21], 10% in Oman

[27], 24.4% in Korea [28], 30.8% in Pakistan [22] and from 8.3% [8] to 27.1% in Japan [7]. Recently, two articles from the USA described a prevalence of 7.7% [29] and 13.2% [30], while an Icelandic population study involving over 5000 individuals showed a DISH rate of 7.8% [31]. However, it should be noted that the different results can be partly explained by the heterogeneity of imaging techniques applied (e.g.: whole-spine CT scan, chest CT, PET/

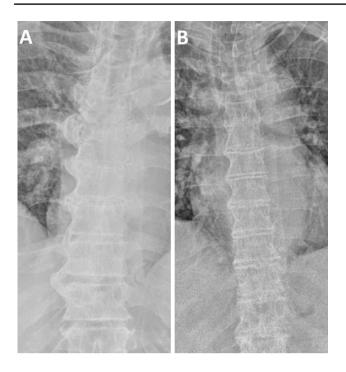


Fig.4 Coarse and smoother ossification patterns in DISH. **a** Anterior–posterior radiograph showing coarse flowing ossification of the lumbar spine with large ossification of the anterior lateral ligament; **b** anterior–posterior radiograph showing bone bridges with smoother ossification pattern

CT, whole-spine lateral radiographs), hampering the comparability between studies.

We confirm that DISH predominantly affects men and that the condition becomes more frequent with ageing [7, 8, 23–26, 28–30]. Indeed, we observed a steady increase across age groups, peaking in the range 70–79 years in men

and 80–89 years in women, consistently with the results of Yoshihara et al. [29]. Then, at least in men, a relative reduction is noted. We have no exhaustive explanation for this finding, but the well-known association between DISH and metabolic disorders with higher rates of cardiovascular risk factors might suggest earlier mortality in DISH patients. A mortality effect for DISH has been hypothesized in past literature [32, 33], but the findings have never been corroborated in subsequent samples. Prospective studies may be warranted to elucidate the correlation between presence of DISH and mortality.

Since patients with DISH were significantly older than individuals without DISH, we compared clinical and radiographic characteristics adjusting for age and we further confirmed a significant link between DISH and components of the metabolic syndrome such as BMI, diabetes and hypertension [8, 9, 22, 30, 31, 34-36]. Metabolic factors are widely recognized as key determinants in patients with DISH, as in the case of other diseases with propensity for new bone formation such as osteoarthritis and psoriatic arthritis [37-40]. Obesity, in particular, is strongly associated with DISH, as well as with a wide range of other musculoskeletal diseases [41–43], and a role of adipokines in the pathogenesis of DISH has been proposed because of their effects on bone metabolism, promoting osteoblasts number and activity [44–46]. Moreover, obesity is associated with type 2 diabetes and with insulin resistance, but the prevalence of diabetes is high in DISH patients independently of the presence of obesity. Several studies analysed the link between DISH and diabetes [47, 48], and a possible pathogenetic mechanism might be that the high levels of insulin or insulin-like growth factors stimulate new bone formation [49, 50]. Indeed, insulin is a bone growth-promoting peptide [51] and it has been

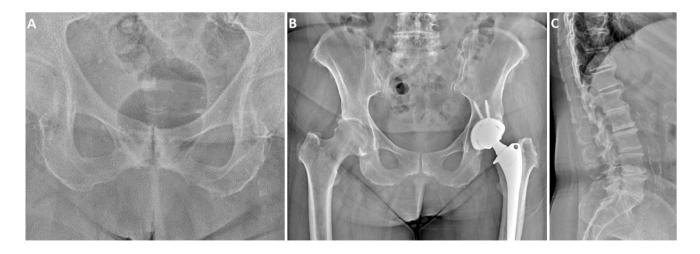


Fig. 5 Osteitis pubis, pelvic enthesopathies and aortic calcification. **a** Anterior–posterior radiograph of the pelvis showing osteitis pubis with sclerosis and erosions of the pubic symphysis; **b** anterior–posterior radiograph of the pelvis showing bilateral enthesopathy of the iliac crest, ischiopubic ramus and greater trochanter. c Lateral radiograph showing flowing bridges involving the thoracolumbar spine, ossification of the interspinous ligament and calcification of the abdominal aortic wall suggested as a key player in the pathophysiology of DISH and of other spinal inflammatory and degenerative disorders, with a potential effect of diet modifications on their management [52-55].

Interestingly, the proportion of individuals presenting features of insertional enthesopathy was elevated in the DISH group. In line with the available literature, we noted a significant association between DISH and ischiopubic enthesopathy, iliac crest enthesopathy, greater trochanter enthesopathy, hip OA, osteitis pubis and calcification of interspinous ligament, remarking how in particular pelvic enthesopathy is highly characteristic of this condition [22, 56]. The entheseal involvement, along with the hyperostotic spinal changes, might generate confusion in the radiological differential diagnosis between DISH and axial SpA, although the two diseases have completely distinct radiographic features [57–59].

Knowing the epidemiology and the associated clinical and radiological characteristics of DISH may help to raise the awareness of rheumatologists and radiologists and to properly identify and report the condition. Indeed, notwithstanding the expertise in musculoskeletal diseases of a tertiary referral centre, in our sample the inter-observer reliability between radiologists was rather good, but not excellent, with a Cohen's kappa of 0.74. The difficulty in making the radiological diagnosis can be partially related to the subjective interpretation of the Resnick and Niwayama criteria [3], in particular when the severity of disc degeneration or the presence of sacroiliac and apophyseal changes have to be evaluated. It is therefore not surprising that previous studies have shown highly heterogeneous results even when populations of the same country were analysed [7, 8, 23-26], nor that inter-observer agreement in the available literature has never been reported to be excellent, but always moderate or good. In Japan, Mori et al. [24] and Hiyama et al. [23] found a kappa value of 0.79, while it was 0.64 in the study by Hirasawa et al. [7]. Reviewing 300 cases, Auðunsson et al. described a kappa of 0.55 [31], while in the study by Oudkerk et al. [60] values substantially improved after a consensus meeting and ranged from 0.51 to 0.86.

Despite providing updated estimates about prevalence of incidentally detected DISH in the general population, our study has some limitations to be acknowledged. First, the design is cross-sectional. As a consequence, the potential effects of DISH on mortality cannot be evaluated. We included in our study the assessment of different radiographic characteristics which might be related to the presence of DISH, as for example insertional enthesopathies and aortic calcifications. However, DISH may also involve the cervical spine [61] and peripheral segments such as the elbow, the shoulders, the knee or the calcaneus [62]. These segments have not been assessed in our study. Since the study was performed retrospectively on patients visiting the ED for acute complaints, history about symptoms related to DISH were not included in the medical evaluation, preventing the possibility to perform analyses based on the clinical presentation. Finally, we acknowledge that individuals visiting an ED are not necessarily representative of the general population. This might have resulted in the introduction of a selection bias in our study sample. However, in order to minimize this risk, unselected patients were enrolled consecutively over a broad period of time and avoiding overly restrictive exclusion criteria.

In conclusion, our study contributes to the knowledge about the epidemiology of incidentally detected DISH in Italy, confirming that the condition is relatively common in the general population. Findings about prevalence are consistent with previous literature but prospective research with longitudinal design is warranted to elucidate the pathogenesis of this entity and its potential effects on mortality.

Author contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by JC, EB, GV, GF and FU. The first draft of the manuscript was written by JC and EB and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethics approval The research was conducted in compliance with the Declaration of Helsinki and its latest amendments. The study was approved by the local Ethics Committee (Comitato Etico Area Vasta Emilia Centrale, Bologna, Italy—approval number: 0008347/2021).

Consent to participate Not applicable.

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References

- Mader R, Baraliakos X, Eshed I, Novofastovski I, Bieber A, Verlaan J-J et al (2020) Imaging of diffuse idiopathic skeletal hyperostosis (DISH). RMD Open 6(1):e001151. https://doi.org/ 10.1136/rmdopen-2019-001151
- Forestier J, Rotes-Querol J (1950) Senile ankylosing hyperostosis of the spine. Ann Rheum Dis 9(4):321–330. https://doi.org/10. 1136/ard.9.4.321
- Resnick D, Niwayama G (1976) Radiographic and pathologic features of spinal involvement in diffuse idiopathic skeletal hyperostosis (DISH). Radiology 119(3):559–568. https://doi.org/10.1148/ 119.3.559
- Sieper J, Rudwaleit M, Baraliakos X, Brandt J, Braun J, Burgos-Vargas R et al (2009) The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. Ann Rheumatic Dis 68(Suppl 2):ii1–ii44. https://doi.org/ 10.1136/ard.2008.104018.
- Nascimento FA, Gatto LA, Lages RO, Neto HM, Demartini Z, Koppe GL (2014) Diffuse idiopathic skeletal hyperostosis: a review. Surg Neurol Int 5(Suppl 3):S122–S125. https://doi.org/ 10.4103/2152-7806.130675
- Kuperus JS, Waalwijk JF, Regan EA, van der Horst-Bruinsma IE, Oner FC, de Jong PA et al (2018) Simultaneous occurrence of ankylosing spondylitis and diffuse idiopathic skeletal hyperostosis: a systematic review. Rheumatology (Oxford) 57(12):2120– 2128. https://doi.org/10.1093/rheumatology/key211
- Hirasawa A, Wakao N, Kamiya M, Takeuchi M, Kawanami K, Murotani K et al (2016) The prevalence of diffuse idiopathic skeletal hyperostosis in Japan—the first report of measurement by CT and review of the literature. J Orthop Sci 21(3):287–290. https:// doi.org/10.1016/j.jos.2016.02.001
- Banno T, Togawa D, Hasegawa T, Yamato Y, Yoshida G, Kobayashi S et al (2018) The controlled study of diffuse idiopathic skeletal hyperostosis for the assessment of physical function in elderly populations. J Orthop Sci 23(6):929–934. https://doi.org/ 10.1016/j.jos.2018.07.017
- Mader R, Novofestovski I, Adawi M, Lavi I (2009) Metabolic syndrome and cardiovascular risk in patients with diffuse idiopathic skeletal hyperostosis. Semin Arthritis Rheum 38(5):361–365. https://doi.org/10.1016/j.semarthrit.2008.01.010
- Mattera M, Reginelli A, Bartollino S, Russo C, Barile A, Albano D et al (2018) Imaging of metabolic bone disease. Acta Biomed 89(1-s):197–207. https://doi.org/10.23750/abm.v89i1-S.7023.
- Scutellari PN, Orzincolo C, Princivalle M, Franceschini F (1992) Diffuse idiopathic skeletal hyperostosis. Review of diagnostic criteria and analysis of 915 cases. Radiol Med 83(6):729–36.
- Pappone N, Di Girolamo C, Del Puente A, Scarpa R, Oriente P (1996) Diffuse idiopathic skeletal hyperostosis (DISH): a retrospective analysis. Clin Rheumatol 15(2):121–124. https://doi.org/ 10.1007/bf02230327
- Pappone N, Lubrano E, Esposito-del Puente A, D'Angelo S, Di Girolamo C, Del Puente A (2005) Prevalence of diffuse idiopathic skeletal hyperostosis in a female Italian population. Clin Exp Rheumatol 23(1):123–124
- Ciaffi J, Gigliotti PE, Festuccia G, Borlandelli E, Facchini G, Chiaravalloti A et al (2021) Can chest imaging be used to draw information about body mass index and obesity status? Obes Res Clin Pract 15(2):187–190. https://doi.org/10.1016/j.orcp.2021.01. 006
- Cohen J (1968) Weighted kappa: nominal scale agreement with provision for scaled disagreement or partial credit. Psychol Bull 70(4):213–220. https://doi.org/10.1037/h0026256

- Resnick D, Niwayama G (1983) Entheses and enthesopathy. Anatomical, pathological, and radiological correlation. Radiology 146(1):1–9. https://doi.org/10.1148/radiology.146.1.6849029.
- Borlandelli E, Ciaffi J, Festuccia G, Facchini G, Miceli M, Brusi V et al (2022) Osteitis condensans ilii: prevalence and characteristics of a neglected mimic of sacroiliitis. Clin Rheumatol 41(2):483– 490. https://doi.org/10.1007/s10067-021-05925-y
- Johnson R (2003) Osteitis pubis. Curr Sports Med Rep 2(2):98– 102. https://doi.org/10.1249/00149619-200304000-00009
- Kellgren JH, Lawrence JS (1957) Radiological assessment of osteo-arthrosis. Ann Rheum Dis 16(4):494–502. https://doi.org/ 10.1136/ard.16.4.494
- World Medical A (2013) World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 310(20):2191–2194. https://doi.org/10. 1001/jama.2013.281053
- Liang H, Liu G, Lu S, Chen S, Jiang D, Shi H et al (2019) Epidemiology of ossification of the spinal ligaments and associated factors in the Chinese population: a cross-sectional study of 2000 consecutive individuals. BMC Musculoskelet Disord 20(1):253. https://doi.org/10.1186/s12891-019-2569-1
- Adel H, Khan SA, Adil SO, Huda F, Khanzada U, Manohar M et al (2020) CT-Based evaluation of diffuse idiopathic skeletal hyperostosis in adult population; prevalence, associations and interobserver agreement. J Clin Densitom 23(1):44–52. https:// doi.org/10.1016/j.jocd.2018.12.001
- Hiyama A, Katoh H, Sakai D, Sato M, Tanaka M, Watanabe M (2018) Prevalence of diffuse idiopathic skeletal hyperostosis (DISH) assessed with whole-spine computed tomography in 1479 subjects. BMC Musculoskelet Disord 19(1):178. https:// doi.org/10.1186/s12891-018-2108-5
- Mori K, Kasahara T, Mimura T, Nishizawa K, Nakamura A, Imai S (2017) Prevalence of thoracic diffuse idiopathic skeletal hyperostosis (DISH) in Japanese: results of chest CT-based cross-sectional study. J Orthop Sci 22(1):38–42. https://doi.org/ 10.1016/j.jos.2016.09.003
- 25. Uehara M, Takahashi J, Ikegami S, Tokida R, Nishimura H, Sakai N et al (2020) Prevalence of diffuse idiopathic skeletal hyperostosis in the general elderly population: a Japanese Cohort Survey Randomly Sampled From a Basic Resident Registry. Clin Spine Surg 33(3):123–127. https://doi.org/10.1097/ bsd.000000000000919
- 26. Kagotani R, Yoshida M, Muraki S, Oka H, Hashizume H, Yamada H et al (2015) Prevalence of diffuse idiopathic skeletal hyperostosis (DISH) of the whole spine and its association with lumbar spondylosis and knee osteoarthritis: the ROAD study. J Bone Miner Metab 33(2):221–229. https://doi.org/10.1007/ s00774-014-0583-9
- 27. Sirasanagandla SR, Al Dhuhli H, Al Abri A, Salmi A, Jayapal SK, Sara C et al (2018) Prevalence of diffuse idiopathic skeletal hyperostosis among elderly subjects referred for radiological investigation in tertiary hospital at Oman. Anat Cell Biol 51(3):174–179. https://doi.org/10.5115/acb.2018.51.3.174
- Kim BS, Moon MS, Yoon MG, Kim ST, Kim SJ, Kim MS et al (2018) Prevalence of diffuse idiopathic skeletal hyperostosis diagnosed by whole spine computed tomography: a preliminary study. Clin Orthop Surg 10(1):41–46. https://doi.org/10.4055/ cios.2018.10.1.41
- Yoshihara H, Nadarajah V, Horowitz E (2021) Prevalence and characteristics of thoracic diffuse idiopathic skeletal hyperostosis in 3299 black patients. Sci Rep 11(1):22181. https://doi. org/10.1038/s41598-021-01092-x
- 30. Oudkerk SF, Mohamed Hoesein FAA, W PTM, Öner FC, Verlaan JJ, de Jong PA et al (2019) Subjects with diffuse idiopathic skeletal hyperostosis have an increased burden of coronary artery disease: an evaluation in the COPDGene cohort.

Atherosclerosis 287:24–9. https://doi.org/10.1016/j.atheroscle rosis.2019.05.030.

- Auðunsson AB, Elíasson GJ, Steingrímsson E, Aspelund T, Sigurdsson S, Launer L et al (2021) Diffuse idiopathic skeletal hyperostosis in elderly Icelanders and its association with the metabolic syndrome: the AGES-Reykjavik Study. Scand J Rheumatol 50(4):314–318. https://doi.org/10.1080/03009742.2020.1846779
- 32. Milner GR, Boldsen JL, Ousley SD, Getz SM, Weise S, Tarp P et al (2018) Selective mortality in middle-aged American women with Diffuse Idiopathic Skeletal Hyperostosis (DISH). PLoS ONE 13(8):e0202283. https://doi.org/10.1371/journal.pone.0202283
- 33. Julkunen H, Heinonen OP, Knekt P, Maatela J (1975) The epidemiology of hyperostosis of the spine together with its symptoms and related mortality in a general population. Scand J Rheumatol 4(1):23–27. https://doi.org/10.1080/03009747509095610
- Coaccioli S, Fatati G, Di Cato L, Marioli D, Patucchi E, Pizzuti C et al (2000) Diffuse idiopathic skeletal hyperostosis in diabetes mellitus, impaired glucose tolerance and obesity. Panminerva Med 42(4):247–251
- Mader R, Lavi I (2009) Diabetes mellitus and hypertension as risk factors for early diffuse idiopathic skeletal hyperostosis (DISH). Osteoarthritis Cartilage 17(6):825–828. https://doi.org/10.1016/j. joca.2008.12.004
- Pillai S, Littlejohn G (2014) Metabolic factors in diffuse idiopathic skeletal hyperostosis - a review of clinical data. Open Rheumatol J 8:116–128. https://doi.org/10.2174/1874312901408010116
- 37. Ciaffi J, Mele G, Mancarella L, Brusi V, Lisi L, Faranda Cordella J et al (2022) Prevalence of Type 2 and Type 1 diabetes in psoriatic arthritis: an Italian study. J Clin Rheumatol 28(2):e324–e329. https://doi.org/10.1097/rhu.000000000001706
- Tripolino C, Ciaffi J, Ruscitti P, Giacomelli R, Meliconi R, Ursini F (2021) Hyperuricemia in Psoriatic Arthritis: epidemiology, pathophysiology, and clinical implications. Front Med (Lausanne) 8:737573. https://doi.org/10.3389/fmed.2021.737573
- Kumthekar A, Ogdie A (2020) Obesity and psoriatic arthritis: a narrative review. Rheumatol Ther 7(3):447–456. https://doi.org/ 10.1007/s40744-020-00215-6
- Bliddal H, Leeds AR, Christensen R (2014) Osteoarthritis, obesity and weight loss: evidence, hypotheses and horizons - a scoping review. Obes Rev 15(7):578–586. https://doi.org/10.1111/obr. 12173
- 41. Lee J, Lee JY, Lee JH, Jung SM, Suh YS, Koh JH et al (2015) Visceral fat obesity is highly associated with primary gout in a metabolically obese but normal weighted population: a case control study. Arthritis Res Ther 17(1):79. https://doi.org/10.1186/ s13075-015-0593-6
- 42. D'Onghia M, Ciaffi J, Lisi L, Mancarella L, Ricci S, Stefanelli N et al (2021) Fibromyalgia and obesity: a comprehensive systematic review and meta-analysis. Semin Arthritis Rheum 51(2):409– 424. https://doi.org/10.1016/j.semarthrit.2021.02.007
- 43. Finckh A, Turesson C (2014) The impact of obesity on the development and progression of rheumatoid arthritis. Ann Rheum Dis 73(11):1911–1913. https://doi.org/10.1136/annrh eumdis-2014-205741
- Lago F, Dieguez C, Gómez-Reino J, Gualillo O (2007) Adipokines as emerging mediators of immune response and inflammation. Nat Clin Pract Rheumatol 3(12):716–724. https://doi.org/ 10.1038/ncprheum0674
- Turner RT, Kalra SP, Wong CP, Philbrick KA, Lindenmaier LB, Boghossian S et al (2013) Peripheral leptin regulates bone formation. J Bone Miner Res 28(1):22–34. https://doi.org/10.1002/jbmr. 1734
- 46. Ruscitti P, Ursini F, Cipriani P, Greco M, Alvaro S, Vasiliki L et al (2019) IL-1 inhibition improves insulin resistance and adipokines in rheumatoid arthritis patients with comorbid type 2 diabetes: An

observational study. Medicine (Baltimore) 98(7):e14587. https:// doi.org/10.1097/md.00000000014587

- Denko CW, Boja B, Moskowitz RW (1994) Growth promoting peptides in osteoarthritis and diffuse idiopathic skeletal hyperostosis-insulin, insulin-like growth factor-I, growth hormone. J Rheumatol 21(9):1725–1730
- Denko CW, Malemud CJ (2006) Body mass index and blood glucose: correlations with serum insulin, growth hormone, and insulin-like growth factor-1 levels in patients with diffuse idiopathic skeletal hyperostosis (DISH). Rheumatol Int 26(4):292–297. https://doi.org/10.1007/s00296-005-0588-8
- Smith LL, Burnet SP, McNeil JD (2003) Musculoskeletal manifestations of diabetes mellitus. Br J Sports Med 37(1):30–35. https:// doi.org/10.1136/bjsm.37.1.30
- Ursini F, Mauro D, Naty S, Gagliardi D, Grembiale RD (2012) Improvement in insulin resistance after short-term treatment with abatacept: case report and short review. Clin Rheumatol 31(9):1401–1402. https://doi.org/10.1007/s10067-012-2034-0
- 51. Akune T, Ogata N, Seichi A, Ohnishi I, Nakamura K, Kawaguchi H (2001) Insulin secretory response is positively associated with the extent of ossification of the posterior longitudinal ligament of the spine. J Bone Joint Surg Am 83(10):1537–1544. https://doi.org/10.2106/00004623-200110000-00013
- Ciaffi J, Mitselman D, Mancarella L, Brusi V, Lisi L, Ruscitti P et al (2021) The effect of ketogenic diet on inflammatory arthritis and cardiovascular health in rheumatic conditions: a mini review. Front Med (Lausanne) 8:792846. https://doi.org/10.3389/fmed. 2021.792846
- Tripolino C, Ciaffi J, Pucino V, Ruscitti P, van Leeuwen N, Borghi C et al (2021) Insulin signaling in arthritis. Front Immunol 12:672519. https://doi.org/10.3389/fimmu.2021.672519
- 54. Ursini F, D'Angelo S, Russo E, Arturi F, D'Antona L, Bruno C et al (2017) Serum complement C3 strongly correlates with whole-body insulin sensitivity in rheumatoid arthritis. Clin Exp Rheumatol 35(1):18–23
- Salaffi F, Carotti M, Barile A (2019) Musculoskeletal imaging of the inflammatory and degenerative joints: current status and perspectives. Radiol Med 124(11):1067–1070. https://doi.org/10. 1007/s11547-019-01004-0
- 56. Slonimsky E, Leibushor N, Aharoni D, Lidar M, Eshed I (2016) Pelvic enthesopathy on CT is significantly more prevalent in patients with diffuse idiopathic skeletal hyperostosis (DISH) compared with matched control patients. Clin Rheumatol 35(7):1823– 1827. https://doi.org/10.1007/s10067-015-3151-3
- Olivieri I, D'Angelo S, Palazzi C, Padula A, Mader R, Khan MA (2009) Diffuse idiopathic skeletal hyperostosis: differentiation from ankylosing spondylitis. Curr Rheumatol Rep 11(5):321–328. https://doi.org/10.1007/s11926-009-0046-9
- Paparo F, Revelli M, Semprini A, Camellino D, Garlaschi A, Cimmino MA et al (2014) Seronegative spondyloarthropathies: what radiologists should know. Radiol Med 119(3):156–163. https:// doi.org/10.1007/s11547-013-0316-5
- 59. La Paglia E, Zawaideh JP, Lucii G, Mazzei MA (2019) MRI of the axial skeleton: differentiating non-inflammatory diseases and axial spondyloarthritis: a review of current concepts and applications : Special issue on "musculoskeletal imaging of the inflammatory and degenerative joints: current status and perspectives." Radiol Med 124(11):1151–1166. https://doi.org/10.1007/ s11547-019-01045-5
- Oudkerk SF, de Jong PA, Attrach M, Luijkx T, Buckens CF, Mali WP et al (2017) Diagnosis of diffuse idiopathic skeletal hyperostosis with chest computed tomography: inter-observer agreement. Eur Radiol 27(1):188–194. https://doi.org/10.1007/ s00330-016-4355-x
- 61. Bécares-Martínez C, López-Llames A, Martín-Pagán A, Cores-Prieto AE, Arroyo-Domingo M, Marco-Algarra J et al (2020)

Cervical spine radiographs in patients with vertigo and dizziness. Radiol Med 125(3):272–279. https://doi.org/10.1007/ s11547-019-01111-y

 Bruno F, Arrigoni F, Palumbo P, Natella R, Maggialetti N, Reginelli A et al (2019) New advances in MRI diagnosis of degenerative osteoarthropathy of the peripheral joints. Radiol Med 124(11):1121–1127. https://doi.org/10.1007/s11547-019-01003-1 **Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.