RESEARCH

A SINGLE-CENTER, CROSS-SECTIONAL PREVALENCE STUDY OF CERVICAL DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS

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Abstract

Introduction: In this study, we aimed to investigate the prevalence and characteristics of cervical diffuse idiopathic skeletal hyperostosis using computed tomography scans of the cervical vertebra.

Materials and Methods: This study was performed using the Picture Archiving and Communication System of our hospital. Computed tomography images of 1744 patients were included in this study. The patients were divided into age groups by decade. The characteristics of the cervical osteophytes and intervertebral bridging were recorded. Cervical diffuse idiopathic skeletal hyperostosis was diagnosed based on the criteria described by Resnick and Niwayama.

Results: The mean age of the study group was 48 years. The prevalence rate of cervical diffuse idiopathic skeletal hyperostosis was 6.3% (6.4% in males and 6.2% in females). The difference between genders was not statistically significant (p=0.908). The prevalence rates significantly increased as age increased. The prevalence rate of cervical osteophytes was 36.5% (33.9% in males and 40.6% in females). The most frequently affected level was C5-6 (16.9%), and the vertebra was C6 (30.6%). Osteophytes were localised in the midline with a rate of 75.5% and was most frequently found in the 70–79 age group (81.2%).

Conclusion: In our study, we detected the prevalence rates of cervical diffuse idiopathic skeletal hyperostosis and cervical osteophytes, which were 6.3% and 36.5%, respectively. In comparison, the most frequently affected vertebra and intervertebral levels were, respectively, C6 (30.6%) and C5-6 (16.9%), and cervical osteophytes was most often formed in the midline (75.5%).

Keywords: Geriatrics; Hyperostosis, Diffuse Idiopathic Skeletal; Prevalence; Cervical Vertebrae; Osteophyte.

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INTRODUCTION

Diffuse idiopathic skeletal hyperostosis (DISH), or Forestier's disease, is a chronic and non-inflammatory disease characterised by diffuse osteophyte formations in the vertebra due to ossification of the anterior longitudinal ligament, which connects the ventral aspects of the vertebrae and surrounding tissues (1, 2). Its diagnosis is based on those criteria described by Resnick and Niwayama, the presence of calcification and ossification along the ventrolateral aspects of at least four adjacent vertebral bodies (3 intervertebral levels); the preservation of disc levels; and the absence of apophyseal joint degeneration or sacroiliac inflammatory changes (3).

DISH's pathophysiology has not yet been clearly described; however, a strong relationships with metabolic diseases, such as obesity and type 2 diabetes mellitus, has been identified in the literature (4). It has been reported that its prevalence ranges between 2.6% and 30.8% in the general population. DISH also increases with age, and it is more commonly seen in males and in developed populations. The male-female ratio was approximately 2:1 (5). Thoracic vertebrae are the most frequently involved region followed by cervical and lumbar vertebrae. The clinical signs of the disease vary depending on the involvement site. The most commonly found symptoms are pain and limited motion in the affected vertebral site (4, 6).

The prevalence of DISH of the cervical vertebrae (C-DISH), or cervical Forestier's disease, was reported as between 0 and 7.9% in various studies (7, 8). C-DISH is usually asymptomatic. However, though rarely, various symptoms and signs may be related with the localisation of pathological ossification and its impact on the neighbouring pharynx, oesophagus and trachea. C-DISH symptoms also include cervical pain, limited motion, dysphagia, dysphonia, snoring, obstructive sleep apnoea, stridor, vocal cord paralysis, coughing, spinal cord compression, pharynx/hypopharynx injury due to post-traumatic osteophyte fracture, dyspnoea, aspiration pneumonia, weight loss, thoracic exit syndrome, Horner's syndrome, spinal fracture, stroke and myelopathy. These symptoms may be accompanied by difficulties in intubation-extubation and airway management. Cardiopulmonary arrest has been also reported, though rarely. The symptomatic patients are mostly male, and dysphagia is the most frequently seen symptom (75%) (6, 9-13).

There are no disease-specific standard laboratory findings. The diagnosis of DISH is established radiologically. The disease is most commonly identified coincidentally in standard radiographies. Computed tomography (CT) is the most important imaging technique in its diagnosis, and it displays the relationship of DISH with neighbouring organs as well as its shape and size (Figure 1A, 1B). The larynx, hypopharynx, trachea and oesophagus can be examined comprehensively using magnetic resonance imaging (MRI), barium oesophagography, video laryngoscopy (Figure 1C), gastroscopy and bronchoscopy (4, 12).

Differential diagnosis of DISH, includes diseases that cause excessive ossification in the axial skeleton, such as ankylosing spondylitis, degenerative spondylosis, seronegative spondyloarthropathy, acromegaly, parathyroid disorders, fluorosis and ochronosis (4).

Symptomatic therapy is primarily applied for its treatment. In the case of failed conservative treatment, surgical therapy can be planned if conditions such as myelopathy and fracture develop (9, 14).

In recent years, some epidemiological research has been carried out among some ethnic groups, particularly in Europe and Far East regions. Most of research on DISH are case reports or case series. There are not yet any adequate comprehensive prevalence studies for all ethnic populations (10). Due to the rapid aging of the world's population, clinicians are increasingly diagnosing C-DISH in

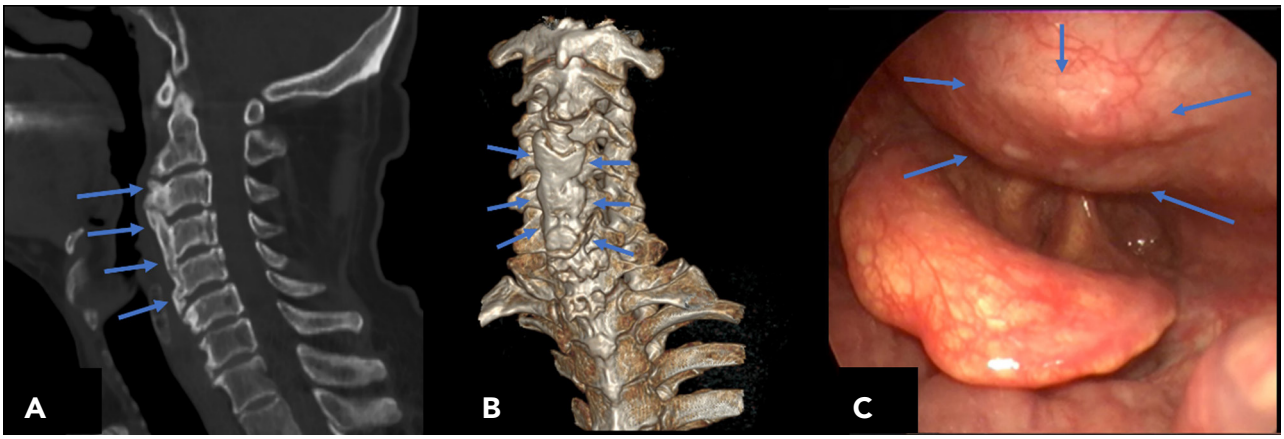

Figure 1. The images of a patient diagnosed with C-DISH

A. Sagittal CV-CT image of a 65-year-old male patient with C-DISH. B. 3D reconstruction of CV-CT image of the same patient. C. Videolaryngoscopic image of the same patient (blue arrows indicate C-DISH).

patients who have cervical complaints. However, sufficient prevalence studies from Türkiye on C-DISH could not be found in the literature. This study aimed to investigate the prevalence and characteristics of C-DISH using computed tomography scans of the cervical vertebra (CV-CT).

MATERIALS AND METHODS

This cross-sectional study was carried out in accordance with the Helsinki Declaration upon receiving approval from the Non-Invasive Clinical Research Ethics Committee of Amasya University (19.01.2022-53136). The study used our hospital's PACS system between February 1, 2022 and May 31, 2022. The study included the images of 2192 patients who underwent CV-CT for any reason between January 1, 2020 and December 31, 2021. First, CT images of 373 patients under the age of 20 were excluded from the study. Then, when CV-CT images were examined, 34 patients with previous cervical surgery findings, 18 patients with severe traumatic cervical injury findings, and 23 patients with cervical disc herniations and severe disc deformities that cause changes in the intervertebral distances findings were excluded from the study. Finally, after the CV-CT images of 448 patients were excluded from the study, the study continued with those of 1744 patients. The patients were divided into the following age groups: 20-29, 30-39, 40-49, 50-59, 60-69, 70-79 and 80 and over. No research was performed addressing aetiology, accompanying comorbid disease and patient complaints.

Radiological Examination

All CV-CT images were obtained with 1.25-mm-thick slices on the axial plane using GE Revolution CT 128-Slice (GE Healthcare, USA), and then sagittal reconstructions were created. CV-CT images were examined based on bone dose using the picture archiving and communication systems (PACS). Cervical vertebrae (C1, C2, C3, C4, C5, C6, C7) and intervertebral distances (C1-2, C2-3, C3-4, C4-5, C5-6, C6-7) were evaluated. The following were then recorded separately: the presence and number of the cervical osteophytes (C-O) in vertebral bodies, the localisation of C-Os in the vertebral body (right, left, medial, right&medial together, left&medial together, right&left&medial together), and the presence and number of intervertebral bridging.

The predominant localisation of osteophytes was taken into consideration for the patients believed to have osteophytes in multiple vertebrae. The relationship between the 7th cervical vertebra and 1st thoracic vertebra was not evaluated. The diagnosis of C-DISH was based on the criteria described by Resnick and Niwayama (3).

All CV-CT images were evaluated by two senior Ear, Nose and Throat specialists. Prior to the study, the researchers twice evaluated the CT images of 50 patients with an interval of 20 days based on the interobserver agreement.

Statistical Analysis

All data were analysed using the Statistical Package for the Social Sciences (SPSS) (IBM) Version 25 software. Student t test, χ^2 tests and Wald Z test were used according to their applicability. A type 1 error level below 5% ($p< 0.05$) was accepted as statistically significant.

RESULTS

The kappa coefficient of the interobserver agreement was 0.89 and 0.94, respectively.

Of the 1744 patients included in the study, 1069 (61.3%) were male and 675 (38.7%) were female. The mean age of the study group was 48±19.7 (20-96) years (males: 45.7±19 [20-95], females: 51.7±20.2 [20-96]). The higher mean age of females in the study group was statistically significant (p=0.001). C-DISH was diagnosed (C-DISH+) in 110 (68 males [61.8%] and 42 females [38.2%]) of all the patients. The C-DISH prevalence was 6.3% (6.4% in males, 6.2% in females). The difference between genders regarding C-DISH prevalence was not statistically significant (p=0.908).

The data on all demographics, affected vertebrae and intervertebral distances are given in Table 1.

In the 110 patients with C-DISH, bridging was observed at 3 levels in 69 (62.7%), 4 levels in 27 (24.6%) and 5 levels in 14 (12.7%) patients.

In the study group, C-O was detected in 636 patients (C-O+), (in min. 1 and max. 7 levels). The prevalence of C-O was 36.5% in the study group (33.9% in males and 40.6% in females). High prevalence rate of C-O+ in females was statistically significant (p=0.004). The difference between age distributions in terms of genders was statistically significant among C-O+ patients (p=0.001). The

Table 1. Descriptive Statistics, C-Osteophyte and C-DISH Characteristics

	Study Group		C-O (+)			C-DISH (+)		
	n/%	Min.-Max.(y)	n/%	Min.-Max.(y)	p	n/%	Min.-Max.(y)	p
Gender Total	1744/100	20-96	636/36.57%	26-96		110/6.3	40-94	
Male	1069/61.3	20-95	362/33.96%	28-95	**0.004**	68/6.4	40-94	0,908
Female	675/38.7	20-96	274/40.69%	26-96		42/6.2	52-94	
	Mean ±SD(y)	Min.-Max.(y)	Mean ±SD(y)	Min.-Max.(y)	p	Mean ±SD(y)	Min.-Max.(y)	p
Age	48±19.7	20-96	64.9±19.7	26-96		72 ±19.8	40-94	
Male	45.7±19	20-95	63.1±19.7	28-95	**0.001**	71.8±19.8	40-94	0,355
Female	51.7±20.2	20-96	67.4±19.7	26-96		74±19.7	52-94	

Table 1 continued.

Table 1. Descriptive Statistics, C-Osteophyte and C-DISH Characteristics

Age Groups									
	Study Group			C-O (+)			C-DISH (+)		
	Total n/%	M. n/%	F. n/%	Total %	M. %	F. %	%	M. %	F. %
20-29	388/22.2	276/71.13	112/28.9	0,8	0,4	1,8	0	0	0
30-39	304/17.4	196/64.5	108/35.5	4,3	6,1	1	0	0	0
40-49	292/16.7	177/60.6	115/39.4	27,1	28,8	24,4	1.4	5,8	7,3
50-59	243/13.9	150/61.7	93/38.3	56,8	58	54,8	5.8	15,9	34,2
60-69	229/13.1	133/58.1	96/41.9	75,1	76,7	73	11.8	18,8	17,1
70-79	149/8.5	79/53	70/47	**81,2**	81	81,4	18.8	30,4	17,1
≥80	139/8	58/41.7	81/58.3	79,1	77,6	80,3	**26.6**	29	41,5
Total	1744/100	1069/61.3	675/38.7	36,5	33,9	40,6	6.3	6.4	6.2
Cervical Osteophyte and Intervertebral Bridge values									
	C1	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**		
n	1	47	130	276	498	533	367		
%	0.1	2.7	7.5	15.8	28.6	**30.6**	21		
	C1-2	**C2-3**	**C3-4**	**C4-5**	**C5-6**	**C6-7**			
n	0	26	73	153	295	285			
%	0	1.5	4.2	8.8	**16.9**	16.3			

(M.: Male, F.:Female, n:number, SD:standart deviation, C-DISH:Cervical diffuse idiopathic skeletal hyperostosis, C-O:Cervical osteophyte, Min.:Minimum, Max.:Maximum, y:year)

mean age of C-O+ patients was 65±19.7 years, whereas the mean was 38±19.7 years in patients who were not C-O+ (p=0.001). The lowest rate of C-O prevalence was detected in the 20-29 (0.8%) age group, whereas the highest rate was determined in the 70-79 (81.2%) age group (Figure 2). The C-O prevalence was 36.5% in the study group, whereas it was significantly higher in the groups aged over 40 and 60 years (58.9% and 78%, respectively) (p=0.001) (p=0.001).

In the study group, the lowest rates of osteophytes were found in C1 (0.1%) and the highest in C6 (30.6%). Intervertebral bridging was monitored in one or more intervertebral levels (min. 1 and max. 5) in 418 (24%) patients. No bridging was encountered in the C1-C2 level, whereas the largest number of bridging was monitored in the C5-C6 level (16.9%) (Figure 3). The C4-5 and C5-6 levels were affected in all of the C-DISH+ patients (Figure 3). When the localisations of osteophytes

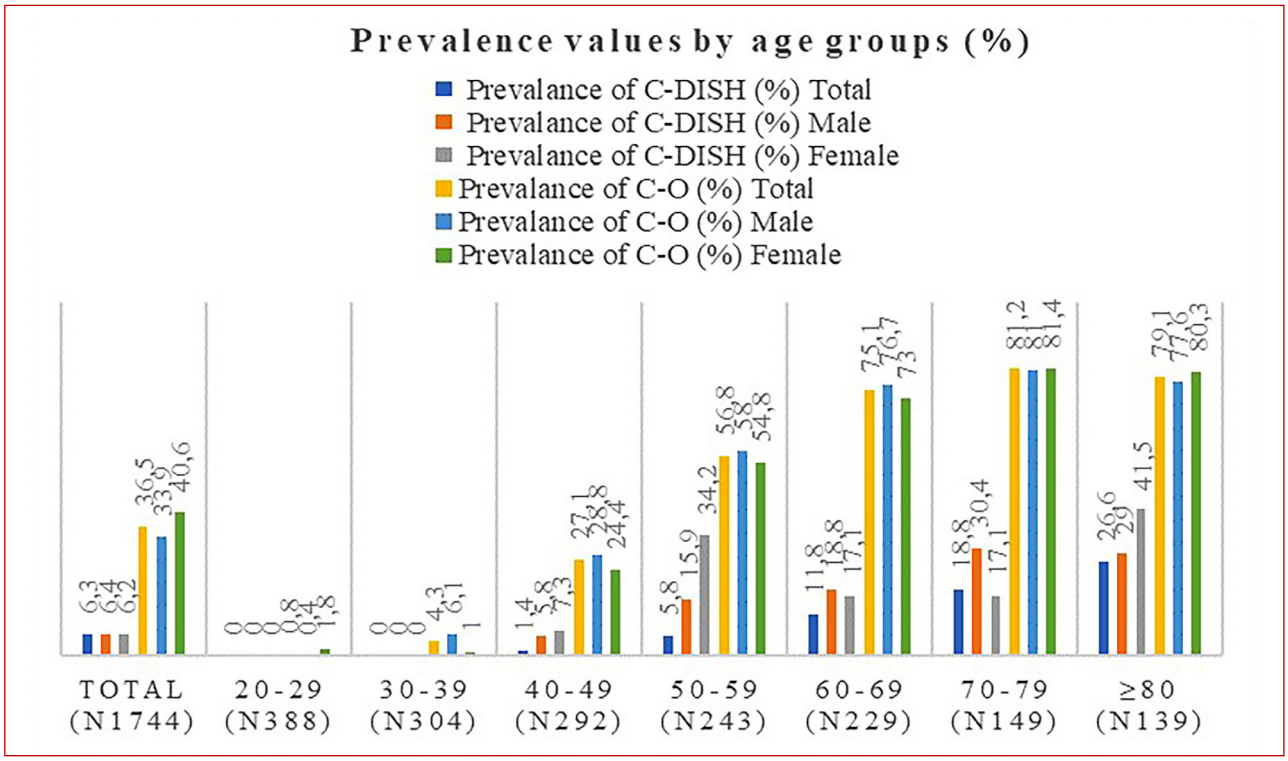

Figure 2. The prevalence values of the affected cervical vertebrae and intervertebral levels in the age groups

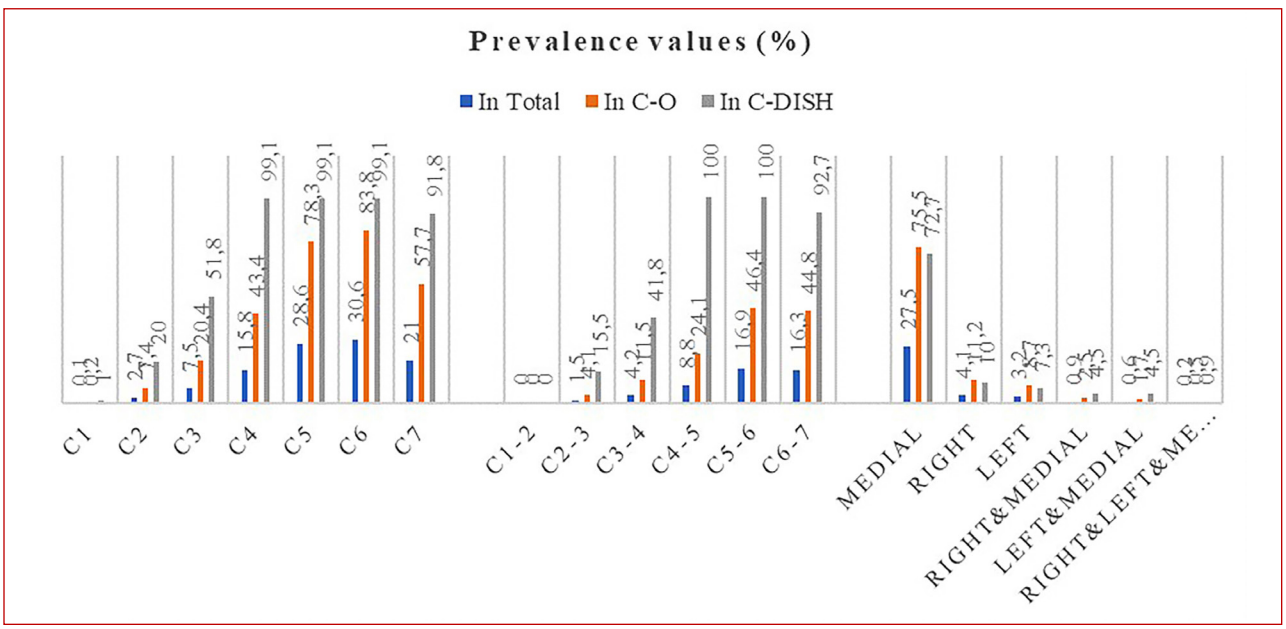

Figure 3. The prevalence values of the affected cervical vertebrae, intervertebral levels and the localisation distribution of osteophytes

were examined, 75.5% of osteophytes were in the midline (Figure 3).

DISCUSSION

In the literature, the overall prevalence of DISH has been reported as between 2.6 and 30.8%. DISH is more common in men, and its prevalence increases in the elderly (even up to 44%). The thoracic spine is most commonly affected, and it has strong associations with metabolic diseases, such as obesity and type 2 diabetes mellitus (15). Studies report the prevalence of DISH belonging to different regions and ethnic groups from most parts of the world. This indicates that DISH is not geographically specific and is common despite differences (16). DISH prevalence may vary depending on age group distributions of study populations, gender, genetic and ethnic variability, imaging techniques used for scanning, lifestyle habits and frequency of examinations. The prevalence of DISH can be expected to increase in the coming years due to the increase of the elderly population and the worldwide increase in obesity and type 2 diabetes mellitus (2, 5, 14, 16). C-DISH prevalence has been reported between 0% and 7.9% in the limited number of studies on the topic (7, 8). Our study will be one of the first to examine the prevalence and characteristics of only C-DISH and C-O using CV-CT in detail.

In the past, direct radiography was used for the diagnosis of DISH, and lower prevalence rates were obtained (17). Today, studies have demonstrated that CT is more advantageous than plain radiography in the diagnosis of DISH and has high sensitivity in showing spinal ligament ossification; it may be the best imaging technique to encounter the exact prevalence (8, 18-20). Hirasawa et al. (19) compared direct radiography and CT evaluations and found a higher prevalence of DISH with CT.

As far as we know, the prevalence of C-DISH has also been reported in four studies using CT for general DISH screening (Table 2). Kim et al. (8), evaluated whole spine CT scans of patients over 16 years of age who were examined at Cheju Halla

Table 2. Previous Reports on C-DISH Prevalence

Author	Year	Modality	Country	n	Age (mean)	Min-max	C-O Prevalence % (Total/Male/ Female)	C-DISH Prevalence % (Total/Male/ Female)
Kagotani et al.	2014	Whole-Spine Radiography	Japan	1647	64.4	NA	NA	0
Kim et al.	2018	Whole Spine CT	Korea	164	NA	16- NA	NA	7.9
Liang et al.	2019	PET-CT	China	2000	48.5	20-95	6.6/7.9/4.1	2/ NA / NA
Hiyama et al.	2018	Whole Spine CT	Japan	1479	54.7	20- >90	NA	Low
Ahmed et al.	2022	Whole Spine CT	India	1815	47.5	20-98	>20/ NA / NA	0
This study	2022	Cervical Vertebra CT	Türkiye	1744	48	20-96	36.5/33.9/40.6	6.3/6.4/6.2

(NA: Not Available, n:number, Min.:Minimum, Max.:Maximum

General Hospital and reported the first and the highest C-DISH prevalence as 7.9%. Liang et al. (18), evaluated subjects who underwent PET/CT for the purpose of cancer screening in a single hospital and determined a C-DISH and C-O prevalence of 2% and 6.6%, respectively. Hiyama et al. (17), evaluated patients who had experienced trauma who had undergone whole-spine CT and stated, without specifying numbers, that C-DISH prevalence was low. In contrast, Ahmed et al. (21), evaluated whole-spine CT scans of polytrauma patients from 2018-2021 above the age of 20 years and found no C-DISH patients in their study. All these studies observed that prevalence increased with age, and it was significantly high in males.

We also used CV-CT to assess C-DISH prevalence. We utilised the criteria described by Resnick ve Niwayama for DISH diagnosis (3). Since our study has a retrospective design, we could not evaluate sacroiliac joint involvement, which was one of the diagnostic criteria. Although the mean age and age distribution of our study group were similar with studies in the literature, which reported C-DISH prevalence using CT, we found prevalence rates of 6.3% and 36.5%, respectively, for C-DISH and C-O, which were higher than the mean values found in the literature. Weinfeld et al. (22) reported that genetic or hereditary differences are the important predisposing factors regarding DISH. They also demonstrated that DISH prevalence was lower in Asian, Black and Indian populations. Kim et al. (8) obtained lower prevalence rates in Korean patients, whereas higher prevalence values were obtained in studies conducted with Japanese patients originating from the same race. Therefore, it is believed that genetic factors influence DISH prevalence more than race (21, 23). We consider that the prevalence values of our study were found to be higher than the other studies performed on mostly Asian study populations because of racial and genetic differences as well as lifestyle habits of the Turkish population. Since CV-CT is an imaging method mainly preferred in patients with cervical complaints in the clinic, the probability of detecting any pathology is higher in these patients. Also, for this reason, we may have found the prevalence rates of DISH to be high in our study.

Most of the previous studies denoted that DISH is more frequently seen in males independently of ethnic origin or genetic factors (2, 5, 7, 23). However, some authors showed that T-DISH prevalence was higher in female patients in the black race population (2). In our study group, the mean age of females was significantly higher than the males' ($p=0.001$). However, this difference decreased in the age groups over 40 and 50. This decrease probably resulted from the high number of hospital admissions in young males, since they work more actively in our population and, therefore, are exposed to more trauma. However, in the studies of Yoshihara et al. (2), Bateman et al. (15) and Pereira et al. (24), the T-DISH prevalence differences between male and female patients were not statistically significant. In our study, the higher prevalence rate of C-DISH in females was not significant ($p=0.908$), whereas the higher prevalence rate of C-O in females was statistically significant ($p=0.004$). In other words, we found that the probability of developing C-DISH in patients does not depend on gender. However, we determined that the difference between genders regarding prevalence rates of C-DISH increased in favour of males as age advanced (11.4% in males and 9.2% in females over 40 years, 20% in males and 15.4% in females over 60 years).

We concluded that advanced age caused an increase in prevalence rates of C-DISH and C-O. The lowest prevalence rates of C-O and C-DISH were identified in the 20-29 age group, and the highest prevalence rates were identified the 70-79 year group and older. The mean ages of the patients who did and did not have C-DISH were 72 and 46 years, respectively, and the mean ages of the patients who did and did not have C-O were 72 and 38 years, respectively ($p=0.001$), ($p=0.001$).

No C-DISH patients were found in males below 40 years old and females below 52 year old. There were no C-O+ patients below 26 year old. The C-DISH prevalence was 10.5% and 17.8% in the groups over 40 and 60 years old, respectively. The increase in the prevalence with advancing age was statistically significant (p=0.001), (p=0.001). Almost 90% of the C-DISH+ patients were 50 years old and over. Approximately 18% of patients 60 years and older had C-DISH, and 80% had C-O.

In their review, Verlaan et al. (16) evaluated the vertebrae affected by C-DISH on dysphagia and/or airway obstruction cases due to C-DISH and identified that C1 (2.9%) was the least affected vertebra, whereas C4 (95.9%) was most affected one. Symptoms were present in 25% of the patients without affecting four adjacent vertebrae. This study showed that essential symptoms may occur without an increase in the number of osteophytes. Some authors reported that slow-growing cervical osteophytes can be reasonably well tolerated by many individuals; however, fast onset complaints may emerge due to suddenly occurring soft tissue oedema due to a triggering condition, such as an upper respiratory tract infection (16). For this reason, we believe that the presence of osteophytes or bridging, even in small numbers, should be considered symptomatic at any time, and this should not be forgotten, especially in elderly patients with symptoms.

In our study group, C-O was present in 36.5% of the patients, whereas only 24% had intervertebral bridging. We consider that the high mobility of cervical vertebrae prevented more bridging. No bridging was monitored in C1-2, whereas the largest number of bridging was observed in C5-6. The least number of osteophytes was found in C1 whereas the largest number of osteophytes was found in C6, C5 and C7. We ascertained that most of the osteophytes (75.5%) were localised in the midline. We speculate that dysphagia most often occurs in the patients with C-DISH, since osteophytes predominantly form in the ventromedial aspect of the lower cervical vertebrae in the cervical region, and this region has a close association with the oesophagus. C-DISH and C-O are the important diagnoses that should be kept in mind, particularly for elderly patients admitted with cervical region complaints, primarily dysphagia, along with comorbid factors. Early diagnosis and an effective multidisciplinary approach can provide appropriate treatment.

Limitations

There are some limitations of our study. First, our study addressed only cervical vertebrae, and other spine regions were not examined. Second, sacroiliac joint involvement, one of the diagnostic criteria of DISH described by Resnick and Niwayama, could not be evaluated (3). Third, the patient's symptoms, comorbidities and etiopathogenetic data could not be obtained because of the study's retrospective design. Finally, our study is not a community screening study (that would be unethical due to radiation from CT). However, these are the scans of patients who applied to the hospital for any reason, and the clinician requested a CT scan. So it is expected that the prevalence is higher than the previous literature since most of them have evaluated patients that do not specifically have neck symptoms – they evaluated acute trauma cases or cancer screening patients.

CONCLUSION

In our study, we detected that C-DISH and C-O prevalence rates were 6.3% and 36.5%, respectively. There was no significant difference between genders in terms of C-DISH prevalence. Prevalence values significantly increased with age; cervical osteophytes were most often localised in the midline, and the most affected cervical vertebra and intervertebral levels were C6 and C5-6, respectively. Given all these data, we conclude that C-DISH is

a geriatric disease. Therefore this fact should be considered, particularly for patients admitted with cervical complaints. Furthermore, the follow-up and treatment of these patients should be performed with a multidisciplinary approach.

Declaration of Conflicting Interests

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