Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/14542
DOI URL: http://dx.doi.org/10.21474/IJAR01/14542

RESEARCH ARTICLE

LOW GRADE LUMBAR SPONDYLOLISTHESIS AT L4&L5 AND L5&S1 VERTEBRAE IN RURAL SOUTH INDIAN POPULATION

Adil Ahmed Karnul[1], Azra Mubeen Karnul[2], Abdul Aziz Riyaz[3] and Mahjabeen H.B[4]

1. MBBS.MS, MCH, Consultant Neurosurgeon at Malnad Lifeline Hospital, Shimoga.
2. MBBS. M.D. Associate Professor Department of Anatomy, East Point College of Medical Sciences, Bangalore
3. MBBS, MS, MCH. Consultant Neurosurgeon at S S Sparsh Hospital, Bangalore.
4. MBBS, MBA. Junior Resident at Department of Neurosurgery at Malnad Lifeline Hospital, Shimoga.

Manuscript Info

Manuscript History
Received: 15 February 2022
Final Accepted: 18 March 2022
Published: April 2022

Key words:-
Spondylilosthesis Myerding's Grade, Vas, Modic Changes, Isthemic And Degenerative

Abstract

Objectives: In heavy workers incidence of low back ache is common. Low grade spondylolisthesis has more options of treatment than high grade spondylilosthesis. Therefore, this study was done to find out clinical profile of low-grade spondylolisthesis at L4-L5 and L5-S1 vertebrae in rural south Indian population. Co-relation between Modic change (MC) and grades of spondylolisthesis was also assessed.

Material and Methods: Study was carried out for a period of 2 years in 40 patients with age 20-70 years with single-level L4/L5 and L5/S1 low grade spondylolisthesis (Meyerding's grade I and II), with clinical and neurological examination, assessment of pain by Visual Analogue Score (VAS) and investigations like X ray, CT scan & MRI.

Results: Out of 40 cases, 27.5% were males and female were 72.5%. The most affected age group was 40-60 years (65%). Lower back pain (LBP) was the most common symptom (100%). Straight leg raise test was positive in 81.25%. Sensory and motar deficit was seen in 45% of patients. L4-L5 level is affected in 60% of low grade spondylolisthesis cases. Incidence of Meyerding's grade I & II were 67.5% & 32.5% respectively. In both grades females were more in distribution than males and L4-L5 vertebral level was involved significantly. Isthmic (IS) & Degenerative (DS) spondylolisthesis was 82.5% & 17.5% respectively and both incidences were more in females. In IS the level affected was L5-S1 and in DS L4-L5 level. Incidence of MC type1 is 15%, type 2 is 85% and in type3 incidence was not found in any cases. Females showed higher incidence in type1 (83.3%)&type 2 (70.6%) as compared to Males (16.6% & 29.4% respectively) but this difference was not significant(p value>0.05).Type2 Modic changes were found significantlyhigh in grade II spondylolisthesis 70%compared to 30% intype 1(p value=0.02).

Summary: Incidence of low spondylolisthesis was more in females and at L4-L5. Modic changes were gender non-specific and grade specific.This study elucidates the clinical presentations of low-grade spondylolisthesis and specific changes associated with it and that will help in tracing factors responsible for it and assessing treatment outcome.

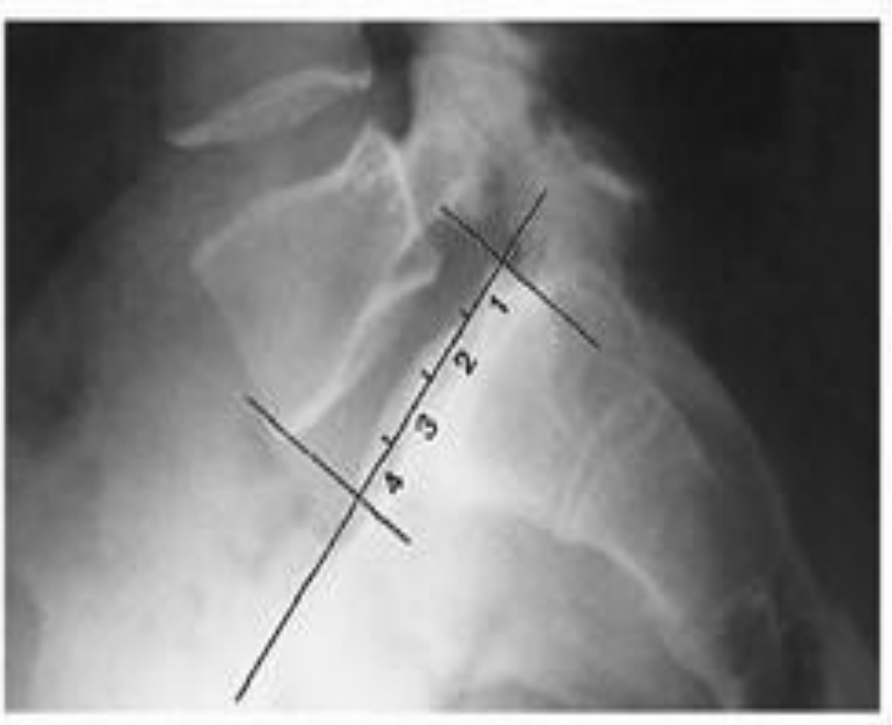
Corresponding Author:- Azra Mubeen Karnul
Address:- MBBS. M.D. Associate Professor Department of Anatomy, East Point College of Medical Sciences, Bangalore.

……

Introduction:-

Spondylolisthesis is displacement of one vertebra over the adjacent lower vertebra in sagittal plane which is due to posture, gravity, repeated stress, and activities that involve repetitive lumbar hyperextensionand sagittal orientation of facets etc. [(1)] The incidence of spondylolisthesis is 5-6 % in the general population & 27-69% familial predisposition, however the increased prevalence up to 12% noted in adult engaged in heavy works, which signifies that mechanical factor is important etiology for this condition. The most affected vertebrae are L4 and L5, which are the keystones of the lumbo-sacral spine, providing stability The risk factors that increase the likelihood of further slippage are younger age, increased BMR, female sex, presence of spina bifida, wedging of the vertebrae, increased pelvic incidence and tilt, rounding of the anterior sacral dome andhype lordosis [(1).] Pain in lower back is commonest symptom of low-grade spondylolisthesis. Sciatica can also be a presentation of spondylolisthesis. Radiological spondylolisthesis is graded into four types (Fig no-1), by Meyerding depending upon the severity of the vertebral slip. He divided the upper surface of inferior vertebra into four equal parts [(2)] and slip of the superior vertebra up to 25%-type I, 25-50% type II, 51-75% type III and 76-100% type IV. Grades 1 and 2 (Fig no-2 & 3) are considered as low grades, grades 3 and 4 are considered as high-grade spondylolisthesis[(2)].

Fig No 1:- Meyerding's Grading system.



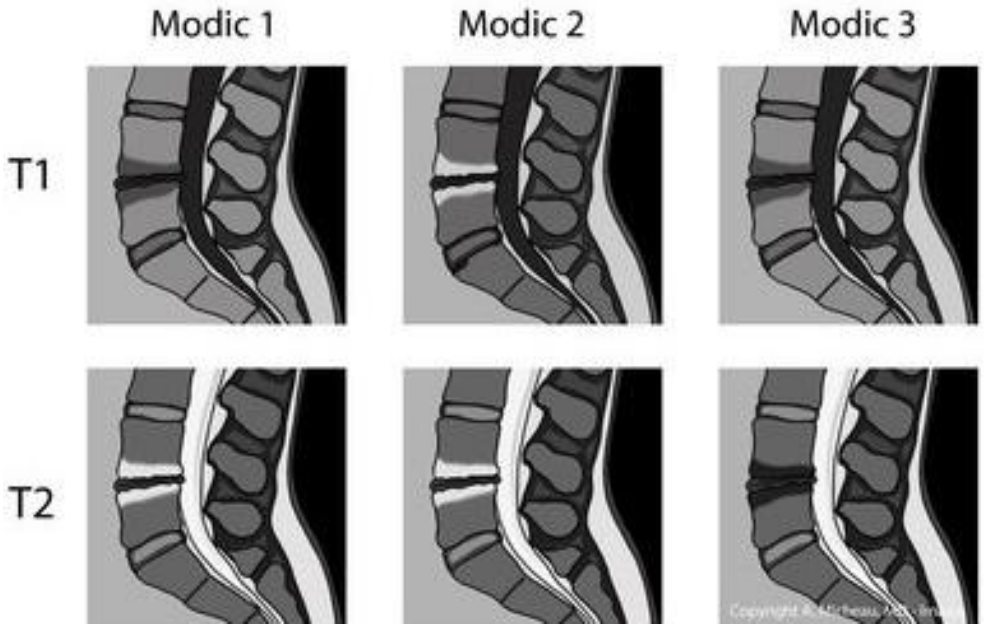
Wiltse et al [(3)] classified into five types Type I-congenital i.e due to dysplasia, Type II-isthmic due to fatigue fractures of pars interarticularis due to repeated trauma, Type III-due to degenerative conditions like arthritis and associated with disc degeneration. Type IV is traumatic to spine, Type V is pathologic and can be caused by lytic bone tumors, osteopetrosis, or osteoporosis. Type VI is iatrogenic spondylolisthesis and is a potential sequela of spinal surgery.

Fig no 2:- Grade I Spodlolisthesis: upto 25% slip.

Fig No 3:- Grade II Spondylolisthesis: 50% slip.

Isthemic spondylolisthesis is congenital or caused by a stress fracture and is frequently seen in adolescents sports person[4].Degenerative spondylolisthesis differs from isthmic/lytic spondylolisthesis by the presence of normal pars interarticularis. Modic changes (M.C) has strong corelation with LBP & is seen as degenerative vertebral endplate and subchondral bone marrow changes are seen in MRI scans of spondylolisthesis cases [4]. M.C are 3 types (Fig No-4), Type-1 - changes are hypointense on T1-weighted imaging (T1WI) and hyperintense on T2-weighted imaging (T2WI) and represent bone marrow oedema and inflammation. Type-2 - hyperintense on T1WI and isointense or slightly hyperintense on T2WI and associated with conversion of normal red hemopoietic bone marrow into yellow fatty marrow because of marrow ischemia. Type-3 - subsequently described as hypointense on both T1WI and T2WI and represent subchondral bone sclerosis [5]. However mixed types are also observed, which is due to conversion of one type to another [6]. Etiology of M.C are not well understood but studies suggest it is due to mechanical stress leading to these degenerative changes. Albert et alreported possibility of anaerobic bacterial infection of disc which has not been proved so far [7]. Further research will dig into finding out therapeutic alternatives in management of this condition.

Fig No 4:- Modic changes.



The management of this condition can be approached in two methods, viz. (1) Conservative method which includes Relaxation, pain management and orthosis, (2) Surgical method which uses Instrumented spinal fusion and decompression. Grade I/II patients can be treated with Conservative methods. It is still not conclusively proven if surgical method is a treatment of choice for higher grades [(8)].

Aims and Objectives:-

To know age of incidence, genderpreponderance, duration of symptoms, motar and sensory deficit, VAS for pain assessment, Meyerding's grading, types of spondylolistheses and co relation of type of Modic changes with gender, level and grade involved in spondylolisthesis.

Materials And Methods:-

A prospective study of 40 patients of low-grade lumbar spondylolisthesis has been conducted in 14 months periods. After meeting all inclusion, exclusion criteria and written consent, patient with age of 20-70 patient with low back ache, sciatica & Single-level L4/L5 and L5/S1 grade I or grade II were included, pathological and traumatic cases were excluded in the study. Neurological examination, assessment of pain by questionnaires and visual analogue score (VAS) and investigations like X ray – AP view, lateral view, flexion and extension, CT scan & MRI were recorded. MRI was done in individuals who were showing neurological symptoms and signs.

Descriptive statistics was done to present the data with mean±SD,data was presented in frequency distribution tables. Analysis was done with IBM SPSS statistics ver.16. To corelate between MC with gender, levels of vertebrae & grades, Chi-square test was utilised. Statistical significance was defined as a p value of <0.05.

Results:-

In our study, out of 40 patients, females were 72.5%, males were 27.5%, the mean age was 49.2 years (S.D is 11.71). The commonest age group affected was between age of 40-49 and 50-60 years 32.5% in each group followed by age group of 60-70 year, 20% cases. In the range of age group of 40-60 there were 50.3% male patients and 65% female patients. There was no male patient below 40 years of age. Spondylolisthesis was higher in females than males in almost all the age groups except 60-70 years where 62.5% males & 37.5% females are affected (Table No.1).

Table 1:- Age and gender wise distribution ofcases.

Age	Males	Females	Total
20-29	0 (0%)	2 (100%)	2(5%)
30-39	0 (0%)	4 (100%)	4(10%))
40-49	3 (23%)	10 (76.9%)	13(32.5%)
50-59	3 (27.3%)	10 (76.9%)	13(32.5%)
60-70	5 (62.5%)	3 (37.5%)	8(20%)
Total	11 (27.5%)	29 (72.5%)	40(100%)

Lower back ache was the commonest symptoms in all 100% cases, radiating pain was 2nd most common symptoms. 81.25% of patients showed unilaterally SLRT test positiveat L4-L5 level andgradeI as compared to 18.65% ofL5-S1 & grade II. 75% had EHL weakness and 25% patient had FHL weakness. Sensory deficits were noted at L5 dermatome in 42.8% patients and 57% patients at S1 dermatome (Table No-2). The duration of symptoms was up to 1 year in 55% patients, 1-2 years in 12.5 % patients, 2-3 years in 12.5 % patients and more than 3 years in remaining 20% of patients.

Table No 2:- Distribution of spondylolisthesis cases for various indices:

Index	L4-L5				L5-S1				Total
Motar deficit: FHL/EHL	3(75%)				1(25%)				4(10%)
Sensory deficit	6(42.8%)				8(57%)				14(35%)
Vertebral levels with grades	L4 -L5 -I		L4 -L5 -II		L5-S-I		L5-S1-II		Total
Gender	Males	Female	Males	Female	Males	Female	Males	Female	
Meyerding's grades	4(10%)	11(27.5%)	4(10%)	5(12.5%)	2(5%)	10(25%)	1(2.5%)	3(7.5%)	40(100%)
Isthmic spodylolisthesis	3(9%)	7(21.2%)	4(12.1%)	5(15.1%)	1(3%)	9(27.3%)	1(3%)	3(9%)	33(82.5%)
Degenerative spodylolisthesis	1(14.2%)	4(57.1%)	0(0%)	0(0%)	1(14.2%)	1(14.2%)	0(0%)	0(0%)	7(17.5%)

FHL: Flexor Hallucis Longus, EHL: Extensor Hallucis Longus

The vertebral level involved in spondylolisthesis is L4-L5, 24 cases (60%) and at L5-S1, 16 cases (40%). Meyerding's grade 1 and 2 spondylolisthesis cases were 67.5% and 32.5% respectively(Table No-2). In grade I, males were 10% and 5% and females were 27.5% & 25% at L4-L5 & L5-S1 levels. In grade II males 10% & 2.5% as compared to females 12.5% & 7.5% in distributions at L4-L5 & L5-S1.

Distribution of Isthmic spondylolisthesis (IS) was 82.5% (Table No-2), out of that at both levels L4-L5 grade I and L5-S1 grade I, males 9% & 3% as compared to females were by 21.2% & 27.3% respectively. L4-L5 and L5-S1 grade II, males 12.1% and 3%as compared to females were more by 15.5% and 9%. IS was seen maximum in females in the grades I spondylolisthesis at L5-S1 level. Distribution of degenerative spondylolisthesis (DS) was 17.5% (Table No-2). Grade I at L4-L5 and L5-S1 males were 14.2% each at both levels and females were 57.1% and 14.2% respectively. No cases were seen in at L4-L5 II and L5-S1 grade II. DS was seen maximum in females in grade I at L4-L5.

Type 1 MC changes are seen in 15% cases out of that 16.6% were of males and 83.3% of females and Type 2 changes were 85% of cases out of that 29.4% of males and 70.6% were of females. Modic type 3 changes were not noted in any patient (Table No-3).

Table no 3:- Modic changes with grade and gender wise distribution.

Levels & grades	Types of Modic changes				Total
	Type 1		Type 2		
	Male	Female	Male	Female	
L4 -L5 -I	0(0%)	0(0%)	2(16.6%)	4(33.3%)	12(30%)
L5-S1 -I	1(8.3%)	1(8.3%)	2(16.6%)	2(16.6%)	
L4 -L5 -II	0(0%)	1(3.57%)	4(14.3%)	12(42.8%)	28(70%)
L5-S1-II	0(0%)	3(10.7%)	2(7.1%)	6(21.42%)	
Total	6(15%)		34(85%)		40(100%)

Table no-4 shows difference in MC in relation to gender was not significant(p value =0.181).MC was seen in 70% of grade II spondylolisthesis cases as compared to 30% in grade I. In grade II, type 2 MC was seen in males 4% and females 62.3% as shown in Table no-4. MC in spondylolisthesis is significantly co-related to grades of vertebrae, p value- 0.02,(Table no-4), indicating Type 2 changes are significantly associated with gradeII spondylolisthesis. MC in relation vertebrallevel at L4-L5 are seen in 42.8% cases and at the L5-S1 levels 21.4% in both grades and in both gender p value 0.181, no significant co relation between MC and levels of vertebra.

Table no 4:- Corelation of modic changes with gender,grades & levels of vertebra.

VARIABLES	**TYPE1**	**TYPE2**	**X^2& P VALUE**
Modic Change (n = 40)	6 (15%)	34 (85%)	-
Gender			
Male	1 (16.6%)	10 (29.4%)	1.792, 0.181
Female	5 (83.3%)	24 (70.6%)	
Grade			
Grade 1	2 (16.6%)	10 (83.3%)	1.050, 0.02*
Grade 2	4 (14.3%)	24 (85.7%)	
Levels affected			
L4-L5	1 (4.3%)	22 (95.6%)	0.037, 0.847
L5-S1	5 (29.4%)	12 (70.6%)	

Values are presented in frequencies & percentages, Statistical significance <0.05.* significant value

Discussion:-

Out of 40 cases, 65% of cases were noted in the age group of 40-60 years. The mean age of the patients in our study is 49years.The mean age in study by Lei Cheng et al [(8)] study was 49 years and Sakeb et al [(9)] were 46 yrs. A study done in South India by Manickam et al [(10)] had similar mean age which was 40.64 years, while as study done by Vatsal et al [(11)] showed most of cases are in the range of 50-59. In our study, 72.5% are females and males 27.5% which indicate female preponderance and M:F ratio 1:3, which could be due to females are lacking in having strong protective muscle strength and ligaments. The female preponderance of our study was comparable with study by Manickam et al(68 %)[(10)] and Sakeb et al(78.8%) [(9).] Females are more in number with lytic (isthemic) spondylolisthesis in our study. It is noted by Ivkovic et al [(12)] that women are at greater risk for stress fractures than men. Though pars interarticularis defects are more common in men than in women, women are more likely to have spondylolisthesis reported by Tallarico et al [(13)]. Males suffer lytic spondylolisthesis more commonly than females [(2,14)]. As most of the females in our study were agricultural laborers engaged in heavy and hard field work causing stress fractures of pars inter articularis. This could be the probable reason for the female preponderance in IS subgroup.

In our study low back pain (LBP) was noted in all 100% cases and radiculopathy 87.5% and. It corelates with study done by Lei Cheng et al [(8)], it was noted 91.3% of patients suffered from LBA and 89% suffered from radiculopathy. Sakeb et al [(9)] documented that 100 % of patients in their study suffered from LBA whereas 86% of patients suffered with radiculopathy. The duration of symptoms was up to 1 year in 55% patients and 2-3 and 3 years equally 20%, our finding does'nt match with study done by Vatsal et al [(11)] and Newman et al [(15)]. SLRT was positive in 82.5% at L4-L5 vertebral level(p value>0.05), no significant difference was noted similar to study done by Banu et al[(16)].

L4-L5 level of spondylolisthesis is noted in our study in 60 % of cases. Our findings are in accordance with study done in south Indian population, Manickam et al [10] the authors noted 56 % of patients had L4-5 and 44 % of L5- S1 spondylolisthesis. Dantas[17] reported equal number of patients involving L4-5 and L5-S1 levels. Debnath et al [18] and Panchal et al [19]reported 84 % of patients were suffering from L5-S1 level and 16% L4-5 level. This inconsistent result could be due to variation in study population.

Like our study, Cheng et al [8], Vatsal et all [11] and Panchal et al [19]reported higher incidence of grade I spondylolisthesis than grade II(67.5% vs 32.5%). Our study shows majority of females were affected in grade I, at L4-L5 then followed by L5-S1 & in grade II spondylolisthesis at L4-L5 indicating that lower grades of spondylolisthesis is gender specific, but our study is limited to low grades of spondylolisthesis, needs further exploration of research to higher grades of spondylolisthesis.

In our study, Isthmic type of spondylolisthesis (82.5%) is more common than degenerative type (17.5%). Similar observation was noted in another study by Devkota et al [20], where they have noted 41 % of IS patients were 22 % of DS patients, in both females were showing more incidence than males. Isthmic spondylolisthesis is found to have no severe disability thus indicates that no surgical requirement is needed [21]. IS found to be more in females at L5-S1 levels because of L5 pars defect, this finding is same as that of Aruna et al [22]. Recurrent trauma because of repeated flexion, hyperextension and rotational movements in women field workers are the factors for development of IS in our study. Similar to our study Yi Xiang reported higher incidence of DS in female gender in grade I at L4-L5, concluded that DS is gender-specific and age-specific [23]. Our finding is also in accordance with Lara-Almunia et al [14].

We noted all the all patients showed Modic changes in the endplates, type 2 changes in 85%. Similar to studies done by Rahme et al [24] and Kuisma et al [25]. According to Yue-Hui Zhang [4] type 1 and type 2 are the most common patterns in the lumbar spine, it is disputed whether type II is more frequent than type 1. Andrew et all [26] reported Modic type 2 changes more common and significantly associated with disc degeneration in lower lumbar vertebrae particularly at L4-L5, our study includes both IS & DS.

All 100% cases showing Modic change, presented with LBP indicating strong association between LBP and Modic changes, particularly to type 2 changes and higher incidence in female gender. Similar to the study done by Yue-Hui Zhang [4]. According to Kuisma et al [25]type 1 MC is associated positively with LBP symptoms, who included only females in their study. Jarvinen et al [27] reported type 1 MC is more common and after adjustment it becomes insignificant and concluded that type1 change with LBP should be considered as specific subgroup of LBP cases, this difference in the occurrence of type of MC could be due to inclusion of disc degenerative cases in their study.

It has been found that most MC type 1 progresses to type 2 in 18–24 months [6]. Type 2 M.C appears to be more stable state however, it may convert to MC type 1 in unstable conditions or may eventually progress to type3 [26,27]. The progress of MC can be ablated by proper management of disease at conservative level or at surgical level.

Exact causes of MC are not clear, their occurrence may be closely related to abnormal load and stress, increased BMI, lax abdominal musculature and lordosis due to multigravida, conditions related to harmones like lactation and menopause are the risk factors that will affect vertebral endplates and the microenvironment of adjacent vertebral bone marrow, resulting in these histological and radiological changes [27]. Low levels of female sex hormones in postmenopausal women can be associated as evidenced by the benefit of regimen of early hormone replacement therapy(HRT) in menopausal women in lumbar degenerative spondylolisthesis may be considered in cases with anatomical high risk of developing DS, such as high lumbar lordosis, vertebral end-plate inclination, severe disc degeneration and loss of height, and facet joint sagittal orientation particularly with symptoms [28].Our study lack in comparing MC in relation to IS and DS. Further research has to be conducted to find out MC in this particular subgroup of spondylolisthesis. In our study incidence of type 2 MC is higher in grade II spondylolisthesis in females involving L4-L5 levels, this co relation between MC & grades of spondylolisthesis was significant(p value-0.03) . Corelation between MC and grades was no done so far in literature, the current study is the first study to present such data. Our study is limited to low grade spondylolisthesis hence further follow up studies should be carried out to co relate MC, mechanism responsible for changes and effect of treatment on thischangewhich will help in deciding the best clinical treatment.

Conclusion:-

Specific radiological assessment in spondylolisthesis shows MC, which could be corelated with extent of slip i.e grades and its conversion could be the indicator of progress of disease and treatment provided. Further studies of MC will explore relationship between symptoms and therapeutic possibilities. Link between clinical features, specific radiological signs and understanding of structural changes will help in taking decision of trearment.

Conflict of interest:
None declared.

References:-

1.Sadiq Shahzad, Meir Adam, Hughes S.P. Surgical management of spondylolisthesis overview of literature. Neurology India Dec 2005; 53:506-511
2. Ramamurthy & Tendon.Textbook ofneurosurgery.3rded. India: Jaypee; 2012:1296 – 1312
3. Wiltse LL, Newman PH, Macnab. Classification of spondylosis and spondylolisthesis. Clin Orthop. Relat Res 1976; 117:23-29
4. Yue-Hui Zhang, Chang-Qing Zhao, Lei-Sheng Jiang, Xiao-Dong Chen, Li-Yang Dai. Modic changes: a systematic review of the literature, eur spine J 2008;17:1289–1299
5. Diagnosis and Treatment of Degenerative Lumbar Spondylolisthesis. NASS Clinical Guidelines 2014 revised; 16-19.
6. Modic MT, Steinberg PM, Ross JS, Masaryk TJ, Carter JR. Degenerative disk disease: assessment of changes in vertebral body marrow with MR imaging. Radiology 1988; 166:193–199
7. Albert HB, Kjaer P, Jensen TS, Sorensen JS, Bendix T, Manniche C. Modic changes: possible causes and relation to low back pain. Med Hypotheses 2018; 70:361–368.
8. Lei Cheng & Lin Nie, Li Zhang. Posterior lumbar interbody fusion versus posterolateral fusion in spondylolisthesis. A prospective controlled study in the Han nationality: Int Ortho (SICOT) 2009; 33:1043–1047
9. Najmus Sakeb, Kamrul Ahsan. Comparison of the early results of transforaminal lumbar interbody fusion and posterior lumbar interbody fusion in symptomatic lumbar instability, Ind J ortho May 2013; 47:255-263
10. Ramanujan Muthu Manickam, Ganesan G. Ram, S. Sundar, A. Prakash. Functional and radiological analysis of posterior lumbar interbody fusion in spondylolisthesis: Int J of Res in Ortho:2015 Dec; 1:11-14
11. DK Vatsal, Rajeev Kainth, Rajeev Kainth, Mazhar Husain. A clinico-etiological study of spondylolisthesis in north Indian population: Int J Med Sci & Cli Inventions 2017; 4: 2884-2887
12. Alan Ivković, Miljenko Franić, Ivan Bojanić, Marko Pećina. Overuse Injuries in Female Athletes: Croat Med J2007; 48:767-78.
13. Tallarico RA, Madom IA, Palumbo MA. Spondylolysis and spondylolisthesis in the athlete; Sports Med Arthrosc 2008; 16:32-38
14. Monica Lara-Almunia, Juan A. Gomez-Moreta, Javier Hernandez-Vicente. Posterior lumbar interbody fusion with instrumented posterolateral fusion in adult spondylolisthesis: description and association of clinico-surgical variables with prognosis in a series of 36 cases. Int J Spine Surg 2015; 9:22
15. P H Newman, K. H. Stone. The etio of spondylolidthesis: J of Bone & Joint surg 1963; 45:39-59
16. Kalpakcioglu Banu, Altınbilek, Turgay, Senel, Kazım: Determination of spondylolisthesis in low back pain by clinical evaluation. Journal of Back and Musculoskeletal Rehabilitation 2009. 22 (1): 27–32
17.Dantas FL, Prandini MN, Ferreira MA. Comparison between posterior lumbar fusion with pedicle screws and posterior lumbar interbody fusion with pedicle screws in adult spondylolisthesis: Arq Neuropsiquiatr 2007; 65:764–770.
18. Ujjwal K Debnath, Atanu Chatterjee, Jeffrey R. McConnell, Deepak K. Jha, Tapas Chakraburtty. Interbody Fusion in Low Grade Lumbar Spondylolsithesis: Clinical Outcome Does Not Correalte with Slip Reduction and Neural ForaminalDimension. Asian Spine J 2016; 10:314-320
19. Panchal L, L Sarukte V, N Bhanushali R. Study of functional outcome in low grade spondylolisthesis operated by pedicular screw instrumentation and fusion. Int j med res rev 2021; 9:34-40
20. P Devkota, SK Shrestha, R Krishnakumar and J Renjithkumar. Posterior lumbar interbody fusion for the management of spondylolisthesis. Nepal Med Coll J 2011; 13:46-49
21. Yasuchika Aoki, Hiroshi Takahashi, Arata Nakajima, Go Kubota, AtsuyaWatanabe, Takayuki Nakajima, Yawara Eguchi, Sumihisa Orita, Hiroyuki Fukuchi, Noriyuki Yanagawa, Koichi Nakagawa & Seiji Ohtori. Scientific reports 2020; 10:6739
22. Aruna Ganju M.D. Isthmic spondylolisthesis. Neurosurg Focus 2002; 13: Article 1

23.Yi Xiang J. Wang a, Zolta´n Kapla'r a, Min Deng a, Jason C.S. Leung. Lumbar degenerative spondylolisthesis epidemiology: A systematic review with a focus on gender-specific and age-specific prev. J of ortho translation 2017; 11:39-52

24. R. Rahme, R. Moussa. The Modic Vertebral Endplate and Marrow Changes: Pathologic Significance and Relation to Low Back Pain and segmental Instability of the Lumbar Spine. Am J Neuro radiol May2008; 29:838-842

25.Kuisma M, Karppinen J, Niinimaki J, Kurunlahti M, Haapea M, Vanharanta H et al. A three-year follow-up of lumbar spine endplate (Modic) changes. Spine 2006; 31:1714–1718.

26. Andrew J. Teichtahl, Donna M. Urquhart, Yuanyuan Wang, Anita E. Wluka, Richard O'Sullivan, Graeme Jones and Flavia M. Cicuttini Lumbar disc degeneration is associated with modic change and high paraspinal fat content – a 3.0T magnetic resonance imaging study. Teichtahl et al. BMC Musclsklt Disord 2016; 17:439-446

27. Järvinen et al. BMC Musculoskeletal Disorders 2015; 16:98

28. Devine JG, Schenk-Kisser JM, Skelly AC. Risk factors for degenerative spondylolisthesis: a systematic review. Evid Based Spine Care J 2012; 3:25-34.