Lumbar Spondylolisthesis in a Sample of Iraqi Patients with Rheumatoid Arthritis

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Abstract

The aim of the study is to assess the prevalence of lumbar spondylolisthesis in rheumatoid arthritis patients. A total of 100 patients with rheumatoid arthritis have been diagnosed according to the 2010 American College of Rheumatology/European League against rheumatism classification criteria, and compared with 100 healthy controls. Lumbar spondylolesthesis was reported in 27% of cases and 18% of controls**.** Males represented 19% of cases and 22% of control group while females represented 81 % of cases and 78% of controls. Among patients with spondylolesthesis, degenerative type was reported in(66.7%), while among controls with spondylolesthesis, the isthmic type was reported in (72.2%). The prevalence of lumbar spondylolesthesis in Rheumatoid arthritis patients with chronic low back pain was significantly higher than in controls. The prevalence of degenerative type was more common in rheumatoid arthritis patients, while the prevalence of isthmic type was more common in controls.

Keywords: *Rheumatoid arthritis,disease activities indices, spondylolysis, spondylolesthesis.*

Introduction

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease characterized by synovial joints destruction leading to severe disability and premature mortality.(1) Rheumatoid arthritis affects approximately 0.5-1% of the population with female to male (3: 1 ratio), and in ages between 40 and 60 years. Approximately 70% of patients have irreversible joint destruction and 80% of active young adults in the labor market are affected by stiffness and devastating pain.(2) American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) developed classification criteria in 2010, which can help a physician-made diagnosis with a total score ≥ 6 points, is considered definite rheumatoid arthritis.(1) Various scoring indices have been used to quantify RA disease activity, including the Simple Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), and Disease Activity Score (DAS). Although none of these is universally accepted as the "gold standard", DAS has been increasingly used in clinical practice. (3) Lumbar spondylolisthesis (LS) is the subluxation or slipping of one vertebral body relative to another. It is a potential cause of back pain and neurologic deficits.(10) Spondylolysis refers to a posterior defect in the vertebral body at the pars interarticularis.Usually, this defect is due to trauma or from chronic repetitive loading and hyperextension. If this instability results in translation of the vertebral body, spondylolisthesis occurs.(5) Certain genetic factors, such as family history, race and athletic activities that involve repetitive lumbar hyperextension have been associated with higher LS risk.(4,6) Isthmic spondylolisthesis (IS) is the most clinically encountered subtype and is seen with an incidence of 5-6% in the adult population and about 12% in the adolescent population. It commonly involves L5 (90**%**). Although the incidence of IS in women is half that of men, women account for >50% of symptomatic cases and have higher LS grades.(4) The incidence of degenerative spondylolisthesis (DS) is about 10% and is 3 to 9 times more common in women than men.(7) Hysterectomy and multi parity, presumably by causing abdominal muscle

deficiency, increase DS.[8] Grading of spondylolisthesis using Meyrding classification is determined by the percentage of slippage of the inferior-posterior corner of the vertebral body above over the superior surface of the vertebral body below. At least 5% slippage must be present for a diagnosis of SPL to be established.[9] Rheumatoid arthritis (RA) Generally spares the thoracic and lumbar portions of the spine. However, a review of literatures showed that rheumatoid synovitis with erosive changes can be developed in these diarthrodial joints. The vertebral bodies and intervertebral discs may be involved through either enthesitis or an extension of the inflammatory process from the apophyseal joints.[10]

Subjects and Method

This is a case-control study conducted at Rheumatology unit of Baghdad Teaching Hospital/ Medical City, Baghdad, Iraq, from August 2018 to June 2019. A total of 100 patients with RA diagnosed according to the 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for Rheumatoid arthritis, with a history of mechanical back pain for more than 3 months, were included in the study and compared with 100 controls.

Exclusion Criteria:

- Age less than 16 years.
- Backache of less than 3 months.
- History of trauma or history of spinal surgery.
- Malignancy.
- Pregnancy.
- Patients with inflammatory back pain.
- History of spondylodiscitis,
- History of systemic infection in the last 6 months requiring intravenous antibiotic.
- Osteoporosis or on anti osteoporotictreatment or with compressed vertebra or osteopenia on X-ray.
- RA patients overlapping with other autoimmune disease such as Systemic lupus erythematosus and inflammatory myopathy.

Data were collected using a data collection sheet containing questionnaires for the patients and controls. The questionnaires included demographic data, obstetric history, education, occupation, marital status and smoking status. The three clinical disease activity indices, CDAI,SDAI and DAS28-(ESR, CRP), were calculated. All patients and control were evaluated for spondylolisthesis by lumbosacral x-ray in lateral view (flexion and extension position), and were taken by radiology institute device, Digital AGFA/DX-D400, made in Belgium in 2013. All X-rays were evaluated by a single radiologist who has been blinded to clinical data, using meyerding classification. Grades were determined by the percentage of slippage of the inferior-posterior corner of the vertebral body above over the superior surface of the vertebral body below. Grade I is 5% to 25%, grade II is 26% to 50%, grade III is 51% to 75%, grade IV is 76% to 100%, and grade V is more than 100% (spondyloptosis).[9]

Statistical Analysis: Statistical Package for the Social Sciences (SPSS) version 23 was used for data entry and analysis. Mean and standard deviation were used to express the numerical data while frequency and percentages were used to express the categorical data. Appropriate tests, independent student t test, chi-square (Fischer exact test if not applicable), Anova test and logistic regression were used to confirm significance. P value ≤0.05 was considered significant.

Result and Discussion

The mean age of RA patients was 48.5±11.7 SD years, of controls was 49.1±15.4 SD. Males represented 46.3% of RA patients and 53.7% of control group, while females represented 50.9% of patients and 49.1% of controls, and this difference was statistically non-significant(p=0.8),**(table 1).** There was no significant association between duration of back pain and groups of study (p=0.2). Leg pain and paresthesia were the most common symptoms reported in two groups. Sensory impairment was significantly higher in RA patients in comparison to controls (p=0.04) as displaced in **(table 2**). Lumbar spondylolisthesis was significantly higher in RA patients in comparison to controls(27% vs. 18%), p=0.03. Anterolisthesis, degenerative type, was more in RA patients while retrolisthesis, isthmic type, was reported more with controls. L4-L5 and L5-S1 were the most commonly involved sites. Grade I & II spondylolisthesis were the most reported grades in both groups. Degenerative disc diseasewas the commonest other abnormal X-ray finding as illustrated in **(table 3)** and (**figure 1)**. The rate of lumbar spondylolisthesis was higher among patients of 40-70 years old and ≥ 70 years but did not reach the significant level(p=0.4). Lumbar

spondylolisthesis was significantly higher(p=0.02) among female patients (29.6%) in comparison to male patients (15.8%). The rate of spondylolisthesis was significantly higher with patients who are at menopause phase as seen in (**table 4**). Spondylolisthesis status in term of present or absent were not significantly associated with RA duration, RF, ACPA, FC, RA disease activity indices,ESR level, and medications (p>0.05). The only significant association was reported with CRP level in term of normal or high level and history of joint replacement surgery(hip or knee), p<0.05, **(table 5)**. Female gender in RA patients, increased disease duration, activity, acute phase reactant and history of joint replacement surgery were considered potential risk factors that might significantly increases the probability of occurrence of spondylolisthesis (p<0.05 for all) (**table 6**). QUEST-RA database that included 6,004 patients from 70 sites in 25 countries that found 79% of included RA patients were females, more than 90% of them were of Caucasians. [11]The increasing incidence of degenerative type in RA patients might be based on facet joint involvement and facet joint synovitis that increases the incidence of SPL among RA patients.[12] Three conditions have been reported as potential patho mechanisms of thoracic and lumbar spondylitis in patients with RA. First, synovitis probably starts in the apophyseal joints, with erosion of cartilage and subchondral bone in exactly the same fashion as in peripheral joints. Second, erosion of the facet joints produces functional incompetence, with resultant anteroposterior and lateral instabilities. Finally, the next lesion probably starts at the disco-vertebral junction as an enthesopathy with the inflammatory degeneration of collagen at the junction between the discs and vertebral endplates, leading to a loss of disc space.[13] Hagege B et al observed that isthmic SPL (which is not affected by facet joint modifications) was less frequent in RA patients in comparison to controls, which suggests that facet joint is mainly involved in the pathophysiology of lumbar SPL in RA patients.[14] Neva MH et al concluded that the possible reason for the significant correlation between history of joint surgery and lumbar spondylolisthesis might be a history of poor control of RA disease activity and increased severity of joint destruction.[15] Because CRP level offers a measure of inflammation, a possible cause of the significant correlation between lumbar spondylolisthesis and serum CRP level is the inflammatory response in the lumbar spine.[16] Occurrence of lumbar spondylolisthesis in RA patients could associate with high disease activity or RA severity.[17] A large meta-analysis study evaluating the prevalence of cervical spine lesions in RA patients found that the incidence of atlanto-axial subluxation decreased over the time (ranging from 36% before 1980 to 24% before 2000) suggesting a role of a better management of RA due to improvement of therapies.[18] Spondylolysis together with spondylolisthesis (isthmic type) was reported in 9 cases (33.3%) of RA patients and 13 cases (72.2%) of control group. Micheli LJ et al were concluded that spondylolysis estimated to be present in 6-13% of the general population. Most, however, are asymptomatic.[19] Several previous studies indicated that degenerative changes of intervertebral discs or facet joint erosion were predictors of listhesis due to RA.[20] To the best of our knowledge, this is the first study in our country which demonstrates the relationship between lumbar spondylolisthesis and rheumatoid arthritis.

Table 1. Socio demographic and obstetric history of females of both groups

		Groups				p-value
		Patients		Control		
		No.	%	No.	%	
Age groups	<40	28	51.9%	26	48.1%	0.6
	40-70	47	47.9%	51	52.1%	
	≥70	25	52.1%	23	47.9%	
Gender	Male	19	46.3%	22	53.7%	0.8
	Female	81	50.9%	78	49.1%	
Educational level	Illiterate	24	37.5%	40	62.5%	0.06
	Primary	41	61.2%	26	38.8%	
	Secondary	23	63.9%	13	36.1%	
	College/Institute	12	36.4%	21	63.6%	

		Groups				p-value
		Patients		Control		
		No.	%	No.	%	
Occupation	Manual worker	80	58.8%	56	41.2%	0.01
	Non-manual worker	20	31.3%	44	68.8%	
Smoking	Yes	3	15.0%	17	85.0%	0.01
	No	97	53.9%	83	46.1%	
BMI (kg/m^2)	Underweight	3	75.0%	1	25.0%	0.01
	Normal	11	23.4%	36	76.6%	
	Overweight	30	42.9%	40	57.1%	
	Obese	55	71%	23	29%	
Parity	Nil	13	43.3%	17	56.7%	0.2
	1-4	49	50.5%	48	49.5%	
	≥5(Grand multipara)	19	59.4%	13	40.6%	
Menstruation	Pre menopause	41	53.2%	36	46.8%	0.8
	Post menopause	40	48.8%	42	51.2%	
Hysterectomy	Yes	3	37.5%	5	62.5%	0.7
	No	78	51.7%	73	48.3%	

BMI; Body mass index, Kg; Kilogram, M2; square meter, P-value; Probability value.

Table 2. Clinical findings of patients and control

		RA	Control	P-value
Duration of back pain	3 months-1 year	9(42.9%)	12(57.1%)	0.2
	1-5 years	49(46.2%)	57(53.8%)	
	> 5 years	42(57.5%)	31(42.5%)	
Leg pain		80(80%)	89(89%)	0.07
Paresthesia		56(56%)	68(68%)	0.8
Neurogenic claudication		34(43%)	37(37%)	0.3
Sphincters' disturbances		10(10%)	4(4%)	0.9
Saddle anesthesia		4(4%)	4(4%)	1.0
Motor-abnormal		53(53%)	51(53%)	1.0
Sensory-abnormal		13(13%)	5(5%)	0.04
Reflexes-abnormal		9(9%)	3(3%)	0.07

RA; Rheumatoid arthritis, P-value; Probability value.

Table 3. Spondylolisthesis characteristics of RA patients and control

		RA	Control	P-value
	Spondylolisthesis	27(27%)	18(18%)	0.03
Spondylolisthesis direction	Anterolisthesis	26(26%)	16(16%)	0.5
	Retrolisthesis	1(1%)	2(2%)	
Spondylolisthesis type	Isthmic	9(33.3%)	13(72.2%)	0.3
	Degenerative	18(66.7%)	5(27.8%)	

		RA	Control	P-value
Site	L4-L5	6(22.2%)	4(22.2%)	0.6
	L5-S1	21(77.8%)	14(77.8%)	
Grade	Grade 1	25(92.6%)	15(83.3)	0.7
	Grade 2	2(7.4%)	3(16.7%)	
Other X-ray findings	Normal	16(16%)	32(32%)	0.02
	Degenerative disc disease	33(33%)	34(34%)	
	Facet joint osteoarthritis	24(24%)	16(16%)	

RA; Rheumatoid Arthritis, P-value; Probability value, L; Lumbar, S; Sacral.

Table 4. Spondylolisthesis rate according to socio demographic characteristics of RA patients

		Spondylolisthesis				p-value
		Yes		No		
		No.	%	No.	%	
Age groups	<40	5	17.6%	23	82.4%	0.4
	40-70	14	29.8%	33	72.8%	
	≥70	8	32%	17	68%	
Gender	Male	3	15.8%	16	84.2%	0.02
	Female	24	29.6%	57	70.4%	
Educational level	Illiterate	7	29.2%	17	70.8%	0.6
	Primary	12	29.3%	29	70.7%	
	Secondary	4	17.4%	19	82.6%	
	College/Institute	4	33.3%	8	66.7%	
Occupation	Manual worker	20	25.0%	60	75.0%	0.3
	Non-manual worker	7	35.0%	13	65.0%	
Smoking	Yes	1	33.3%	2	66.7%	0.8
	No	26	26.8%	71	73.2%	
BMI (kg/m^2)	Underweight	1	33.3%	2	66.7%	0.7
	Normal	4	36.4%	7	63.6%	
	Overweight	10	25.6%	29	74.4%	
	Obese	12	25.5%	35	74.5%	
Parity	Nil	3	23.1%	10	76.9%	0.6
	1-4	16	32.7%	33	67.3%	
	≥5	8	42.1%	11	57.9%	
Menopause	Pre menopause	6	17.6%	28	82.4%	0.01
	Post menopause	21	44.7%	26	55.3%	
Hysterectomy	Yes	1	4.1%	2	3.5%	0.3
	No	23	95.9%	55	96.5%	

No; Number, BMI; Body mass index, Kg; Kilogram, M^2, square meter, P-value; Probability value.

Table 5. Spondylolisthesis rate according to disease activity and used medications of RA patients

			Spondylolisthesis	p-value
		Yes	No	
RA duration	<6 months	1(3.7%)	5(6.8%)	0.5
	≥6 months	96.3%))26	68(93.2%)	
RF Positive		21(77.7%)	56(76.7%)	0.9
ACPA positive		22(81.5%)	56(76.7%)	0.6
FC	I	12(44.4%)	45(61.6%)	0.2
	II	8(29.6%)	20(27.4%)	
	III	7(25.9%)	7(9.6%)	
	IV	0(0.0%)	1(3.7%)	
CDAI	Low	3(11.1%)	10(13.7%)	0.7
	Moderate	15(55.6%)	38(52.0%)	
	High	9(33.3%)	25(92.6%)	
SDAI	Low	2(7.4%)	11(15.1%)	0.6
	Moderate	16(59.3%)	42(57.5%)	
	High	9(33.3%)	20(27.4%)	
DAS28-ESR	Low	1(3.7%)	4(5.5%)	0.2
	Moderate	21(77.8%)	38(52.0)	
	High	5(18.5%)	31(42.5%)	
DAS28-CRP	Remission	0(0.0%)	2(2.8%)	0.6
	Low	1(3.7%)	5(6.8%)	
	Moderate	20(70.1%)	52(71.2%)	
	High	6(22.2%)	14(19.2%)	
ESR	Normal	7(25.9%)	33(45.2%)	0.1
	High	20(74.1%)	40(54.8%)	
CRP	Normal	6(22.3%)	37(50.9%)	0.02
	High	21(77.7%)	36(49.1%)	
NSAIDs	Used	7(25.9%)	28(38.4%)	0.7
Steroids (mean dose of prednisolone 6.6±3.2 mg)	Used	12(44.4%)	55(75.3%)	0.1
DMARDs (mean dose of MTX 20±11.2 mg))	Used	25(92.6%)	69(94.5%)	0.2
Biology	Used	19(70.4%)	57(78.1%)	0.6
Joint surgery	Yes	1(3.7%)	3(4.1%)	0.01

RA; Rheumatoid Arthritis, RF; Rheumatoid Factor, ACPA; Anti-citrullinated peptide antibody, FC; Functional class, CDAI; Clinical Disease Activity Index, SDAI; Simplified Disease Activity Index, DAS28-CRP; Disease Activity Score 28- C - reactive protein -DAS28-ESR; Disease Activity Score 28- Erythrocyte Sedimentation Rate, ESR; Erythrocyte Sedimentation Rate, CRP; C - reactive protein, NSAID; Non-Steroidal Anti Inflammatory Drugs,DMARD; Disease Modifying Anti Rheumatic Drugs, P-value; Probability value.

Table 6. Logistic regression for spondylolisthesis in RA patients

	OR	P-value	95% C.I. for OR	
			Lower	Upper
Age	0.9	0.5	0.8	1.2
Gender/female	6.3	0.01	2.4	9.8

	OR	P-value	95% C.I. for OR	
			Lower	Upper
RA Duration	3.6	0.04	1.9	4.07
CDAI moderate & high	4.7	0.02	2.8	7.8
SDAI moderate & high	3.9	0.03	2.4	6.2
DAS28ESR moderate & high	3.7	0.03	2.2	6.4
DAS28CRP moderate & high	3.8	0.03	2.1	5.8
ESR	4.2	0.02	1.8	6.8
CRP	4.8	0.01	2.7	6.6
Hysterectomy	1.1	0.4	1.0	5.4
Joint surgery	1.7	0.03	0.9	1.9

RA; Rheumatoid Arthritis, CDAI; Clinical Disease Activity Index, SDAI; Simplified Disease Activity Index, DAS28-CRP; Disease Activity Score 28- C - reactive protein, DAS28-ESR; Disease Activity Score 28- Erythrocyte Sedimentation Rate, ESR; Erythrocyte Sedimentation Rate, CRP; C - reactive protein, CI; Confidence interval, OR; Odds ratio.

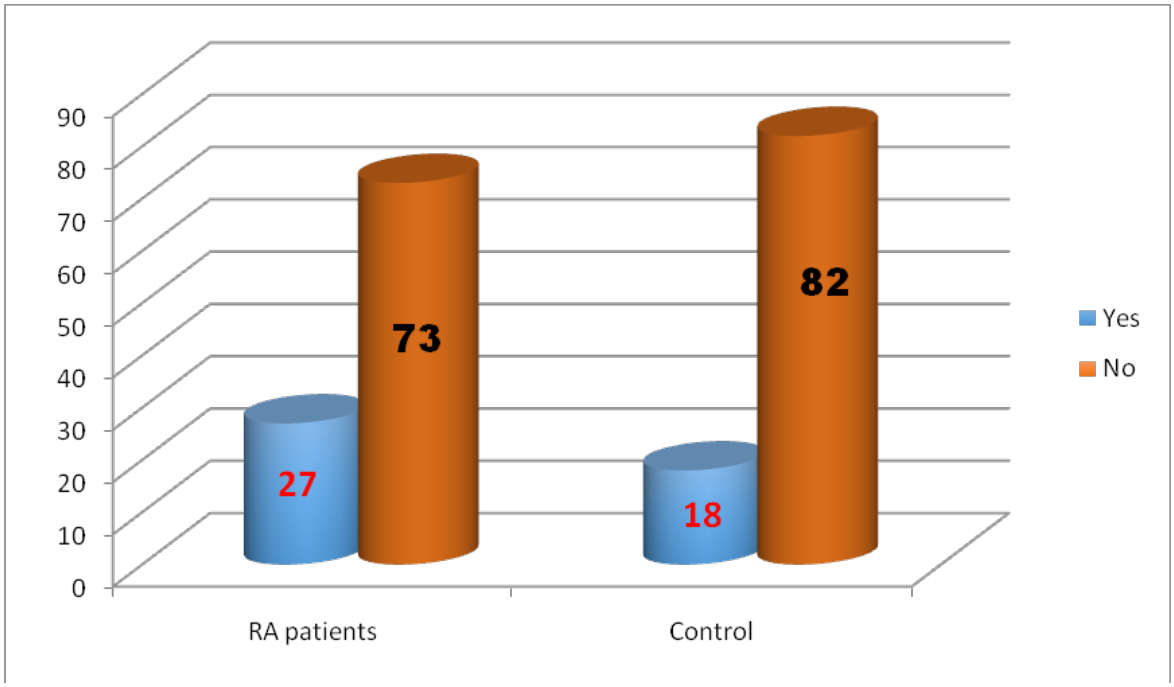

Figure 1. Prevalence of spondylolisthesis for RA patients and control

Conclusions

Prevalence of lumbar SPL among rheumatoid arthritis patients with chronic low back pain was significantly higher than control group. Degenerative type of SPL was more common in RA patients while the isthmic type was more common in healthy controls.

Limitations of the Study:

1. Data collection had been done in one single institute.
2. Small sample size.

Conflict of Interest: Nil.

Source of Funding: Self-funding.

Ethical Clearance: Consent was obtained from each participant included in this study according to the declaration of Helsinki. Ethical approval was obtained from the Ethics Committee in Medical Department, College of Medicine, Baghdad University.

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