




Ossification of Posterior Longitudinal Ligament in Cervical Spine and Its Association With Ossified Lesions in the Whole Spine: A Cross-Sectional Study of 2500 CT Scans

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Abstract

Study Design: A retrospective study.

Objective: To identify the prevalence and characteristics of ossified posterior longitudinal ligament (OPLL) in the cervical spine and its association with other spinal ligament ossifications.

Method: This study is a retrospective review of whole spine CT scans of polytrauma patients from 2009 to 2018. Patients were screened for cervical OPLL (C-OPLL), thoracolumbar OPLL, thoracic ossified ligamentum flavum (OLF), cervical and thoracolumbar ossified anterior longitudinal ligament (C-OALL AND T-L OALL), ossified nuchal ligament (ONL) and, diffuse idiopathic skeletal hyperostosis (DISH) using CT scans. Their prevalence and distributions were assessed using statistical tools. Chi-square tests were used to determine statistical association between the categorical parameters.

Results: Out of 2500 patients, 128 had C-OPLL with a prevalence rate of 5.12% with mean age of 55.89 year. The most commonly affected level was C5, followed by C6, and C4. The segmental OPLL was highest in number (77.7%), followed by localized type (14.8%). While the prevalence rate of thoracic OPLL was 0.56%, OLF was 9.9%. Ossifications that coexisted along with C-OPLL were thoracic OPLL (7.81%), thoracic OLF (36.71%), cervical OALL (29.68%), thoracolumbar OALL (37.5%), DISH (27.34%) and, ONL (7.03%).

Conclusion: Our study indicated a prevalence rate of 5.12% for C-OPLL with a predominance of segmental OPLL (77.7%). Among these patients, approximately 36% had coexisting thoracic OLF. In patients with symptomatic OPLL induced cervical myelopathy, MRI analysis of whole spine with relevant CT correlation may help in detecting additional ossification sites of compression.

Keywords

ossified posterior longitudinal ligament, ossified ligamentum flavum, ossified anterior longitudinal ligament, diffuse idiopathic skeletal hyperostosis, cervical myelopathy

Introduction

Ossified posterior longitudinal ligament (OPLL) is a hyperostotic condition characterized by ossification within the posterior longitudinal ligament. OPLL causes spinal canal stenosis, which leads to different degrees of neurological manifestations.¹ OPLL, one of the important causes of cervical myelopathy, is also known as “Japanese disease” as it was first noticed in the Japanese population.² The exact etiopathogenesis of OPLL is not

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entirely understood to date. A broad spectrum of metabolic, genetic, and environmental factors have been studied and implicated for its development and progression. So far, the published literature suggests an association of OPLL with DISH (Diffuse idiopathic skeletal hyperostosis), ankylosing spondylitis and, diabetes mellitus.³ Various genomic studies showed that multiple genetic variations are associated with the occurrence and severity of OPLL; it includes BMP9 and BMP4 haplotypes, COL6A1, and TGF3 gene.^{4,5} OPLL has a long course of presentation with variable degrees of neurological involvement. This makes it challenging to lucidly understand the natural course of the disease.

OPLL can involve any region of the spine; with the cervical spine being the most commonly affected level followed by the thoracic spine. Traditionally, plain radiographs were used to diagnose and classify OPLL. Unlike the thoracic vertebral segments, cervical spine is not overlapped by shoulders and ribs. Therefore, cervical OPLL are relatively more easily identified on plain radiographs than their thoracic counterparts. Computed tomography (CT) is diagnostically more accurate in identifying ossified spinal ligaments, especially in the thoracic spine and junctional regions.^{6,7}

The epidemiology of OPLL has been the subject of many studies. Initially, it was believed to be endemic to the Asian population. The incidence of OPLL was reported about 1.9-4.3% in the Japanese and 0.16% in the non-Asian population.² However, increased knowledge of OPLL and usage of multi-slice CT scans globally has led to an increase in reported prevalence rates in other races. Recent literature has reported C-OPLL prevalence of 2.5% in the US population, higher than any other previously reported radiograph-based studies.³

Other ossified spinal ligaments such as thoracic OPLL, ossified anterior longitudinal ligament (OALL), ossified nuchal ligament (ONL), ossified ligamentum flavum (OLF) coexist with C-OPLL. Various studies have used neck CT scans of patients done for trauma screening and fluorodeoxyglucose positron emission tomography (FDG-PETCT) for cancer screening to assess the prevalence and coexistence of spinal ligament ossification accurately.^{8,9} Published literature from the Indian subcontinent has focused upon treatment options and outcomes.¹⁰ Till this date, there is no study available in the literature showing prevalence in the Indian population. The current study is a cross-sectional survey in the local geographic sample from the Indian population to estimate the disease burden and its association with other spinal ligament ossifications.

Material and Methods

A cross-sectional single institute study was conducted with institutional review board approval. The CT scan data from 2009 to September 2018 was included.

Sample Size

Skeletally mature polytrauma patients (>18 years) who underwent whole-body CT scans from 2009-2018 were enrolled for

the study. We calculated the required sample size based on the assumption of the prevalence rate at 1.5%, which resulted in a requirement of at least 2270 participants. A sample size (N) calculated using the following formula,¹¹

$$N = \frac{(z^2)P(1 - P)}{d^2}$$

Where z = statistic for the level of confidence (1.96), P = expected prevalence (0.015), and d = allowable error (0.005).

SPSS version 20 was used for the statistical analysis. The level of significance was set at 5% level, so P -values less than 0.05 were considered statistically significant. Chi-square tests were used to determine the association between categorical variables. Descriptive statistical analyses were done, and categorical measurements were presented as percentages.

Radiological Assessment and Identification of Ligament Ossification

A whole body or whole spine helical CT scan was performed in the supine position. A commercial Seimens Emotion 6 slice CT system was used with the following parameters: slice thickness was 4.00 mm; pixel size 6x0.5 mm; tube rotation speed was 1.5 seconds; beam pitch of 0.875 mm; Eff mAS of 170 and, tube voltage of 130kV. The scan range went from the head to the whole pelvis. PACS (Picture Archiving and Communication System) software was used to analyze axial and sagittal plane images. All these CT scans were screened by a spine surgeon and a fellow to look for the presence of C-OPLL, T-OPLL, OALL, ONL, OLF and DISH changes.

Diagnostic Criteria for Ligament Ossification and Level Confirmation

OPLL. It was identified as an ossification of posterior longitudinal ligament greater than 2 mm on either the axial CT section of the cervical and thoracic spine.⁷ Counting of OPLL was started at the originating vertebral level. OPLL extending to disc space or localized type of OPLL was counted as per the criteria of Tsuyama et al.¹²

OALL. It was identified with a thickness of greater than 6 mm in the thoracolumbar spine and with thickness greater than 4 mm in the cervical spine at the bridged intervertebral level. OALL must bridge adjacent intervertebral bodies to fulfill the diagnostic criteria of Resnick.^{8,13}

OLF. It was ossification of ligamentum flavum with greater than 4 mm in thickness in axial sections. Counting of OLF started at the originating lamina level.⁸

ONL. The presence of bone density between external occipital protuberance and C7 spinous process in the mid-sagittal cervical spine section. The level was determined by drawing horizontal lines along the superior and inferior endplates of the

vertebral bodies. Ossification lying between these horizontal lines corresponds to the respective cervical vertebral level.

DISH. DISH changes were identified as 3 consecutive OALL bridging 4 vertebral bodies.

Results

Of the 2500 patients (1712 men and 788 women), 128 patients were with C-OPLL (97 men and 31 women). The overall prevalence of OPLL was 5.12% (4.3-6.1; 95% CI) [male-5.66% and female-3.93%]. The most commonly affected age group was the sixth decade, followed by the fifth decade. (Table 1, Figure 1) There was no statistically significant difference in the sex distribution ($P = 0.103$). The most common type was the segmental type (99), localized type (19), mixed type (8), and

continuous type (2) (Figure 2). The most commonly affected level was C5, followed by C6, C4, C3, C7, and C2 in the descending order of involvement. The most common involved level in localized type OPLL was the C5/6 level. The overall prevalence of T-OPLL was 0.56% (male-0.53% and women-0.63%). The most commonly affected level was T1-T2, followed by T5-T6. (Figure 3)

Ossified Ligamentum Flavum (OLF)

The prevalence of OLF was most significant in the sixth decade, followed by the fifth decade in both men and women. There were 247 patients with thoracic OLF (203 men and 44 women). (Table 2) The overall prevalence of thoracic OLF was 9.90% (8.7-11.1%; 95% CI) [men-11.86% and women-5.58]. The most common level involved was T11 lamina, followed by T10 lamina and T5 lamina. (Figure 4) OLF was more prevalent in males than females, which was statistically significant ($P < 0.001$).

Table 1. Cervical OPLL Characteristics.

Cervical OPLL Age distribution			
Age Group	Overall	Male	Female
18-30	0	-	-
31-40	12	10	2
41-50	18	14	4
51-60	38	26	12
61-70	39	28	11
71-80	17	15	2
>81	4	3	1
Cervical OPLL types			
	N = 128	(%)	
Segmental	99	77.7	
Localized	19	14.8	
Mixed	8	6.25	
Continuous	2	0.54	

OALL, DISH and ONL

There were 135 patients with cervical OALL (109 men and 26 women). The prevalence of cervical OALL was 5.4% (4.5%-6.4%; 95% CI). The prevalence rate was 6.36% in men and 3.29% in women. (Figure 5) The prevalence of thoracolumbar OALL was 32% (30.2%-33.9%; 95% CI). The prevalence of thoracolumbar OALL was 36.97% (633 cases) in men and 21.19% (167 cases) in women. (Figures 6–8) One hundred and seventy-three (173) patients had DISH (141 men and 32 women) with an overall prevalence of 6.92% (8.24% in men and 4.06% in women). ONL was found in 12 patients (9 men and 3 women). The prevalence of ONL was found to be 0.48% (0.52% in men and 0.38% in women). The prevalence of

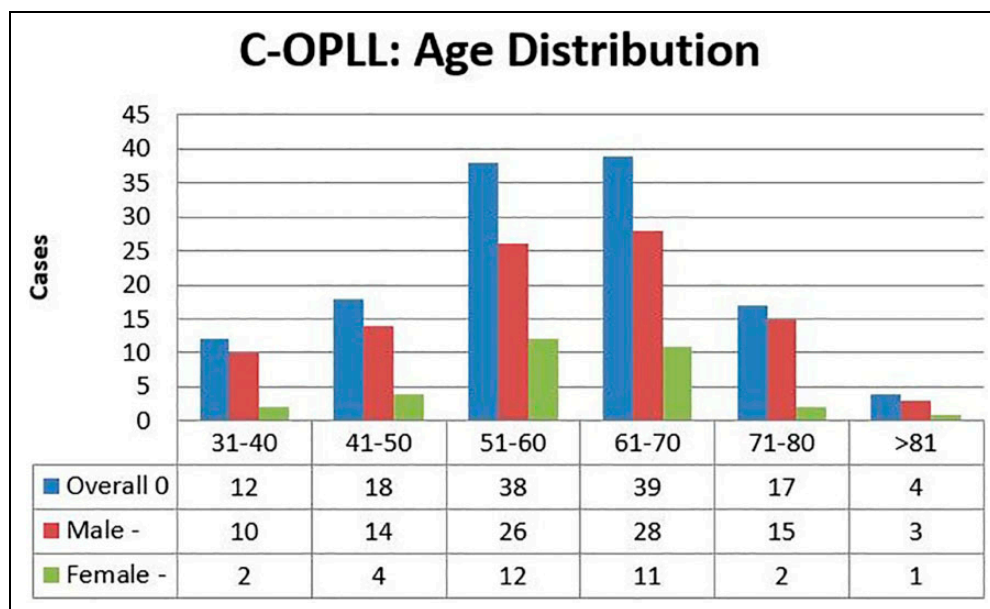


Figure 1. Cervical OPLL age distribution.

C-OPLL, ONL, thoracic OLF, and DISH was significantly higher in men than women.

Distribution Level of Ossifications

Cervical OPLL was most frequent at C5 vertebra (78 cases), followed by C6 (67 cases) and C4 (45 cases). (Figures 9 and 10) The distribution pattern was similar between men and women. Overall, the thoracic OPLL was most frequently observed at the T1/2 level (T1/2 in male and T5/6 in female). Thoracic OLF most commonly found at the T11 lamina (110 cases), followed by T10 lamina (76 cases), followed by T5 (42 cases) without gender discrepancy. For Cervical OALL, the C5-C6 (69 cases) is the most common level, followed by the C6-C7 (35 cases). Thoracic OALL had the highest frequency at T8/T9 intervertebral level (464 cases), followed by T10/T11 (411 cases) and T9/T10 (361 cases). Finally, the distribution pattern was similar between men and women. ONL was most commonly found at the C5 level with no gender discrepancy.

Concomitance of Spinal Ligament Ossifications

For ligament ossification concomitance, 36.71% of C-OPLL cases also had thoracic OLF, 7.81% of C-OPLL cases also had thoracic OPLL, 29.68% of C-OPLL had cervical OALL and, 37.5% had T-L OALL, 27.34% of C-OPLL also had DISH, and 7.03% of C-OPLL also had ONL. For thoracic OLF, 19.43% patients had coexisting C-OPLL, 3.64% had thoracic OPLL, 12.55% had cervical OALL, 21.45% had T-L OALL, 10.93% had DISH and, 2.43% had ONL. (Table 3; Figures 11 and 12)

Discussion

The present study comprehensively examines the prevalence of OPLL and other spinal ligament ossifications in the Indian population. The first documented reports of OPLL goes back to mid-nineteenth century literature by Key, who reported 2 cases with paraplegia, secondary to ossification of the thoracolumbar spinal ligament.¹⁴ In 1942, Oppenheimer reported 18 cases with ossification of the anterior and posterior spinal ligaments diagnosed on X-rays.¹⁵ The next published literature on comparative pathology was in 1960 when Tsukimoto documented an autopsy proving the narrowing of the cervical canal due to OPLL. Following this, numerous missed OPLL cases

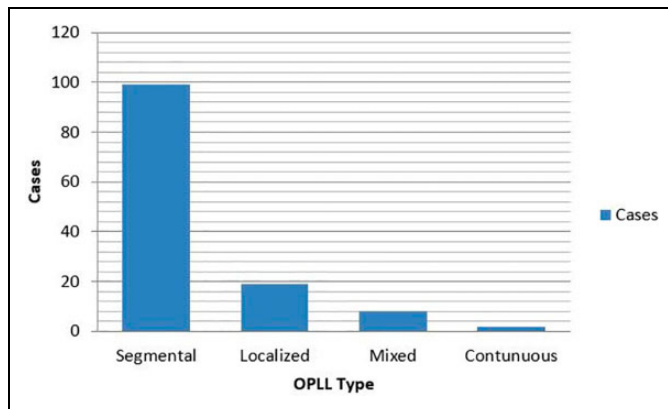


Figure 2. Types of cervical OPLL.

Table 2. OLF Age Distribution.

Age Group	Overall	Male	Female
18-30	4	4	0
31-40	24	20	4
41-50	26	22	4
51-60	72	51	21
61-70	83	71	12
71-80	33	30	3
>81	5	5	0

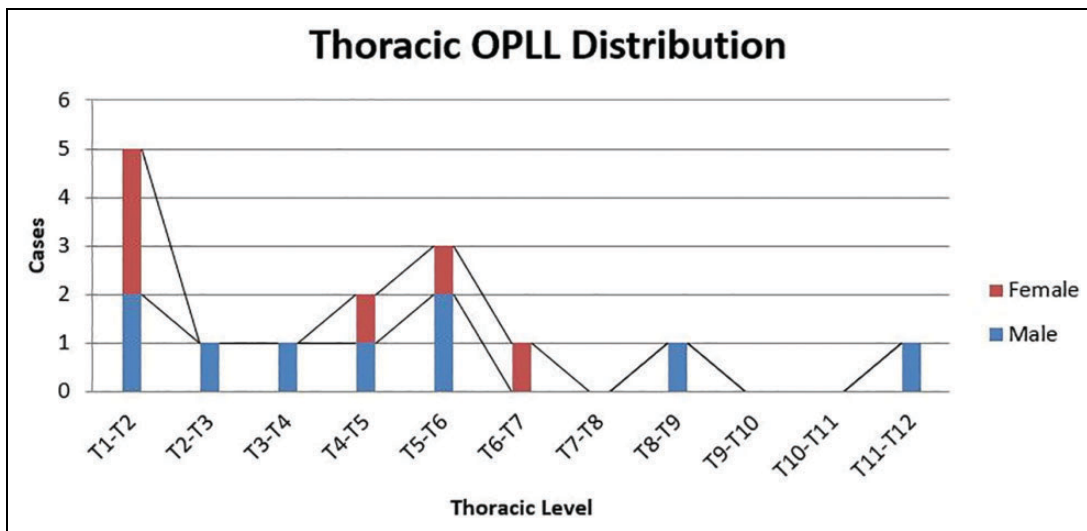


Figure 3. Thoracic OPLL level distribution pattern.

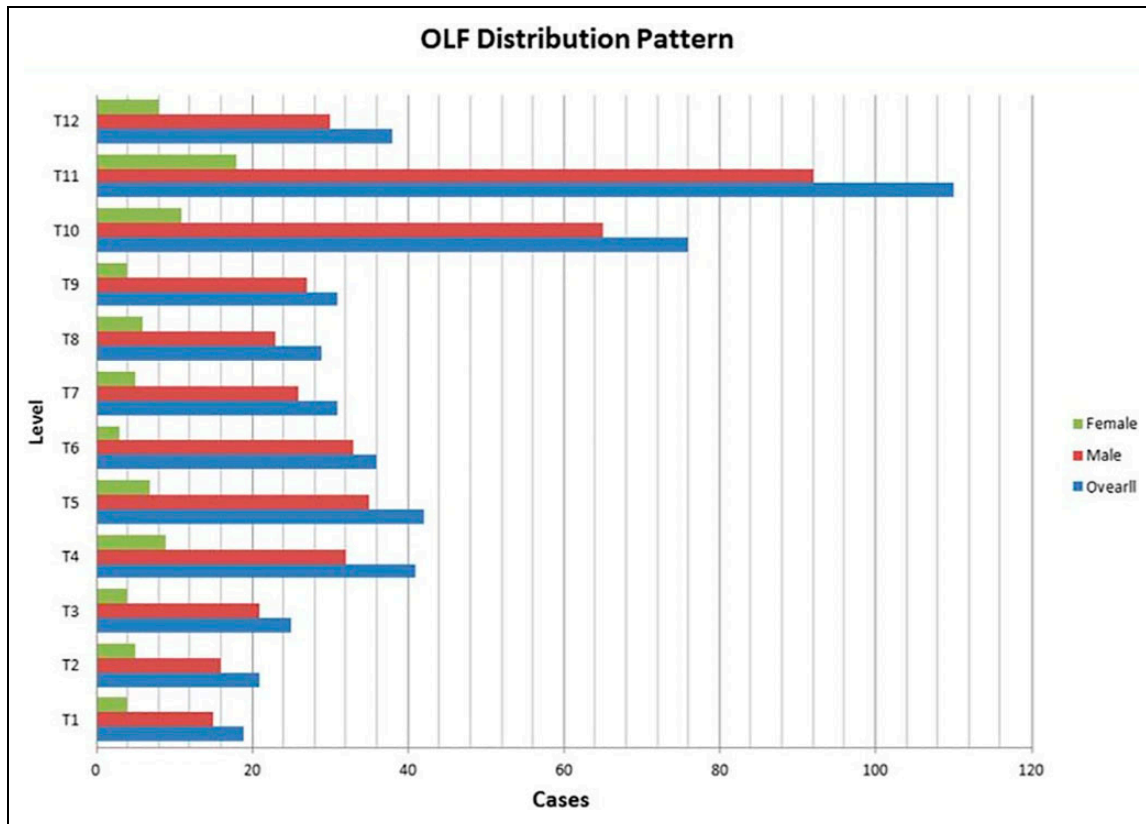


Figure 4. OLF level distribution pattern.

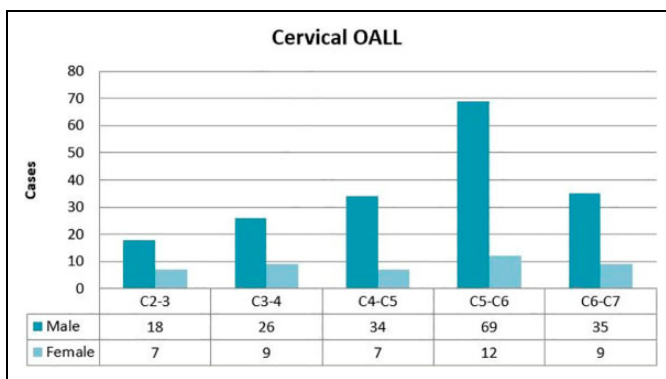


Figure 5. Cervical OALL level distribution pattern.

were retrospectively identified by the Japanese surgeons on radiographs.¹⁶

The most severe neurological manifestation of OPLL is myelopathy, especially in the case of cervical spine involvement and, other symptoms include subaxial neck discomfort and level-specific radiculopathy. The presence of OPLL per se causes static canal compromise, but dynamic factors (range of motion) appear to be very important for myelopathy evolution.² Approximately one-fourth of the patients belonging to the elderly age group with a history of incomplete spinal cord injury without vertebral fractures, often secondary to low energy trauma were cases of undiagnosed OPLL.¹⁷ Current

study demonstrates the overall prevalence of C-OPLL as 5.12% (Male-5.66% and Female-3.93%). The prevalence of other spinal ligament ossification were 0.56% in thoracic OPLL (Male-0.53% and Female-0.63%), 9.9% in thoracic OLF (Male-12.44% and Female-5.58%), 32% in thoracolumbar OALL (Male-45% and Female-26%), 5.4% in cervical OALL (Male-6.36% and Female-3.29%), 6.92% in DISH (Male-8.24% and Female-4.06%), 0.48% in ONL (Male-0.52% and Female-0.38%). Information from other scientific studies is coherent with our findings. (Tables 4 and 5) Gender differences were observed in the prevalence of C-OPLL, with higher numbers being in men, which corroborates with the observations made in the previous studies¹⁸; however, it is not statistically significant. All cases are of same the race and ethnicity; hence racial differences could not be studied.

OPLL Characteristics and Differences

Since CT scans can identify even small ossifications with greater precision as compared with the other modalities (plain radiographs and MRI), the distribution patterns of OPLL classified on the basis of CT is different from those observed using MRI or X-rays. A significant percentage of the patient population, 25 (19.53%), belongs to age less than 50 years while earlier studies do not say so.^{7,19} Previous studies found that with routine use of CT scan, the prevalence of segmental type

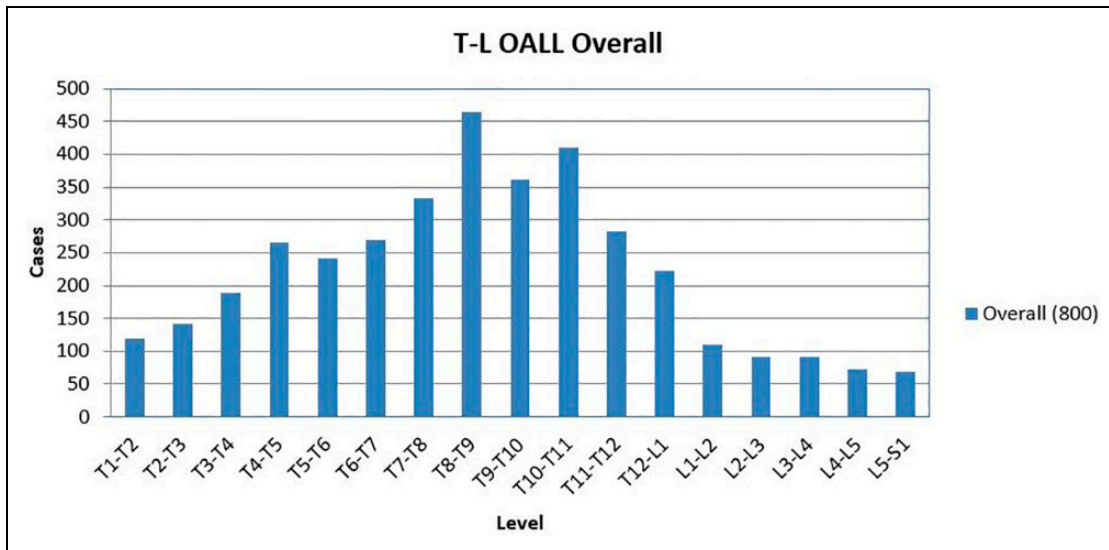


Figure 6. T-L OALL level distribution pattern (overall).

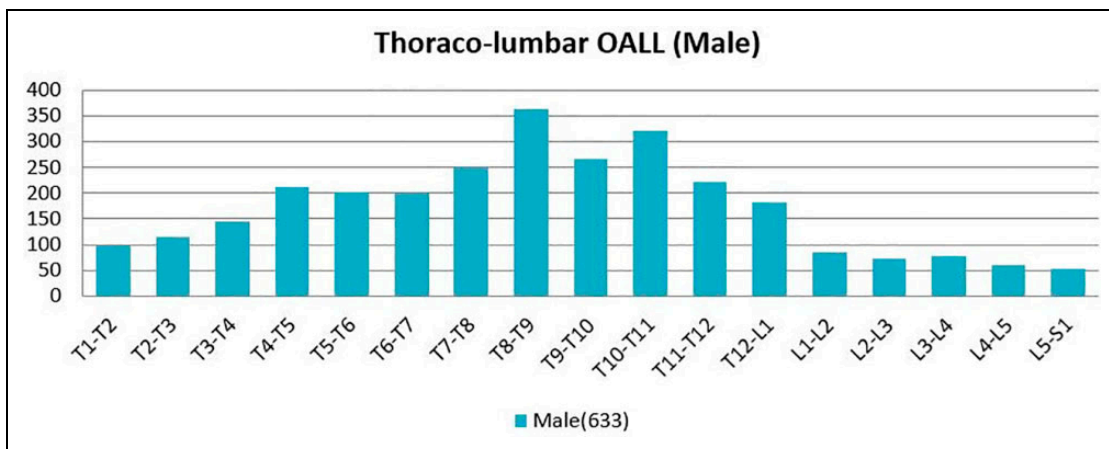


Figure 7. T-L OALL level distribution pattern (male).

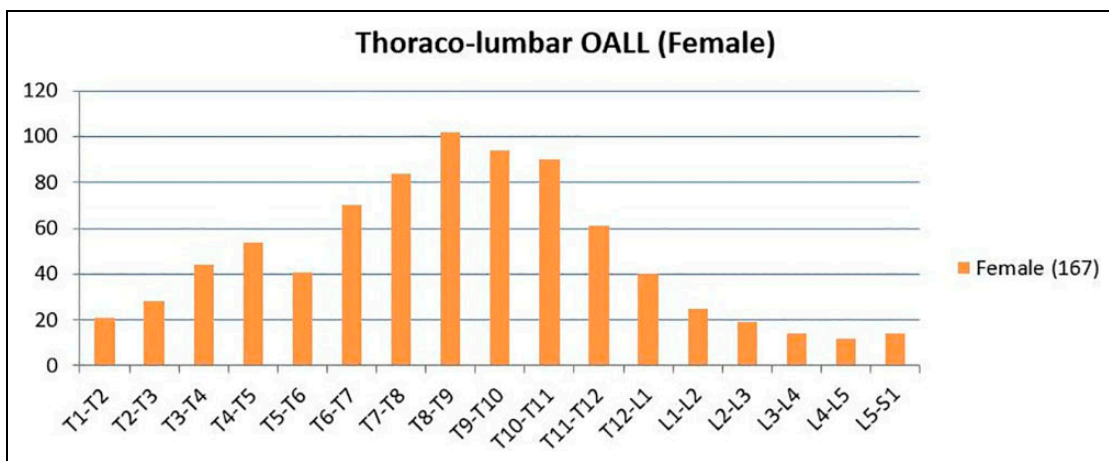


Figure 8. T-L OALL level distribution pattern (female).

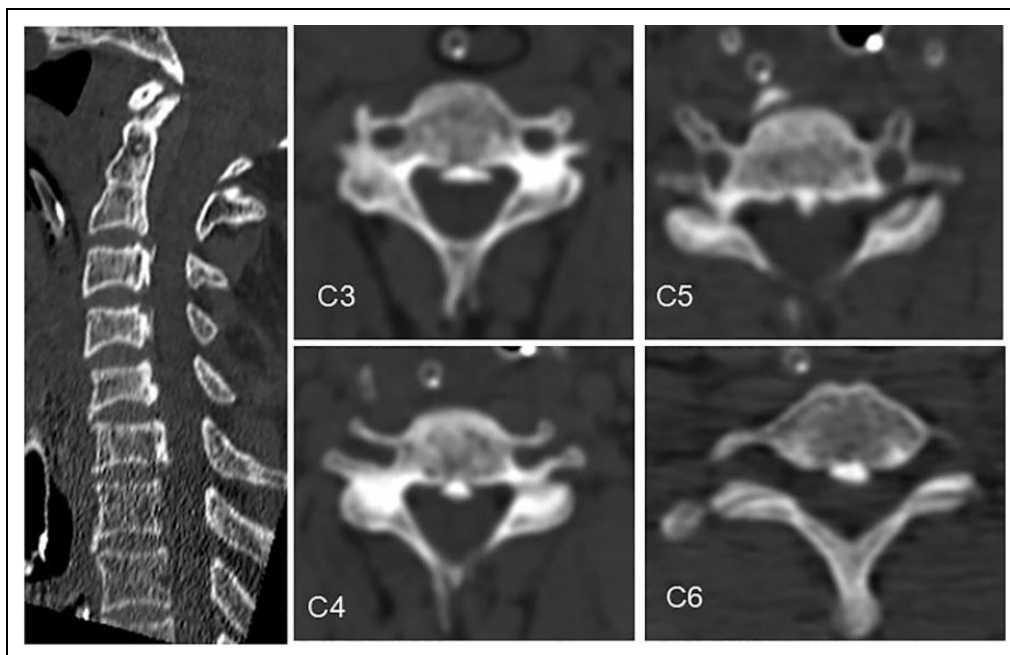


Figure 9. Cervical segmental OPLL.

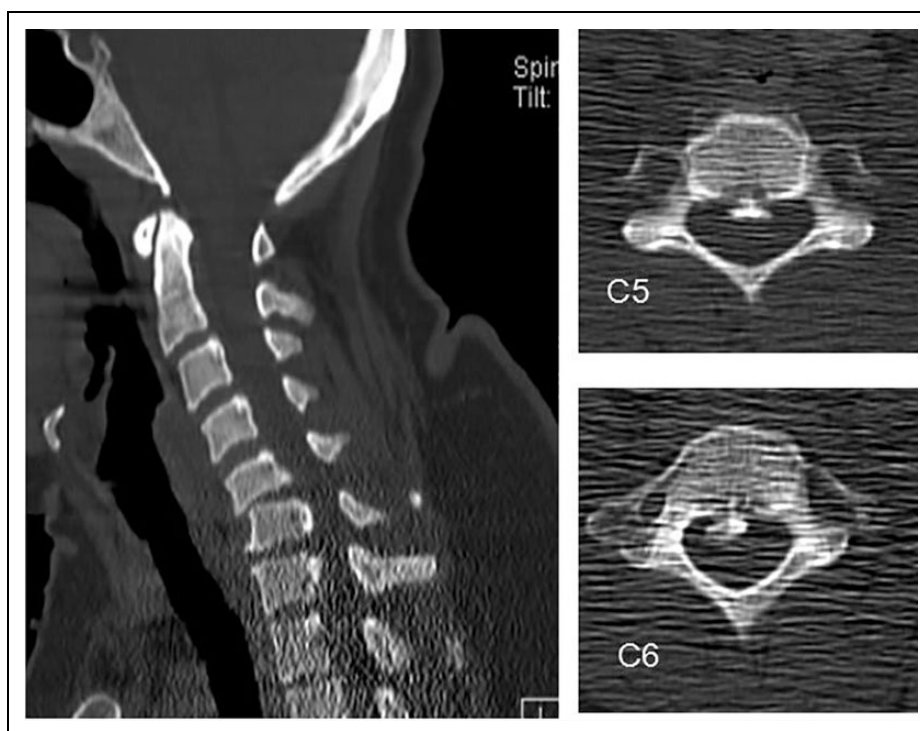


Figure 10. Cervical segmental OPLL with coexisting ONL.

Table 3. Concomitance of Each Type of Spinal Ligament Ossification.

Co-existence	C-OPLL	T-OPLL	T-OLF	C-OALL	T-L OALL	DISH	ONL
With C-OPLL	-	7.81%	36.71%	29.68	37.5	27.34%	7.03
With T-OLF	19.43	3.64	-	12.55	21.45	10.93	2.43

C-OPLL, cervical ossified posterior longitudinal ligament; T-OLF, thoracic ossified ligamentum flavum.

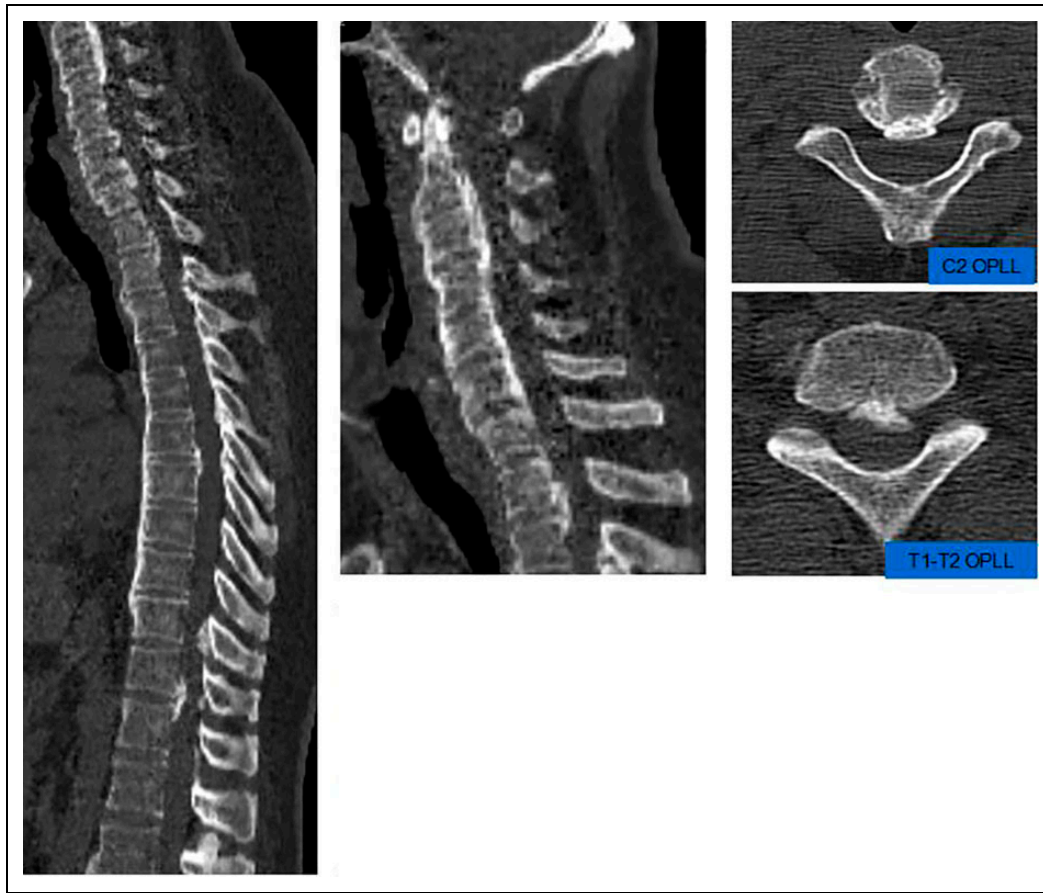


Figure 11. Coexisting of multiple ossified spinal ligament (cervical and thoracic OPLL, OLF and DISH).



Figure 12. Coexisting cervical OPLL and thoracic OLF.

has increased while the continuous type has decreased.^{8,9} We found segmental type OPLL in 77.7% of cases, followed by localized, mixed, and continuous-type OPLL. The most commonly involved level was C5, followed by C6, C4, C3, C7, and C2 levels. C-OPLL commonly affects the lower cervical spine level, which attributes to the anatomical characteristic of the posterior longitudinal ligament (PLL). PLL is thicker and broader at the cervicothoracic junctional area and down the spine; it is thin.⁸ In a study by Ohtsuka et al., the prevalence of T-OPLL in a Japanese population was 0.8% in men and 0.6% in women, which was done using plain thoracic radiographs.²⁰ Mori et al. found a prevalence of 1.6% for T-OPLL in a Japanese sample upon CT chest analysis.¹⁹

The prevalence of T-OLF was found to be 12% in a Japanese sample by Fujimori et al.,⁸ and 16.9% in a Korean sample reported by Moon et al.²¹ In this study, a 9.9% prevalence rate was found for T-OLF (12.44% in men and 5.58% in women), with the most commonly affected level being T11 lamina, followed by T10 and then T5. We found T-OLF is more common among men (12.44%) than women (5.44%), these findings are in coherence with previous studies.²² T-L OALL is commonly seen on the right side of the spine as aortic pulsations on the left half of the spine will forbid the development of the ossifications.²³ Kagotani et al. reported that the prevalence of DISH in a Japanese population was 10.8% (22% in men and 4.8% in

Table 4. Prevalence of Cervical OPLL in Various Studies.

Prevalence of Cervical OPLL							
Author	Country	Race	Investigation Modality	Prevalence (%)	Subjects (Male)	OPLL Case	Mean Age (Year)
Bakhsh W et al (3)	USA	White	Cervical Spine CT	2.5	2917	74	47.9
Sohn et al (6)	Korea	Asian	Thyroid CT	5.7	3240 (1084)	185	50.7
Fujimori et al (8)	Japan	Asian	PET CT	6.3	1500 (888)	95	57 ± 12
Shingyouchi et al (17)	Japan	Asian	Cervical x-ray	4.1	4802 (4802)	198	51.4
Yoshimura et al (18)	Japan	Asian	Cervical x-ray	1.9	1562 (524)	30	70.3 ± 11
Liang H et al (20)	China	Asian	PET CT	4.1	2000 (1335)	82	48.5 ± 9.9
Current Study	India	Asian	Whole Body CT	5.12	2700 (1712)	128	55.89

Table 5. Prevalence of Thoracic OPLL in various studies

Prevalence of Thoracic OPLL								
Author	Country	Race	Investigation Modality	Prevalence (%)	Subjects (Male)	OPLL Case	Mean Age (Year)	Most common Level
Fujimori et al (8)	Japan	Asian	PET CT	1.6	1500 (888)	24	57 ± 12	T1/T2(M) T5-T6 (F)
Mori et al. (17)	Japan	Asian	Chest CT	1.9	3013 (1752)	56	65	T3-T4
Ohtsuka et al (18)	Japan	Asian	X ray	0.8	1058 (440)	34	62.8	T6
Liang et al (20)	China	Asian	PET CT	2.25	2000 (1335)	45	48.5 ± 9.9	T1-T2
Current Study	India	Asian	Whole body CT	0.56%	2500 (1712)	14	55.89	T1-T2

women), using whole spine radiographs and, Westerweld et al. found a prevalence of 17%. In this study, we found a prevalence of 6.92%.^{24,25} In view of the associated pathologies of ossification at other spinal levels, it is important to screen the rest of the spine for concomitant compression elsewhere. Although CT scans are more accurate in identifying these lesions of ossification, the radiation exposure associated with whole spine CT can be significantly high. Our routine protocol is to obtain whole spine MRI scan to screen the rest of the spine, and to procure limited CT cuts only at levels of radiologically or clinically severe cord compression.

There were a few limitations in the current study. First, the study population was selected from a tertiary care hospital instead of random selection from the general population, which has created a sample selection bias (Berksonian's bias). Simultaneously, polytrauma patients tend to be younger and likely to be males. Therefore, they may not represent the general population accurately as a whole. However, obtaining a CT in healthy individuals might be unethical and hazardous. Second, anthropometric correlation and biochemical affiliation not considered. Third, the study does not provide clinical correlation with ligament ossifications. Regardless of the restrictions, our study's results revealed important epidemiological data regarding patients with OPLL and its association with other spinal ligament ossifications.

Conclusion

OPLL is not so uncommon in India; however, the literature lacks knowledge of its distribution and prevalence pattern. This is the first study using a large sample population in the Indians, showing the prevalence of cervical OPLL and intraspinal ossification's coexistence in significant proportion. Segmental type OPLL is the most common pattern with affection toward the lower cervical spine. In patients with symptomatic OPLL induced cervical myelopathy, imaging to screen the rest of spine (preferably whole spine MRI or relevant level CT sections) would be prudent for the early detection of additional sites of ossification. Further investigations ought to look at different ethnic groups to clarify the disease's pathogenesis and better epidemiological understanding.

Declaration of Conflicting Interests

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Institutional Review Board

Ganga Medical Centre & Hospital Pvt Ltd Institutional Review Board (Reg No IRB 00004503); IRB Application No: 2019/06/02. Ganga Medical Centre & Hospital Pvt Ltd. IRB Application No: 2019/06/02.

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