Prevalence of diffuse idiopathic skeletal hyperostosis among elderly subjects referred for radiological investigation in tertiary hospital at Oman

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Abstract: Diffuse idiopathic skeletal hyperostosis (DISH) is characterized by calcification of different entheseal sites including the anterior longitudinal ligament of the spine. There is no documented information about DISH in Oman. This study determined the prevalence of DISH and associated factors among elderly subjects in a national tertiary care referral hospital in Oman. This retrospective study reviewed chest X-rays of all patients aged more than 50 years, referred to the radiology department of Sultan Qaboos University Hospital in the year 2016, based on the Resnick’s criteria. The prevalence was expressed as proportions across age groups and sex. Chi-square test and logistic regression analysis was done to determine the association of the age and sex with DISH. A total of 1305 chest X-rays of patients were reviewed. The overall prevalence of DISH was 10%, with male to female ratio of 1.56:1. The odds ratio for males and increasing age were 1.63 (95% confidence interval [CI], 1.12–2.3; P<0.05) and 1.34 (95% CI, 1.14–1.58; P<0.001) respectively. The prevalence increased with age to maximum of 13% in the age group of ≤80. The pre-stage DISH prevalence was 9.3% and more frequently observed among males. Prevalence of DISH in the national tertiary care referral center in Oman is lower than in Jewish population, almost similar to Japanese, but higher than in Koreans. DISH prevalence is positively associated with age and sex. It is necessary to take appropriate precautionary measures to target the ageing population in Oman, especially elderly males.

Key words: Chest X-ray, Diffuse idiopathic skeletal hyperostosis, Prevalence, Oman, Calcification

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Introduction

Diffuse idiopathic skeletal hyperostosis (DISH) is a systemic non-inflammatory, musculoskeletal disorder characterized by calcification of various entheseal sites of the body [1]. The reported prevalence of DISH is higher among elderly and predominantly seen in males [2, 3]. In comparison to ankylosing spondylitis and other ankylosing disorders, there is limited data available on DISH. It usually manifests as an asymptomatic condition with mild symptoms [4]. It is well
known to be associated with serious clinical manifestations viz. myelopathy, radiculopathy, vertebral canal stenosis, spinal cord injury subsequent to spinal fracture, complete spinal arthrodesis, cervical airway obstruction, entrapment of peripheral nerves and dysphagia [5-8].

Recently DISH has drawn increasing attention among researchers and clinicians. Although DISH is considered as an asymptomatic condition, increasing evidence suggests that it is an important indicator of underlying pathological osseous changes. DISH progression may alter the biomechanics of the spine, which subsequently results in several serious complications [5-8]. In spite of its increasing clinical significance, the prevalence of DISH is largely unknown in most of the Asian countries.

The etiology of the disease lacks clarity. Various factors have been hypothesized to be involved in the pathogenesis of DISH such as exposure to environmental factors (retinol and fluoride), mechanical factors, genetic factors (human leukocyte antigen genes), excess growth factors (insulin-like growth factor), obesity and type 2 diabetes, mellitus and drugs (vitamin A derivatives, acitretin, isotretinoin, and etretinate) [9-14]. Current theories suggest that calcification of anterior longitudinal ligament is due to the altered function and growth of the osteoblasts [15].

Clinically the diagnosis of DISH is made using radiological investigations and based on following criteria: presence of ossified or calcified ligament over at least four contiguous vertebrae, no significant degenerative changes in the intervertebral disc with preservation of its relative height in the affected areas, complete absence of sacroiliac or apophyseal joint ankyloses and non-fusion of intraarticular areas [2]. DISH is often seen in the thoracic region, followed by cervical and lumbar regions [16].

There is no established successful treatment available for the disease. Physical therapy, anti-inflammatory medication, analgesics, and sedation are reported to be effective in the management of the disease [17, 18]. The prevalence of DISH has been explored in different populations all over the world, including in Asian population (Table 1) [19-29]. DISH studies in literature have studied samples from above 40 to 50 years of age (Table 1). To the best of our knowledge, only one study has been conducted in Middle East region more than three decades ago [20]. The total number of general X-ray (plain X-ray and intravenous urogram) at Department of Radiology, Sultan Qaboos University Hospital (SQUH) as per last report available is 47,021 [30]. Of these only plain chest X-rays of those over 50 years in the year of study was 6,500. The database was readily available to conduct this first study in Oman to determine the prevalence of DISH and its associated factors in Omani elderly population.

### Materials and Methods

This retrospective study is based on the compilation of relevant information from the Track Care database of SQUH related to all indoor and outpatients aged more than 50 years referred for chest X-ray to Department of Radiology, SQUH, from January 2016 to December 2016. These patients were included in the study. The age and sex of the patients were documented. Patients with inconclusive chest X-rays, history of spinal fractures were excluded from the study. The postero-anterior and lateral chest radiograms of these patients were

| Study | Country | Target, total number | Age (y) | Diagnostic criteria | Screening method | Prevalence (male/female/total) (%) |
|-------|---------|----------------------|---------|---------------------|-----------------|----------------------------------|
| Julkunen et al. (1975) [19] | Finland | GP, 8993 | >40 | Julkunen | Chest XR (L) | 3.8/2.6/2.6 |
| Bloom (1984) [20] | Israel | P, 1236 | >40 | Resnick | Chest XR (L) | 22.4/13.4/17.9 |
| Boachie-Adjei et al. (1987) [21] | USA | P, 75 | >45 | Forestier | Autopsy, Chest XR (AP, L, Ob), CT | 31/23/28 |
| Cassim et al. (1990) [22] | South Africa | P, 1500 | >40 | Resnick and Bloom | Chest XR (L) | 3.8/4.2/3.9 |
| Weinfeld et al. (1997) [23] | USA | P, 2364 | >50 | Resnick | Chest XR (PA, L) | 25/15/NA |
| Kiss et al. (2002) [24] | Hungary | GP, 635 | >50 | Resnick | Chest XR (PA, L), dorsal XR, lumbar XR | 3.8/4.2/3.9 |
| Kim et al. (2004) [25] | Korea | P, 3595 | >50 | Resnick | Chest XR (L) (PACS) | 5.4/0.8/2.9 |
| Pappone et al. (2005) [26] | Italy | GP, 93 | >40 | Resnick | Dorsal XR, lumbar XR | NA/NA/15.1 |
| Westerveld et al. (2008) [27] | Netherlands | P, 501 | >50 | Resnick | Chest PA and lateral | 22.7/12.1/17 |
| Kagotani et al. (2015) [28] | Japan | GP, 1647 | >23 | Resnick | Whole spine XR (AP, L) | 22/4.8/11 |
| Mori et al. (2017) [29] | Japan | P, 3013 | >16 | Resnick | Chest CT | 13/2.5/8.7 |

DISH, diffuse idiopathic skeletal hyperostosis; GP, general population; XR, standard radiographs; L, lateral; P, patients; AP, anterior-posterior; Ob, oblique; CT, computed tomography; PA, posterior-anterior; NA, not available; PACS, Picture Archiving and Communication System.

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reviewed by the same radiologist using Picture Archiving and Communication System (PACS, ver. 4.4.516.21), manufactured by Philips Company (Foster City, CA, USA). The diagnosis of DISH was based on Resnick’s definition [2]. The positive cases of DISH were established when there was a contiguous ossified ligament over at least four consecutive vertebrae. Presence of three level involvement of ossification was considered as pre-stage DISH [27]. Assuming a DISH prevalence of 20% in our population, the sample size calculated for a single proportion for a finite population, considering relative precision of 10% was 1,223. Institutional Ethical Committee (SQU-EC/093/17) has approved the study.

Statistical analysis

The data was analyzed using SPSS Statistics software ver. 23 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to describe the distribution pattern of DISH among different age groups and sex. The association between DISH with age and gender was determined using Chi square analysis. Logistic regression was performed to determine the odds of age and sex with DISH.

Results

A total of 1,305 patients referred for chest X-ray to SQUH in Oman were included in the study. Among the study subjects, 694 (53.2%) were men. The overall prevalence of DISH in the cohort was 10% (n=130). The DISH prevalence was more frequent in men (n=83, 12%) than in women (n=47, 7.7%) and male to female ratio was 1.56:1. The overall pre-stage DISH prevalence was 9.3% (n=122) and male to female ratio was 1.14:1. Age (chi-square=14.6, df=4, P<0.05) and sex (chi-square=6.5, df=1, P<0.05) were found to be significantly associated with DISH. The DISH prevalence significantly increased with increasing age from 4% to 13%, except for >90s age group where it remained constant (12.9%). The odds ratio for gender and increasing age was 1.63 (95% confidence interval [CI], 1.12–2.3; P<0.05) and 1.34 (95% CI, 1.14–1.58; P<0.001), respectively. These results indicate that elderly men are more prone to develop DISH (Tables 2, 3, Figs. 1, 2).

Discussion

DISH was recognized few decades ago and was described with various synonyms. Initially, in 1938 Meyer and For ester [31] introduced the term moniliform hyperostosis to describe the thoracic spine hyperostosis and calcification. In 1950, Forestier and Rotes-Querol [1] used another term senile ankylosing vertebral hyperostosis or ‘Forestier’s disease’ to differentiate it from other spinal diseases. Later in 1975, Resnick et al. [2] introduced the term DISH to describe the disease more appropriately. They have proposed a diagnostic criterion for DISH after their study on spines of 215 cadavers and 100 patients. Most of the clinicians and researchers have used Resnicks’s criteria to diagnose DISH (Table 1), but few authors have also used Julkunen’s and Utsinger criteria [19, 32].

Most of the studies have used plain chest X-rays (postero-anterior and lateral chest X-rays) as screening method (Table 1). Few authors have preferred cadaveric autopsy [21], computed tomographic scan [29] and magnetic resonance imaging [33]. In our study, lateral chest X-rays were reviewed. In our study lateral chest X-rays were reviewed mainly because

| Variable | Odds ratio | 95% Confidence interval | P-value |
|----------|------------|-------------------------|---------|
| Sex      | 1.63       | 1.12-2.3                | 0.05    |
| Age      | 1.34       | 1.14-1.58               | 0.001   |

Fig. 1. Prevalence of diffuse idiopathic skeletal hyperostosis (DISH) and pre-stage DISH at different age groups.
DISH was found to be more prevalent in thoracic spine. Also, chest X-ray investigations have better patient acceptability, are convenient and readily available, have low amount of radiation, are safe and the findings are relatively consistent. Furthermore, it has been demonstrated that the lateral chest X-rays have relatively high specificity and sensitivity [31]. In our study, screening of chest X-rays was carried out on PACS system. PACS presents the complex data in simplified manner and images can be stored indefinitely and retrieved on request [34].

The prevalence of the DISH has been reported in various selected populations all over the world (Table 1). Weinfeld et al. [23], have studied the prevalence among different ethnic groups including white, Asian, black, native-American, and Hispanic population and have noted a low prevalence in Asians. Further, they concluded that genetic and/or hereditary difference could influence the prevalence of the DISH. Utsinger also described such influence based on the findings on Prima Indians from Arizona [32].

The prevalence of DISH in Asian population is variable in comparison to other ethnic groups and/or Western population. Among Asians, in Koreans the reported prevalence is 2.9% to 4.1% according to different criteria used for diagnosis [25]. In Jewish population from the Middle East [20], a higher prevalence of 22.4% among men and 13.4% among women has been documented. Two studies in Japan noted prevalence estimates of DISH as 11% [28] and 8.7% [29]. The prevalence in the present study (11%) is lower than Jewish population and higher than Koreans, but nearly similar to Japanese. In European countries, the prevalence of DISH varied between 2.6 % and 17% [19, 24, 26, 27]. Prevalence of DISH in Oman is lower than Italy [26] and Netherlands [27] but it is much higher than Finland [19] and Hungary [24].

Even though the pathogenic process of DISH begins at early part of life, the disease is observed most commonly in elderly people older than 40 years of age (Table 1). However, the evidence suggests that although calcification of enthuses beings between 20 to 40 years of age, the complete progression of disease to fulfill the diagnostic criteria requires several decades [3]. In a study by Mata et al. [35], the disease was reported in population older than 70 years of age. Holton et al. [36], have reported high prevalence in men aged older than 65 years. Cassim et al. [22] demonstrated that patients older than 70 years would have prevalence higher than 10%. In a study by Henrard and Bennett [37], prevalence increased to a maximum of 54 in men and 14% in women aged 65 years. Bloom [20] have noted an increased trend in prevalence with increasing age to a maximum of 46% in males and 30% in females aged 80 years. Weinfeld et al. [23] compared the prevalence at two different age groups (50 and 70) and found approximately 10% increase in prevalence with increasing age. From the above reports, it is clear that the prevalence and age are positively correlated. Similar to previous reports in the present study prevalence increased with increasing age. With regard to the available evidence, the well-known male dominance is also being seen in our study. However, it is lower than the expected male/female ratio of 2:1 [3].

In our study, we have recorded the pre-stage DISH to understand the progression and natural course of the disease. In Netherlands population, Westerveld et al. [27], have found that pre-stage DISH was more frequent in women and raised with increasing age. Their findings suggested that women most likely develop ligament ossification at a later life but does not progress into a complete DISH. Contrary to their findings, in our results pre-stage DISH was found to be more frequent in men and was not influenced by age. There is a
need for more studies to draw inference for conclusive evidence regarding the same.

Our findings need to be interpreted with caution. Our study being single-centered, there is a possibility of underestimation of prevalence due to selection bias in our study, as we included only those subjects who underwent radiological investigation at this center, and this sample may not be representative of all the elderly subjects.

Prevalence of DISH in Oman is lower than in Jewish population, almost similar to Japanese but higher than in Koreans. It may perhaps support the hypothesis that ethnic factors influence the DISH prevalence. In addition, DISH prevalence is positively associated with age and gender in our study. We recommend that appropriate precautionary measures need to be taken to target the ageing population, with special emphasis on elderly men.

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References

1. Forestier J, Rotes-Querol J. Senile ankylosing hyperostosis of the spine. Ann Rheum Dis 1950;9:321-30.
2. Resnick D, Shaul SR, Robins JM. Diffuse idiopathic skeletal hyperostosis (DISH): Forestier's disease with extraspinal manifestations. Radiology 1975;115:513-24.
3. Nascimento FA, Gatto LA, Lages RO, Neto HM, Demartini Z, Koppe GL. Diffuse idiopathic skeletal hyperostosis: a review. Surg Neurol Int 2014;5(Suppl 3):S122-5.
4. Mata S, Fortin PR, Fitzcharles MA, Starr MB, Joseph L, Watts CS, Gore B, Rosenberg E, Chhem RK, Esdaile JM. A controlled study of diffuse idiopathic skeletal hyperostosis: clinical features and functional status. Medicine (Baltimore) 1997;76:104-17.
5. Nelson RS, Uurguhart AC, Faciszewski T. Diffuse idiopathic skeletal hyperostosis: a rare cause of dysphagia, airway obstruction, and dysphonia. J Am Coll Surg 2006;202:938-42.
6. Caron T, Bransford R, Nguyen Q, Agel J, Chapman J, Bellabarba C. Spine fractures in patients with ankylosing spinal disorders. Spine (Phila Pa 1976) 1990;15:131-2.
7. Mader R. Clinical manifestations of diffuse idiopathic skeletal hyperostosis of the cervical spine. Semin Arthritis Rheum 2002;32:130-5.
8. Westerveld LA, Verlaan J, Oner FC. Spinal fractures in patients with ankylosing spinal disorders: a systematic review of the literature on treatment, neurological status and complications. Eur Spine J 2009;18:145-56.
9. DiGiovanna JJ, Helfgott RK, Gerber LH, Peck GL. Extraspinal tendon and ligament calcification associated with long-term therapy with etretinate. N Engl J Med 1986;315:1177-82.
10. DiGiovanna JJ. Isotretinoin effects on bone. J Am Acad Dermatol 2001;45:5176-82.
11. Moskowitz RW, Boja B, Denko CW. The role of growth factors in degenerative joint disorders. J Rheumatol Suppl 1991;27:147-8.
12. Denko CW, Malemud CJ. Body mass index and blood glucose: correlations with serum insulin, growth hormone, and insulin-like growth factor-I levels in patients with diffuse idiopathic skeletal hyperostosis (DISH). Rheumatol Int 2006;26:292-7.
13. Kiss C, Szlágyi M, Paksy A, Póó G. Risk factors for diffuse idiopathic skeletal hyperostosis: a case-control study. Rheumatology (Oxford) 2002;41:27-30.
14. Troillet N, Gerster JC. Forestier disease and metabolism disorders: a prospective controlled study of 25 cases. Rev Rhum Ed Fr 1993;60:274-9.
15. Atzeni F, Sarzi-Puttini P, Bevilacqua M. Calcium deposition and associated chronic diseases (atherosclerosis, diffuse idiopathic skeletal hyperostosis, and others). Rheum Dis Clin North Am 2006;32:413-26.
16. Resnick D, Shapiro RF, Wiesner KB, Niwawayma G, Utsinger PD, Shaul SR. Diffuse idiopathic skeletal hyperostosis (DISH) [ankylosing hyperostosis of Forestier and Rotes-Querol]. Semin Arthritis Rheum 1978;7:153-87.
17. Al-Herz A, Snip JP, Clark B, Esdaile JM. Exercise therapy for patients with diffuse idiopathic skeletal hyperostosis. Clin Rheumatol 2008;27:207-10.
18. Umerah BC, Mukherjee BK, Ibekwe O. Cervical spondylosis and dysphagia. J Laryngol Otol 1981;95:1179-83.
19. Julkunen H, Heinonen OP, Knekt P, Maatela J. The epidemiology of hyperostosis of the spine together with its symptoms and related mortality in a general population. Scand J Rheumatol 1975;4:23-7.
20. Bloom RA. The prevalence of ankylosing hyperostosis in a Jerusalem population: with description of a method of grading the extent of the disease. Scand J Rheumatol 1984;13:181-9.
21. Boachie-Adjei O, Bullough PG. Incidence of ankylosing hyperostosis of the spine (Forestier's disease) at autopsy. Spine (Phila Pa 1976) 1987;12:739-43.
22. Cassim B, Mody GM, Rubin DL. The prevalence of diffuse idiopathic skeletal hyperostosis in African blacks. Br J Rheumatol 1990;29:131-2.
23. Weinfeld RM, Olson PN, Maki DD, Griffiths HJ. The prevalence of diffuse idiopathic skeletal hyperostosis (DISH) in two large American Midwest metropolitan hospital populations. Skeletal Radiol 1997;26:222-5.
24. Kiss C, O'Neill TW, Mituszevova M, Szilágyi M, Póó G. The prevalence of diffuse idiopathic skeletal hyperostosis in a population-based study in Hungary. Scand J Rheumatol 2002;31:226-9.
25. Kim SK, Choi BR, Kim CG, Chung SH, Choe JY, Joo KB, Bae SC, Yoo DH, Jun JB. The prevalence of diffuse idiopathic skeletal hyperostosis in Korea. J Rheumatol 2004;31:2032-5.
26. Pappone N, Lubrano E, Esposito-del Puente A, D'Angelo S, Di Girolamo C, Del Puente A. Prevalence of diffuse idiopathic skel-
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27. Westerveld LA, van Ufford HM, Verlaan JJ, Oner FC. The prevalence of diffuse idiopathic skeletal hyperostosis in an outpatient population in The Netherlands. J Rheumatol 2008;35:1635-8.

28. Kagotani R, Yoshida M, Muraki S, Oka H, Hashizume H, Yamada H, Enyo Y, Nagata K, Ishimoto Y, Teraguchi M, Tanaka S, Nakamura K, Kawaguchi H, Akune T, Yoshimura N. 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 2015;33:221-9.

29. Mori K, Kasahara T, Mimura T, Nishizawa K, Nakamura A, Imai S. Prevalence of thoracic diffuse idiopathic skeletal hyperostosis (DISH) in Japanese: Results of chest CT-based cross-sectional study. J Orthop Sci 2017;22:38-42.

30. Annual report 2013 [Internet]. Muscat: College of Medicine and Health Sciences and Sultan Qaboos University Hospital; 2013 [cited 2017 Aug 1]. Available from: https://www.squ.edu.om/Portals/6/AnnualReports/AnnualReport%202013LowRes.pdf?ver=2015-04-13-084000-653.

31. Meyer M, Forester E. Considerations pathogeniques sur l’hyperostose moniliforme du flanc droit de la colonne dorsale. Rev Rhum Mal Osteoartic 1938;5:286-93.

32. Utsinger PD. Diffuse idiopathic skeletal hyperostosis. Clin Rheum Dis 1985;11:325-51.

33. Cammisa M, De Serio A, Guglielmi G. Diffuse idiopathic skeletal hyperostosis. Eur J Radiol 1998;27 Suppl 1:S7-11.

34. Strickland NH. PACS (picture archiving and communication systems): filmless radiology. Arch Dis Child 2000;83:82-6.

35. Mata S, Hill RO, Joseph L, Kaplan P, Dussault R, Watts CS, Fitzcharles MA, Shiroky JB, Fortin PR, Esdaile JM. Chest radiographs as a screening test for diffuse idiopathic skeletal hyperostosis. J Rheumatol 1993;20:1905-10.

36. Holton KE, Denard PJ, Yoo JU, Kado DM, Barrett-Connor E, Marshall LM; Osteoporotic Fractures in Men (MrOS) Study. Diffuse idiopathic skeletal hyperostosis and its relation to back pain among older men: the MrOS Study. Semin Arthritis Rheum 2011;41:131-8.

37. Henrard JC, Bennett PH. Epidemiological study of vertebral hyperostosis. Survey in an adult population of American Indians. Rev Rhum Mal Osteoartic 1973;40:581-91.