Nonarticular Tenderness and Functional Status in Patients with Diffuse Idiopathic Skeletal Hyperostosis

REUVEN MADER, IRINA NOVOFASTOVSKI, EHUD ROSNER, MUHAMMAD ADAWI, PAULA HERER, and DAN BUSKILA

ABSTRACT. ***Objective.*** To investigate the degree of nonarticular tenderness and functional status in patients with diffuse idiopathic skeletal hyperostosis (DISH). We assessed these variables' correlation with their clinical, radiographic, and constitutional measurements and with metabolic syndrome (MS).

Methods. Eighty-seven patients with DISH were compared with 65 controls without DISH. Examination of nonarticular tenderness was performed by thumb palpation. Tenderness was scored for the 18 fibromyalgia tender points (TP), and 4 control points. Nonarticular tenderness was expressed by the number of TP and by the total tenderness score (TTS). The Short Health Assessment Questionnaire (HAQ II) was administered to all participants. Clinical and laboratory data were collected from all patients. Patients were classified as having MS by both the National Cholesterol Education Program and World Health Organization definitions.

Results. There was a statistically significant difference in TTS between controls and patients with DISH. The mean tenderness of many individual TP was significantly higher in the DISH group compared with the control group. TP counts, TTS, and body mass index (BMI) positively correlated with the HAQ II. There was a linear trend in intensity of T-spine bony bridges (BB) and the total number of TP as well as many individual TP. Patients with DISH were more likely to be affected by MS. No correlation was found between TP count, TTS, and MS.

Conclusion. Patients with DISH have a lower pain threshold than patients who do not have DISH. TP count and TTS correlate with the functional status, BMI, waist circumference, and high-grade BB. No correlation was observed between pain threshold and MS. (J Rheumatol First Release JUNE 15 2010; doi:10.3899/rheum.091008)

Key Indexing Terms:
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Diffuse idiopathic skeletal hyperostosis (DISH) is a condition characterized by calcification and ossification of soft tissues, mainly ligaments and enthesis. The main pathologic process is within the enthesis, in particular that of the axial skeleton. However, involvement of peripheral joints led researchers to use the name DISH[1,2]. Because this condition is more prevalent in older individuals, DISH and osteoarthritis (OA) often coexist. Although they have some common clinical features, several manifestations of DISH may distinguish it from primary OA[3]. However, nonarticular tenderness and functional status have rarely been reported in this group of patients. A single controlled study showed that patients with DISH had a higher Health Assessment Questionnaire (HAQ) score compared with healthy individuals despite similar fibromyalgia (FM) tender point (TP) counts. However, no differences in HAQ score or TP counts were observed between patients with DISH and patients with spondylosis[4].

Because of many constitutional and metabolic abnormalities, patients with DISH have often been reported to have metabolic syndrome (MS)[5]. Recently, the association between chronic pain and MS in women has been reported[6].

Our aim was to assess tenderness threshold and functional status in patients with DISH compared to patients with OA. We also investigated the relationships between soft tissue tenderness, functional status, and the degree of vertebral bony bridges (BB) and MS.

MATERIALS AND METHODS

Eighty-seven patients who fulfilled the Resnick classification criteria for DISH[7], and 65 controls with OA (23 with multiple site OA, 20 with large joint OA, 15 with small joint OA, and 7 with spinal OA) and no evidence for DISH were included in the study. Examination of tenderness was performed by thumb palpation, exerting a pressure of about 4 kg. Tenderness was scored for the 18 FM TP[8] and 4 control points: the right distal radius, thumb nailbed, dorsal midtarsal, and the forehead. FM TP were numbered

From the Rheumatic Diseases Unit, Department of Medicine, Ha'Emek Medical Center, Afula; and the Department of Medicine, Soroka Medical Center, Beer Sheva, Israel.

R. Mader, MD, Senior Clinical Lecturer, Head; M. Adawi, MD, Rheumatic Diseases Unit, Ha'Emek Medical Center; I. Novofastovski, MD; E. Rosner, MD, Department of Medicine, Ha'Emek Medical Center; P. Herer, MSc, Biostatistician, Ha'Emek Medical Center; D. Buskila, MD, Professor of Medicine, Department of Medicine, Soroka Medical Center.

Address correspondence to Dr. R. Mader, Rheumatic Diseases Unit, Ha'Emek Medical Center, Afula 18101, Israel. E-mail: Mader_r@clalit.org.il

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from top (occiput) to bottom (knee medial fat pad) with even numbers for the left side and odd numbers for the right side (Table 1). Tenderness was scored as 0 (no pain); 1 (mild, expressed pain but no withdrawal); 2 (moderate, expressed pain plus withdrawal); 3 (severe, immediate exaggerated withdrawal); and 4 (patient untouchable)[8]. Soft tissue tenderness was expressed by the number of TP, and by the sum of the TP score, called the total tenderness score (TTS). The thoracic spine BB were scored by a single observer as 1 = none, 2 = mild, 3 = moderate, 4 = severe. The intensity of the bridges was judged by the thickness of the ossification on anteroposterior or lateral thoracic spine radiographs. By definition, patients without DISH had no spinal bony bridges. The Short HAQ (HAQ II) was administered to all participants[9]. Demographic, clinical, and laboratory data including fasting glucose levels, serum insulin levels (Immulite 2000 Insulin; EURO/DPC Ltd., Llanberis, UK), and serum lipids profile were collected from all patients. The mean systolic and diastolic blood pressure of 3 consecutive measurements at 5-minute intervals were recorded.

Based on these data, patients were classified as having MS by the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP)[10] and the World Health Organization (WHO)[11,12]. Insulin resistance was defined by either diabetes mellitus (DM), fasting glucose ≥ 110 mg/dl, or a homeostasis model assessment index (HOMA) in the top quartile of a nondiabetic population. This last measurement was calculated from the nondiabetic patients from the entire cohort [fasting glucose (mmol/l) × fasting insulin (μU/ml)/22.5].

The study was approved by the local Institutional Review Board.

Data analysis was performed using the SPSS statistical package (SPSS Inc., Chicago, IL, USA). The relationships between the 2 study groups and categorical data were examined using chi-squared tests or Fisher's exact tests, where appropriate. The t-test or Mann-Whitney test (where appropriate) were used to compare continuous data between the 2 independent groups. Spearman's correlations were performed to assess the associations between the variables studied. Significance was set at $p < 0.05$.

RESULTS

The 2 groups had similar ethnic origin makeup, marital status, and number of children. The comparator group was made up of patients with OA. Patients with DISH were significantly more often affected by DM (40.2% vs 12.3%; $p = 0.001$). The main demographic, constitutional, and laboratory findings are given in Table 2. The upper quartile of the HOMA index in patients without DM was 2.6.

There was a statistically significant difference in TTS between controls and patients with DISH and the difference between TTS and total control point score. TP count ≥ 11 was higher in the DISH group, but did not reach statistical significance ($p < 0.06$). The data regarding soft tissue tenderness are given in Table 3. The mean tenderness of 9 of the 18 individual TP was significantly higher in the DISH group compared with the control group (TP 5–12 and 17; Figure 1). The groups had similar sex distribution; women had increased tenderness compared with men.

TP counts, TTS, and body mass index (BMI) positively correlated with the HAQ II ($r = 0.62$, $r = 0.64$, $r = 0.32$, respectively, $p < 0.001$; Figure 2). The correlation between HAQ II and soft tissue tenderness was maintained after removing the effect of BMI.

There was a linear trend in intensity of T-spine bony bridges and the total number of TP as well as many individual TP (Table 1). This was particularly true for patients with grade 4 bridges (Figure 3).

BMI and waist circumference were related to both BB and tenderness. After adjusting for BMI, there was no relationship between TP count and BB, but there was a relationship between TTS and BB ($p < 0.01$). Adjusting for waist circumference, no relationship was found between TP count and BB, but there was a relationship between TTS and intensity of BB ($p < 0.005$). Patients with DISH were more

Table 1. Mean tenderness of tender points, number of tender points, and tenderness score in relation to the intensity of T-spine bony bridges.

Tender Point	Intensity of Bony Bridges				p
	No Bridges	Grade 2 Bridges	Grade 3 Bridges	Grade 4 Bridges	
1- occiput right	0.48 ± 0.72	0.39 ± 0.50	0.45 ± 0.83	0.97 ± 1.06	NS
2- occiput left	0.44 ± 0.64	0.61 ± 0.78	0.42 ± 0.71	0.91 ± 1.03	NS
3- trapezius right	0.68 ± 0.83	0.56 ± 0.86	0.82 ± 0.98	1.53 ± 1.32	0.02
4- trapezius left	0.61 ± 0.78	0.61 ± 1.04	0.70 ± 0.83	1.37 ± 1.34	NS
5- neck base right	0.27 ± 0.61	0.50 ± 0.79	0.64 ± 0.99	0.91 ± 1.03	0.01
6- neck base left	0.23 ± 0.50	0.44 ± 0.70	0.52 ± 0.91	0.88 ± 1.04	0.03
7- supraspinatus right	0.59 ± 0.6	0.94 ± 0.94	0.73 ± 1.10	1.44 ± 1.22	0.009
8- supraspinatus left	0.54 ± 0.79	1.00 ± 1.24	0.94 ± 1.12	1.47 ± 1.39	0.02
9- 2nd rib right	0.61 ± 0.84	0.72 ± 0.83	0.82 ± 1.13	2.41 ± 5.75	0.04
10- 2nd rib left	0.53 ± 0.70	0.72 ± 0.90	0.82 ± 1.07	1.34 ± 1.43	NS
11- lateral epicondyle right	0.73 ± 0.96	1.22 ± 1.35	0.85 ± 1.12	1.53 ± 1.19	0.008
12- lateral epicondyle left	0.76 ± 0.95	1.17 ± 1.04	1.03 ± 1.21	1.44 ± 1.39	NS
13- gluteus right	0.69 ± 0.99	1.06 ± 1.16	0.73 ± 1.13	1.34 ± 1.36	NS
14- gluteus left	0.79 ± 1.01	0.89 ± 0.83	0.88 ± 1.19	1.25 ± 1.37	NS
15- trochanter right	0.58 ± 0.93	0.89 ± 1.08	0.76 ± 1.15	1.12 ± 1.21	NS
16- trochanter left	0.72 ± 0.97	1.00 ± 1.19	0.76 ± 1.03	1.06 ± 1.22	NS
17- medial knee right	0.81 ± 1.11	1.50 ± 1.58	1.15 ± 1.23	1.63 ± 1.45	NS
18- medial knee left	0.89 ± 1.15	1.44 ± 1.38	1.09 ± 1.36	1.50 ± 1.41	0.08
No. tender points	7.21 ± 5.98	9.06 ± 6.33	7.48 ± 6.56	10.56 ± 7.08	0.11
Total tenderness score	11.10 ± 11.32	15.67 ± 12.31	14.09 ± 15.54	24.09 ± 20.38	0.03

NS: not significant.

Table 2. Patient characteristics, and clinical and laboratory values.

Variables	DISH, n = 87	Non-DISH, n = 65	p
Mean age, yrs, ± SD	64.1 ± 8.7	63.3 ± 9.1	NS
Men/women (% men)	29/63 (31.5)	14/55 (20.3)	0.14
Years since diagnosis	3.6 ± 3.4	6.6 ± 7.4	0.001
Body mass index	33.3 ± 5.8	29.6 ± 6.0	0.001
Waist circumference, cm	107.2 ± 11.7	98.0 ± 10.6	0.001
Waist circumference, men, cm	110.3 ± 14.0	96.2 ± 7.2	0.01
Waist circumference, women, cm	105.8 ± 10.3	98.5 ± 11.3	0.001
Systolic BP, mm Hg	140.0 ± 18.1	131.8 ± 19.0	0.004
Diastolic BP, mm Hg	81.7 ± 9.4	79.2 ± 10.0	0.23
Glucose, mg/dl	111.7 ± 35.5	94.3 ± 18.7	0.001
HOMA index	3.04 ± 2.26	1.97 ± 1.33	0.004
Total cholesterol, mg/dl	200.6 ± 38.8	205.0 ± 34.4	NS
LDL, mg/dl	116.8 ± 33.4	123.6 ± 30.5	NS
HDL, mg/dl	51.0 ± 12.6	52.8 ± 12.7	NS
HDL men, mg/dl	44.9 ± 9.7	42.4 ± 6.3	NS
HDL women, mg/dl	53.9 ± 12.8	55.1 ± 12.4	NS
TG, mg/dl	153.0 ± 67.7	133.1 ± 59.4	NS

DISH: diffuse idiopathic skeletal hyperostosis; BP: blood pressure; NS: not significant; HOMA: homeostasis model assessment index; LDL: low-density lipoprotein; HDL: high-density lipoprotein; TG: triglyceride.

Table 3. Nonarticular tenderness in patients with diffuse idiopathic skeletal hyperostosis (DISH) vs patients without DISH.

Variable	DISH	Non-DISH	p
Tender point score	18.82 ± 17.33	10.74 ± 11.26	0.02*
Number of tender points	8.82 ± 6.84	7.03 ± 6.06	NS*
Patients with ≥ 11 tender points	40 (43.5%)	20 (29%)	< 0.06**
Control point score	0.89 ± 1.59	0.51 ± 0.95	NS*
Δ between tender and control points	16.92 ± 16.38	10.22 ± 10.66	0.02*

*Mann-Whitney test. ** Fisher exact test. NS: not significant.

likely to be affected by MS by both the WHO definition (52.9 vs 18.8%; p = 0.001) and the NCEP definition (58.6 vs 40.0%; p = 0.02). No association was found among TP count, TP score, and MS.

DISCUSSION

DISH has been established as a radiologic entity. However, the clinical manifestations have not yet been investigated in depth and it is still considered by some authors as a state and not a disease[13]. Other authors have suggested that in some cases, radiographic involvement of peripheral joints might be symptomatic, while in others it might be asymptomatic[14,15]. It has been suggested that patients with DISH have similar characteristics of pain and stiffness to patients with spondylosis. FM TP count did not differ among patients with DISH, spondylosis, and "healthy" controls[4]. In our study, the sample size was larger than previous studies and the control group was not composed of "healthy" individuals. We believe that in this older group of patients (mean age 64.1 yrs), it would be extremely difficult to find healthy

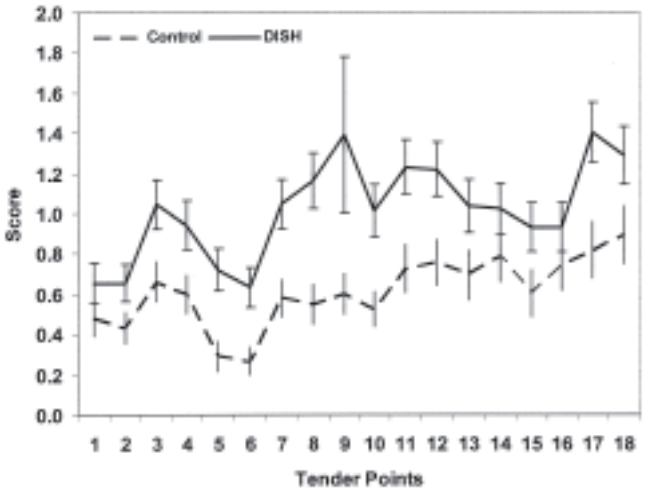

Figure 1. Tenderness scores of the individual fibromyalgia tender points in patients with diffuse idiopathic skeletal hyperostosis (DISH) versus controls.

subjects. Therefore, the control group was composed of patients with OA who were discriminated from the DISH group by the absence of the characteristic thoracic spine BB. As opposed to the TP count, TTS was significantly higher in patients with DISH, suggesting a lower tenderness threshold in these patients. The TTS directly correlated with the intensity of BB, and in particular to grade 4 BB. The correlation with milder forms of BB was weak, probably caused by the subjective aspect of the grading, based on the impression of the observer. It could well be that with a more accurate and validated measurement of the intensity of BB, the results might have reached statistical significance also for milder forms of BB.

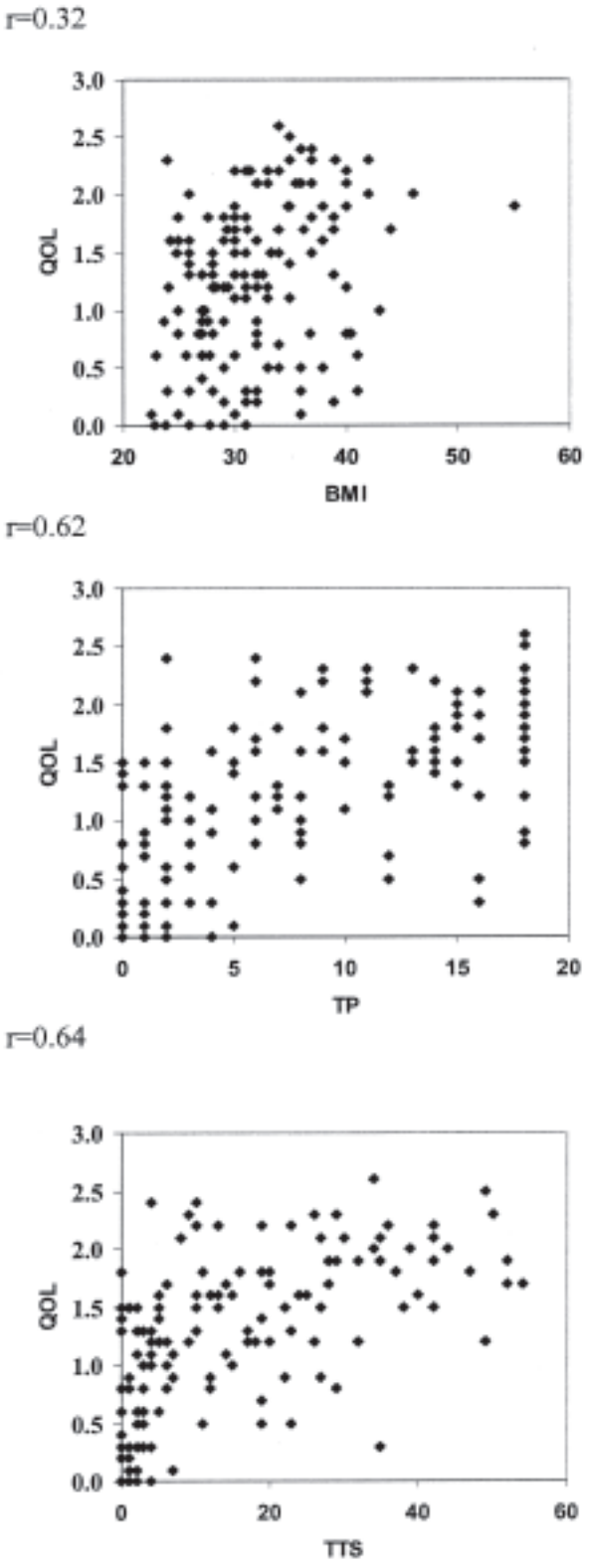

Figure 2. Correlations between quality of life (QOL) and body mass index (BMI), number of tender points (TP), and total tenderness score (TTS; Spearman, $p < 0.001$). QOL was scored by the Short Health Assessment Questionnaire.

The HAQ is a widely used and accepted measure of functional status in rheumatic diseases[16]. The HAQ is also capable of predicting work disability, medical costs, joint replacement, and mortality[17,18,19,20,21]. Recently, it was shown that a shorter questionnaire, the HAQ II, performs as well as the more extensive HAQ[9]. It has recently been shown that nonarticular tenderness and poor functional status are directly associated with elevated BMI[22]. In our study, BMI, TP count, and TTS correlated with poor functional status. The relationships between tenderness scores and poor functional status were maintained after correction for BMI, suggesting that patients with DISH have poor functional status independent of BMI. Further, the correlation between high-grade BB and TTS was preserved after adjusting for BMI, suggesting that the intensity of the spinal entheseal ossification is the main contributor to the soft tissue tenderness and poor functional status. It has been suggested and recently reiterated that mechanical factors arising from the cervical and lumbar spine determine patterns of symptoms and tenderness in many subjects with regional and general pain syndromes[23]. We did not investigate the upper and lower portions of the spine, although they are often involved in DISH. The role played by involvement of the thoracic spine has not been investigated. However, a significantly increased tenderness, for grade 4 BB, was observed between the upper and lower margins of the thoracic cage (Table 1). It is therefore conceivable that the T-spine could be at least a contributor for the generation of low tenderness threshold in this region.

DISH has long been known to be associated with metabolic and constitutional disorders such as obesity, high blood pressure, glucose intolerance, or overt DM, hyperuricemia, and others. It was recently shown that these patients have a significantly higher likelihood to be affected by MS, and bear a higher risk for cardiovascular morbidity[5]. A recent study showed that women with chronic pain were more often affected by MS[6]. Those patients were significantly younger than the prevalent age group of patients with DISH, and patients with DM were excluded from this analysis. It is conceivable, therefore, that chronic pain might further enhance the risk for MS. Of interest is the higher mortality rate associated with widespread pain disorders[24,25]. The mortality was ascribed mainly to cancer, and to a lesser extent to cardiovascular morbidities. Interestingly, the risk of death increased as the number of reported pain sites increased. Although we do not have, at present, enough data to demonstrate a higher mortality rate among patients with DISH, we did demonstrate a higher TTS in patients with high-grade BB. Whether increased tenderness further amplifies the known cardiovascular risk in patients with DISH remains to be investigated. Elevated BMI is a risk factor *per se* for FM[26], but the role of MS as a risk factor for the development of widespread pain has not yet been investigated.

Our study shows that patients with DISH have increased

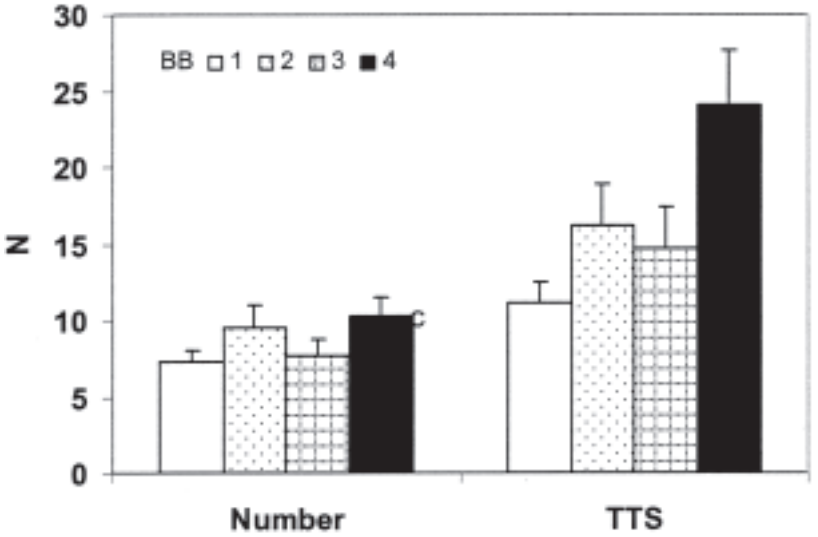

Figure 3. The number of tender points and the total tenderness score (TTS) in relation to the intensity of bony bridges (BB): 1 = none, 2 = mild, 3 = moderate, 4 = severe. TTS in patients with grade 4 bridges was significantly higher compared to patients with no bridges ($p < 0.001$).

nonarticular tenderness. A high degree of BB is associated with a lower pain threshold and as a consequence, with a lower functional status. The increased prevalence of MS, and the augmented cardiovascular risk, might be enhanced by the lower tenderness threshold. While we have no known methods to reverse the entheseal calcification and/or ossification, early diagnosis combined with standard care for treatment of nonarticular tenderness might prove useful in improving the quality of life and functional status of these patients. Additional improvement can be obtained by controlling risk factors for MS, in particular BMI and waist circumference. Forestier, *et al*, in a description of 9 cases, considered DISH to be nearly asymptomatic except for a well tolerated stiffness[27]. This statement, as well as others in that study, should be challenged by further studies.

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