Clinicoradiological Correlation of Serum Procalcitonin Values in Degenerative Lumbar Disc Disease

Abhijeet Bele[1], Jigmisha Acharya[2], Manoj Singhal[2], Piyush Kumar Panchariya[3]

[1] Brain and spine clinic, Amarawati, Maharashtra. India
[2] Department Of Anesthesiology, Government Medical College, Kota, Rajasthan, India
[3] Department Of Neurosurgery, MGM Medical College and Superspeciality Hospital, Indore,

Date of submission: 16th October 2023 Date of Acceptance: 10th January 2024 Date of publication: 15th January 2024

Abstract

Introduction: Low back pain (LBP) as a result of prolapsed intervertebral disc is one of the common causes of the morbidity and disability in current population.We assessed any association of inflammatory marker serum procalcitonin in degenerative disc disease.
Materials & Methods: A prospective analytical study carried out at our tertiary care institute over one year from Dec 2021 to Dec 2022 after clearance from institute ethical committee. Total of 68 patients aged 18 to 65 years with low back pain with lumbar disc herniation on MRI imaging were included in the study. Serum procalcitonin levels were assessed using electrochemiluminescence technique on e411 Elecsys 2010.
Results: The median values of serum procalcitonin were higher in early phase of disease tends to stabilising with chronicity of symptoms. There was a positive correlation between mean VAS scores and procalcitonin levels, those patients with higher procalcitonin values clinically had positive straight leg raising test and in the long run required more operative interventions.
Conclusions: Lumbar degenerative disc disease has a strong inflammatory basis and serum values of procalcitonin can be useful objective marker to predict extent of inflammation with prediction of possible clinical course of disease.

Keywords: Degenerative Lumbar Disc Disease, Serum Procalcitonin.

Introduction

Low back pain (LBP) as a result of prolapsed intervertebral disc is one of the common causes of the morbidity and disability in current population. Conventionally a disease of ageing process due to degenerative process, it is now commonly seen in the younger population as well and younger patients may have different mechanism than the elderly.

In all degenerative spine there is changes in annulus fibrosus and nucleus pulposus. These radiological changes due to reduced disc height resulting from changes in hydrostatic pressure within the disc, may be restricted to the disc or may extend to the vertebral bodies too. Such These changes have been described in the literature as Modic changes 1 MRI.

These patients may present with low back ache, radicular pain, and paresthesia or at times with neurological deficit. It has been proposed that the extent of the clinical presentation may have direct correlation with the presence of various inflammatory markers. Some of the markers which has been studied are IL-6, IL-10, HSCRP and PCT. Recent literature also suggest that primary infection in the disc material may be the cause of low back ache and may precipitate early degenerative changes in the spine.[2,3] Several types of bacterial infection have been proposed in the development of low back pain. Believing the hypothesis of infection as cause of degenerative disc disease, it is likely that there will be presence of inflammatory markers in serum. It can be further contemplated that presence of inflammatory markers will affect the clinical profile of patients as well as changes in the disc/vertebral bodies on MRI. Serum procalcitonin is a very commonly used inflammatory marker used in clinical practice.

We therefore took up this study to find out if there is an actual association of inflammatory marker serum procalcitonin in degenerative disc disease. It may further widen the scope of our understanding of such prevalent disease condition and may also change the way of treatment at various stages of disease.

Materials & Methods

A prospective analytical study carried out at our tertiary care institute over one year from Dec 2021 to Dec 2022

Access this article online

Website: https://www.nepjol.info/index.php/NJN

DOI: https://doi.org/10.3126/njn.v20i4.56878

HOW TO CITE
Abhijeet Bele, Jigmisha Acharya, Manoj Singhal, Panchariya PK. Clinicoradiological Correlation of Serum Procalcitonin Values in Degenerative Lumbar Disc Disease. NJNS. 2023;20(4):39-43

Address for correspondence:
Dr. Piyush Kumar Panchariya,
Assistant Professor, Department Of Neurosurgery
MGM Medical College and Superspeciality Hospital, Indore, Madhya Pradesh, India
E-mail: drpiyushpanchariya@gmail.com

ISSN: 1813-1948 (Print), 1813-1956 (Online)

after clearance from institute ethical committee. Total of 68 patients aged 18 to 65 years with low back pain with lumbar disc herniation on MRI imaging were included in the study. Patients with diagnosed inflammatory diseases, diabetics, other immunocompromised patients, who received intradiscal injections, receiving antibiotic therapy or with history of previous spine trauma or spine surgery were excluded.

Patients as per inclusion and exclusion criteria were examined clinically, neurologically, biochemically and radiologically. Patients were assessed for duration and severity of pain (VAS/ NRS), associated neurological signs (SLR/ Cross SLR) and symptoms and sensory/ motor deficits.

Serum procalcitonin levels were assessed using electrochemiluminescence technique on e411 Elecsys 2010(Roche diagnostic, Germany). The value above 0.05 ng/ml are considered abnormal indicating inflammatory response.

Disc herniation ranging from focal to disc extrusion causing compression of neural structures as seen on MRI were graded as per MODIC changes as per the following classification:

Modic changes according to MRI appearance of vertebral body end plates

Type	T1 weighted	T2 weighted
0	No changes	No changes
1	Hypointense	Hyperintense
2	Hyperintense	Iso/hypointense
3	Hypointense	Hypointense

The patients who presented with any neurological deficit or had failed conservative management over period of 6 weeks or those who developed neurological deficit of any kind during conservative management were subjected to the operative management as per anaesthesia fitness. All other patients given conservative management including pharmacological and physical therapies.

Statistical evaluation was done using Statistical Product and Service Solutions (SPSS) 22.0 software (SPSS Inc, USA) was used for the statistical analyses. Quantitative data is expressed in mean and standard deviation. Chi-square test is used for qualitative data and ANNOVA for quantitative data. Non parametric independent data was evaluated with median values, inter quartile (IQ) range and Kruskal Wallis test.

Observation and Results

There was total 68 patients with age group 18 to 65 year. There were 42(61.76%) male and 26(38.23%) female patients in the study. All the patients were having disc prolapse on the MRI but at different levels: L3-L4 7(10.29%); L4-L5 21(30.88%); L5-S1 30(44.11%); multiple level 10(14.70%). All patients presented with low back ache, pain radiating to limb or neurological deficit. Among 31 operated patients, 13 (41.9%) had some neurological deficit and 18 (58.06%) had failed conservative management over period of 6 weeks. 59 (86.76%) patients were SLR positive and 40 (58.82%) patients were cross SLR positive.[13] patients who developed neurological deficit, all were SLR positive.

The patients included in the study were of chronic low back ache with pain duration of more than 3 months having lumbar dis herniation. The mean duration of presentation was 6.78±3.05 months. Majority of the patients presented between 3-6 months (55.88%) followed by 7-9 months (26.47%).

Overall, 86.76% patients were SLR positive. The SLR was more positive if patients presented early i.e., between 3-6 months (p value 0.05).

Table 1: Association of duration of symptoms with SLR

Duration of symptoms	SLR positive		SLR negative		Total	P Value
	No.	%	No.	%		0.05
3-6 months	36	61.0	2	22.2	38	
7-9 months	15	25.4	3	33.3	18	
10-12 months	4	6.8	3	33.3	7	
>12 months	4	6.8	1	11.1	5	

SLR was compared at the different disc level. 28(93.33%) out of 30 patients of L5-S1 disc prolapse were SLR positive followed by 19(90.47%) out of 21 patients of L4-L5 disc prolapse. SLR was also positive at L3-L4 and in cases of multiple disc prolapses. It indicates that SLR may be positive at other disc levels and may not only positive to L5-S1 level as common saying. There was no significant difference in SLR positivity between different disc levels compared to L5-S1 level (p value>0.05).

Table 2: Association between disc level and SLR positivity compared to L5-S1 level.

Level of disc herniation	Chi-square value	P value
L4-L5	0.1395	0.70
L3-L4	2.8244	0.092
MULTIPLE LEVEL	3.7333	0.053

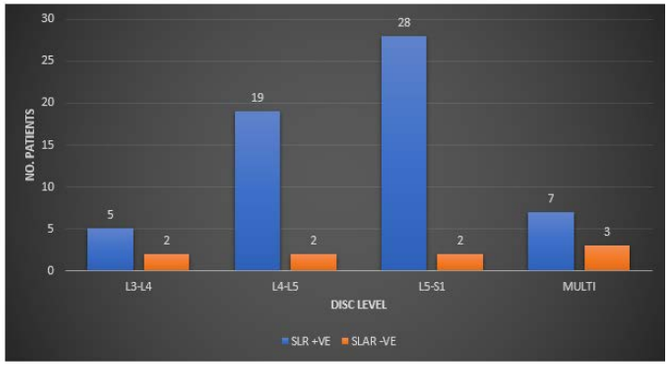

Figure 1: SLR positivity and negativity with disc level.

SLR angle was noted in all the patients it was categorized into different category. It was calculated in the supine position and noting the angle between the raised leg and the horizontal surface. The angle >70 degrees was considered negative SLR as per definition. Most of the patients were having SLR degree between 31 to 70 degrees.

Table 3: SLR Degree in study subjects.

SLR Degree	No. of patients	%
<30	6	8.8
31-50	32	47.1
51-70	26	38.2
>70/-ve	4	5.8
Total	68	100.0

We divide the patients into 3 categories according to the pain score; 0-4 indicating mild pain, 5-7 indicating moderate pain and the 8-10 sever type of pain. Most of the patients in our study were having moderate to severe pain (n=59, 86.76%).

The mean VAS score in our study was 6.79±1.64. The mean VAS score for patients who were SLR positive was 6.90±1.56 and for SLR negative patients was 6.11±1.17 VAS score was having significant difference with the SLR positivity and negativity (p value of 0.04).

Table 4: Mean VAS score in SLR positive and negative patients.

SLR	POSITIVE		NEGATIVE		
	MEAN	**SD**	**MEAN**	SD	p value
VAS	**6.90**	**1.56**	**6.11**	1.17	0.04

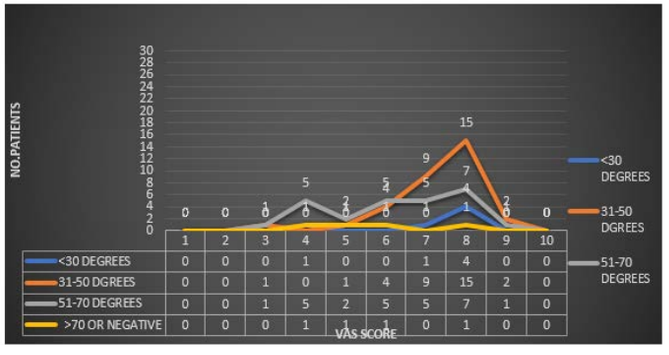

Figure 2: VAS score in study subjects

Modic changes in the vertebral end plates were assessed in each patient on T1 and T2 weighted MRI images. Most common MODIC change in our study population was the TYPE 1 (n=33; 48.5%) followed by the type 2 (n=16; 23.5%). All 33(100%) patients who were having Modic type 1 changes on MRI were also SLR positive while only 1 patient out of 16 was SLR negative in the type 2 Modic changes. If compared with the no changes on MRI with type 1 and 2 changes on MRI, there was significant difference between these groups for SLR. Type 1 and type 2 Modic changes are associated with the SLR positivity while type 3 does not depict the association with SLR.

We found that there was significant difference in the mean values of VAS sore in different types of Modic changes. The mean VAS score was higher in type 1 Modic change (7.47±1.37) as compared to other changes (p value 0.001) indicating that inflammatory changes on MRI is associated with the high pain score.

Table 5: Association of Modic changes with VAS score

SLR	MODIC Changes				p value
	No change	**Grade 1**	**Grade 2**	Grade 3	
VAS Score	**5.58±1.31**	**7.47±1.37**	**6.75±1.39**	5.86±1.34	<0.001

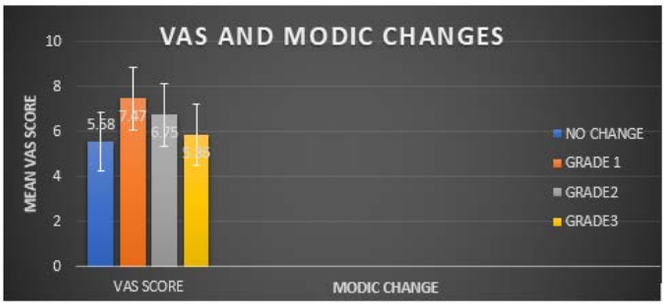

Figure 3: Association of Modic changes with VAS score.

To support hypothesis of the inflammatory and infective pathology in lumbar disc herniation we did the serum levels of procalcitonin in all patient pre-operatively. Its correlation with duration, VAS, SLR and Modic changes were found out.
The median values of the serum PCT were higher than reference range in early periods and values goes on stabilising as chronicity of the symptoms increases. There was no significant difference in the median value of serum PCT at different time duration.

Table 6: Number of patients and duration of symptoms

Duration of symptoms	No. of patients	%	NEGATIVE	PCT (< 0.05 ng/ml)
			Median	IQ range
3-6 months	**38**	**55.88**	**0.054**	0.039
7-9 months	**18**	**26.47**	**0.049**	0.026
10-12 months	**7**	**10.29**	**0.05**	0.04
>12 months	**5**	**7.35**	**0.043**	0.031

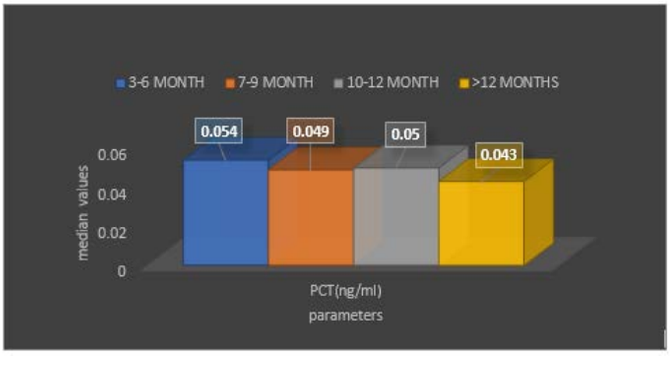

Figure 4: Association of Procalcitonin level with duration of symptoms

The median values of serum PCT was found to be elevated in the patients with higher pain score. PCT had weaker positive correlation with the VAS score. As the pain increases values also tends to increase.

Table 7: Correlation of serum procalcitonin value with VAS score for pain

VAS SCORE	0-4	5-7	8-10
PCT	**0.04±0.032**	**0.048±0.025**	**0.06±0.07**
R Value	**0.1893**		

The median values of PCT were higher in SLR positive patients as compared to the SLR negative patients. The difference was

statistically significant with p value <0.01. Values PCT was higher than reference range in SLR positive patients. Serum PCT level has stronger negative correlation with the degree of SLR (R=-0.35); indicating that as the patients with lesser degree of SLR has higher level of the serum PCT.

Table 8: PCT and SLR

	SLR Positive		SLR Negative		P Value
	Median	IQ range	Median	IQ Range	
PCT (ng/ml)	0.056	0.032	0.043	0.032	<0.01

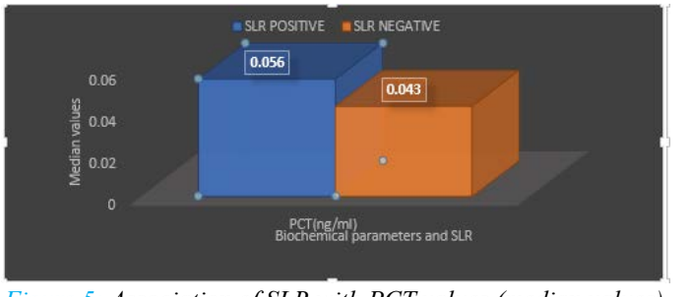

Figure 5: Association of SLR with PCT values (median values).

Median level of PCT (0.068 ng/ml) found to be elevated in type 1 Modic changes as compare to other types. Their values are lowest in type 3 changes. The difference is statistically significant (p value 0.001).

Table 9: Association between Modic changes and PCT values

	Modic Changes				P Value
	No Change	Grade 1	Grade 2`	Grade 3	
PCT	0.04±0.0.02	0.068±0.107	00.049±0.03	0.045± 0.029	0.001

The median values of PCT are found to be on higher side in patients who underwent operative management as compared to non-operated patients. This difference is statistically significant with p value 0.002.

Table 10: Association of Operative procedure with PCT value

	Operated		Non-Operated		P Value
	Median	IQ Range	Median	IQ Range	
PCT Values	0.059	0.045	0.043	0.035	0.002

Discussion

In our study, there were 68 patients with complaints of chronic low back ache (pain more than 3 months duration). The male to female ratio in our study population was 1.6:1 (males 61.76%; females 38.23%). Ben-Galim et al.7, Albert et al.4 and Agarwal et al.5 reported similar male to female ratio except Arndt et al.6 where females patients were more. The age ranged from 18 years to 65 years. The mean age in our study was.37.16 years which was relatively younger as compared to that reported in other studies. We also found that VAS score was significantly higher in SLR positive (6.90±1.56) patients as compare to SLR negative (6.11±1.17) patients. Most of the patients having higher pain score were also having reduced degree of SLR angle. Indicating that SLR pain and low back ache may be having common pathology for pain generation.The inflammatory changes occurring nearby the nerve roots may be the cause for same along with anatomical substrate. R. F. McCarron et al. and K. Olmarker et al. 8 did the separate studies for the inflammatory properties of nucleus pulposus. They suggest that leakage of nucleus pulposus into the spinal canal after disc herniation may initiate immunological and inflammatory responses close to the nerve-roots that increase the activity in nociceptive pathways. This inflammatory influence has been attributed to an upregulation of interleukins (ILs), tumour necrosis factor (TNF), matrix metalloproteinases (MMPs), nitric oxide (NO), and prostaglandins (PGs) in or around the herniated disc. [8,9,10] Previous studies have studied role of inflammatory cytokines like IL6, IL8 in prolapsed disc cases. L. M. Pedersen et al.[11] found out that IL-6 and IL-8 in almost all patients were increased the first weeks after disc herniation. Demircan MN et.al.[12] also noted a clear increase in cytokine levels in the patients that developed chronic pain. Upon extensive literature review no study was found which directly correlated serum procalcitonin with clinical and radiological profile of degenerative lumbar disc disease.

In our study, serum procalcitonin levels in relation of duration of symptoms were raised in early periods of disease in initial 3-6 months but tends to stabilise after that. There was no statistically significant correlation between serum procalcitonin values and duration of symptoms.

Pain is one of the commonest presentations of lumbar degenerative disc disease. We evaluated mean pain scores based on visual analogue score and correlated it with serum procalcitonin values. There was a steady rise in serum values of procalcitonin with increased mean VAS scores and this difference was significant in statistical terms but a weaker correlation as per R values.

Serum procalcitonin levels has significant correlation with SLR findings. The patients with restricted SLR on examination have higher serum procalcitonin values as compared to those who does not have a positive SLR test. This difference has been found significant statistically in our study. Although PCT has significant association with clinical predictability of SLR and patients who will need operative interventions for relief. Also PCT has a negative correlation with degree of SLR. Upon radiological evaluation, serum procalcitonin values are similar and follows similar trends over various levels of involvement in lumbar disc disease. Although the mean serum procalcitonin values were higher in patient with type 1 modic changes and tend to stabilise with higher grades, serum procalcitonin levels were lowest in modic grade 3 changes patients. The finding was not reported significant in statistical terms but follows similar pattern as with duration of symptoms that serum procalcitonin values are higher in initial phase of disease but tends to stabilise with time. Those patients who required operative intervention during due course of time in management

of degenerative lumbar disc disease has higher mean values of serum procalcitonin values as compared to those who were managed on conservative lines. This difference was significant statistically in our study. This may open a new insight into the pathogenesis of disease and its management keeping the hypothesis of extent of inflammation and subsequent damage to neural tissue and resultant insult and needful management.
Since procalcitonin is a marker of infection in body, correlating PCT values may point to infective pathogenesis of prolapsed disc disease although this needs to be studied further.

Conclusion

Lumbar degenerative disc disease has a strong inflammatory pathogenetic basis. Serum procalcitonin values can be a valuable non-invasive parameter to correlate extent of inflammation. There is a positive correlation of serum procalcitonin values with mean VAS score for pain, positive SLR finding and the need of operative intervention in further course of disease. Although it does not have any correlation with radiological pattern of disease including level of involvement, extent of involvement and modic changes on MRI.

Reference

1. Modic MT, Steinberg PM, Ross JS, Masaryk TJ, Carter JR. Degenerative disk disease: assessment of changes in vertebral body marrow with MR imaging. Radiology [Internet]. 1988 Jan 1;166(1 Pt 1):193–9. PMID: 3336678
2. Stirling A, Worthington T, Rafiq M, Lambert PA, Elliott TS. Association between sciatica and Propionibacterium acnes. The Lancet [Internet]. 2001 Jun 23;357(9273):2024–5. doi: 10.1016/S0140-6736(00)05109-6. PMID: 11438138.
3. Stirling A, Rafiq M, Mathur K, Elliott T, Worthington T, Lambert P. Association between sciatica and skin commensals. Orthop Procs. 2003 Mar 1;85-B(SUPP_III):191-192. https://doi.org/10.1302/0301-620X.85BSUPP_III.0850191d
4. Albert HB, Sorensen JS, Christensen BS, Manniche C. Antibiotic treatment in patients with chronic low back pain and vertebral bone edema (Modic type 1 changes): a double-blind randomized clinical controlled trial of efficacy. European Spine Journal. 2013 Feb 13;22(4):697–707. PMID: 23404353
5. Agarwal V, Golish SR, Alamin TF. Bacteriologic Culture of Excised Intervertebral Disc From Immunocompetent Patients Undergoing Single Level Primary Lumbar Microdiscectomy. Journal of Spinal Disorders & Techniques. 2011 Aug;24(6):397–400. PMID: 21150662.
6. Arndt J, Yann Philippe Charles, Koebel C, Ioan Bogorin, Steib JP. Bacteriology of Degenerated Lumbar Intervertebral Disks. Journal of Spinal Disorders & Techniques. 2012 Oct 1;25(7):E211–6. PMID: 2283255
7. Peleg Ben-Galim, Rand N, Giladi M, Schwartz DR, Ashkenazi E, Millgram M, et al. Association Between Sciatica and Microbial Infection: True Infection or Culture Contamination? Spine. 2006 Oct 1;31(21):2507–9. PMID: 17023862.
8. Kjell Olmarker, Blomquist J, Joakim Strömberg, Ulf Nannmark, Thomsen P, Björn Rydevik. Inflammatogenic Properties of Nucleus Pulposus. Spine. 1995 Mar 1;20(6):665–9. doi: 10.1097/00007632-199503150-00006. PMID: 7604342
9. Goupille P, Jayson MIV, Valat JP, Freemont AJ. Matrix Metalloproteinases: The Clue to Intervertebral Disc Degeneration? Spine. 1998 Jul;23(14):1612–26. doi: 10.1097/00007632-199807150-00021.
10. Toru Takebayashi, Cavanaugh JM, A. Cüneyt Özaktay, Srinivasu Kallakuri, Chen C. Effect of Nucleus Pulposus on the Neural Activity of Dorsal Root Ganglion. Spine. 2001 Apr 1;26(8):940–4. doi: 10.1097/00007632-200104150-00018. PMID: 11317117.
11. Pedersen LM, Schistad E, Jacobsen LM, Røe C, Gjerstad J. Serum levels of the pro-inflammatory interleukins 6 (IL-6) and -8 (IL-8) in patients with lumbar radicular pain due to disc herniation: A 12-month prospective study. Brain, Behavior, and Immunity. 2015 May;46:132–6. PMID: 25653193 DOI: 10.1016/j.bbi.2015.01.008
12. Demircan MN, Asir A, Cetinkal A, Gedik N, Kutlay AM, Çolak A, et al. Is there any relationship between proinflammatory mediator levels in disc material and myelopathy with cervical disc herniation and spondylosis? A non-randomized, prospective clinical study. European Spine Journal. 2007 May 3;16(7):983–6. doi: 10.1007/s00586-007-0374-2