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PJBS

ISSN 1028-8880

**Pakistan
Journal of Biological Sciences**

ANSI*net*

Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

Discriminating Extrusive and Bulging Disk Herniations by Using Serum Hs CRP

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Abstract: It has been proposed that because there is inflammation around the nerve roots in disk herniation, there might be an association between serum C Reactive Protein (CRP) with this disease. This study aimed to distinguish between two forms of disk herniation (extrusion, bulging) by comparing the level of serum high-sensitivity CRP (hs CRP). In this perspective study, a total of 62 candidates for lumbar disk herniation surgery were recruited in Tabriz Imam Reza Hospital from 2012 to 2013. The patients categorized in two groups; with extrusion (n = 34) and with bulging (n = 28). Pre-operative serum hs CRP was measured by turbidimetric immunoassay. Both extrusion and bulging groups were matched for their patients' sex (males: 61.8% vs. 57.1%, respectively; p = 0.71) and age (mean: 52.22±7.32 years vs. 49.69±9.40 years, respectively; p = 0.48). The mean serum hs CRP was significantly higher in the extrusion group (3.56±2.90 with a range of 0.1 to 19 mg dL⁻¹ vs. 0.74±0.91 with a range of 0 to 5 mg dL⁻¹; p<0.001). Based on the results of the receiver operator characteristics (ROC) curve, a cut-off point of hs CRP was =2.6 was highly indicative of extrusion, with a sensitivity and specificity of 66 and 63%, respectively. Based on the findings of the present study, the mean serum hs CRP is significantly higher in the patients with extrusive disk herniation vs. those with bulging. The proposed cut-off point may be useful as a preliminary indicator of the type of herniation, before more detailed imaging becomes available.

Key Words: Disk herniation, extrusion, bulging, serum hs CRP, optimal cut-off point

INTRODUCTION

Any disk material, such as nucleus, cartilage, bone and annular tissue may become displaced locally beyond the limits of the intervertebral disk. In this case, a very common pathological condition known as a herniated disk develops (Fardon and Milette, 2001).

Diverse etiological factors may underlie the development of a herniated disk, such as aging, loading forces on different parts of the spine (Moore, 2006) and even congenital anomalies of two neighboring vertebrae (Pouriesia *et al.*, 2013).

Whatever the cause is, a disk herniation can be seen in different forms: (1) Bulging disc in which the disc tissue lies in a circular form and passes the edges of the ring apophyses (many does not consider this type as a real herniation), (2) Protrusion in which the gap between the edges of the base is more than the gap between the edges of the herniation, (3) Extrusion in which the gap between the edges of the base is less than the gap between the edges of the herniation, (4) Migration in

which the disk material is displaced from the site of herniation, with or without sequestration (Haaga *et al.*, 2008).

C Reactive Protein (CRP), is an important acute phase proteins which indicates inflammation. It is synthesized in the liver in response to various factors, especially interleukins and other mediators released by macrophages and fat cells (Thompson *et al.*, 1999; Baradaran and Nasri, 2005; Nasri *et al.*, 2006).

In disk herniation, it is believed that cytokines such as interleukin-1 and interelukin-6, which in part are produced by inflammatory cells such as macrophages and monocytes around the tissue damage to herniation, induce CRP synthesis in the liver (Gabay and Kushner, 1999; Woertgen *et al.*, 2000).

However, conventional methods are not able to measure this CRP, so it may be reported that the serum level of CRP is normal in the cases with lumbar disk herniation. A high-sensitivity CRP (hs CRP) test, on the other hand, measures low levels of CRP and so, it has been recommended in patients with disk herniation. (Sugimori *et al.*, 2003).

The main objective of the present study is to compare the serum level of hs CRP in the patients with extrusive vs. bulging lumbar disk herniations. This is the first study in the literature in this regard.

MATERIALS AND METHODS

In this prospective study, a cohort of 81 patients with lumbar disk herniation was recruited during a 12-month period (2012-2013) in Tabriz Imam Reza Teaching Hospital. Patients with previous surgery in the lumbar region (n = 12) and those with a positive history of inflammatory disease/malignancy (n = 5) or active infection (n = 2) were excluded, leaving 62 cases for the final survey. Based on the findings of Magnetic Resonance Imaging (MRI) the patients were categorized in two groups: the patients with extrusion (n = 34) and the patients with bulging (n = 28). The Ethics Committee of Tabriz Azad University confirmed this study. A written consent was obtained from all the patients before operation.

A blood sample was taken from all the patients before operation. Surgery was performed by a skilled neurosurgeon through a similar appropriate technique.

For each patient, 2 mL of preoperative serum was refrigerated at -70°C. After sampling was completed in all patients, a turbidimetric immunoassay kit of an autoanalyser (Aptec Diagnostics, Belgium) was employed for quantitative assay of high sensitive CRP (hs CRP). Mean serum hs CRP was compared between the two groups with extrusion or bulging.

Statistical analysis: Data were shown as Mean±Standard Deviation or number (%). The SPSS software for Windows (ver.16) was used. Independent samples t test (for age and serum hs CRP) and the Chi-square test (for sex) were employed for analyzing. Receiver Operator Characteristic (ROC) curve was used for determining optimal cut-off points. The p≤0.05 was considered statistically significant.

RESULTS

In the extrusion group, there were 21 males (61.8%) and 13 females (38.2%) with a mean age of 52.22±7.32 (range: 38-64) years. In the bulging group, there were 16 males (57.1%) and 12 females (42.9%) with a mean age of 49.69±9.40 (range: 29-62) years. The two groups were comparable in terms of their patients' sex (p = 0.71) and age (p = 0.48).

Error bar of the mean serum hs CRP in two studied groups are shown in Fig. 1. Accordingly, the mean serum

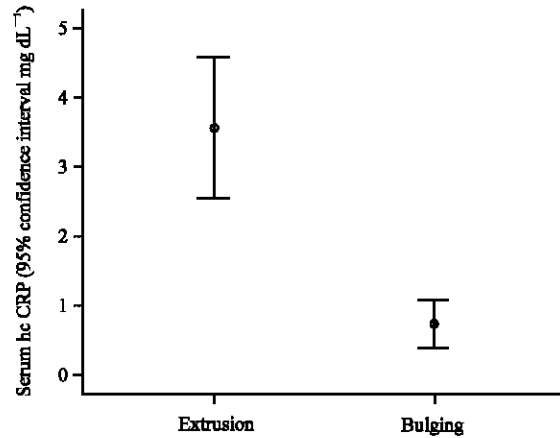


Fig. 1: Error bar of the mean level of serum hs CRP in patients with extrusive and bulging lumbar disk herniation

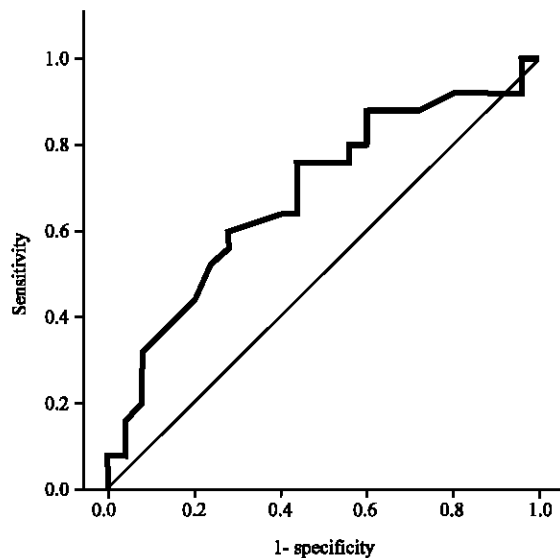


Fig. 2: Receiver Operator Characteristics (ROC) curve of serum hs CRP in discriminating patients with extrusive and bulging lumbar disk herniation

hs CRP was significantly higher in the extrusion group (3.56±2.90 with a range of 0.1 to 19 mg dL⁻¹ vs. 0.74±0.91 with a range of 0 to 5 mg dL⁻¹; p<0.001).

The ROC curve of serum hs CRP in discriminating patients with extrusion from those with bulging is shown in Fig. 2. The under the curve area was 0.70 with a p-value of 0.03, i.e., the serum hs CRP was an appropriate parameter for distinguishing the two groups (extrusion vs. bulging). Based on the results of this curve, the optimal cut-off point of hs CRP was = 2.6, with a sensitivity and specificity of 66 and 63%, respectively.

DISCUSSION

CRP is one of the most useful markers of acute inflammation, because its serum concentration could increase to hundreds fold just within 2 days after tissue injury (Foglar and Lindsey, 1998).

Le Gars *et al.* (2000) showed that the mean level of CRP, which was measured by an ultrasensitive method, was significantly higher in 35 patients with disk herniation in comparison with that in a group of well-matched healthy controls.

In other reports in the patients with lumbar disk herniation, serum hs CRP has been reported a useful tool for different proposes, such as predicting the efficacy of pain relief (Ackerman and Zhang, 2006), or an indicator for the safety of different types of operation (Chao *et al.*, 2007; Zhang *et al.*, 2006).

Sugimori *et al.* (2003) measured the serum level of hs CRP in 48 patients with lumbar disk herniation and 53 normal counterparts. According to their ultrasensitive method of measurement, the mean hs CRP was significantly higher in the patients with lumbar disk herniation. They did not find a significant correlation between the level of serum hs CRP and the level of herniation. They finally concluded that higher concentration of serum hs CRP may indicate a systemic inflammatory which was possibly due to the impingement of the nerve root after disk herniation.

Based on the reported role of CRP in the patients with disk herniation, the present study aimed to compare it between two major and clinically important type of herniation. To the best of our knowledge, the present study is the first one which has claimed that it is possible to distinguish between extruded and bulging lumbar disk herniations only by serum hs CRP. Based on our results, the mean serum hs CRP was significantly higher in the cases with extrusion than in the patients with bulging (3.56 ± 2.90 mg dL⁻¹ vs. 0.74 ± 0.91 mg dL⁻¹; $p < 0.001$). In addition, we also calculated an optimal cut-off point in this regard which seems to be of great practical use for neurosurgeons. Based on this calculation, a serum hs CRP = 2.6 mg dL⁻¹ is an indicator of extrusion rather than bulging (sensitivity = 66%, specificity = 63%). It should be born in mind that this mediocre accuracy rate is possibly due to rather small number of the patients recruited. However, this study is a pioneer for further large scale studies in this regard, which possibly will end up in more accurate results and hence, a value with good sensitivity and specificity.

According to available data, there might be an inflammatory reaction around the nerve roots in lumbar disk herniation. Histopathological examinations have

revealed that inflammatory cells such as macrophages are abundant in herniated disk tissue. These cells usually produce various inflammatory mediators, which in turn, increase the serum CRP concentration. (Gronblad *et al.*, 2000; Virri *et al.*, 2001; Doita *et al.*, 2001; Kawaguchi *et al.*, 2001, 2002). These data support our finding, because it is clear that extrusion is more severe than bulging in terms of tissue injury and hence, indicates a more severe inflammatory response, which is translated into higher levels of CRP in the sera of patients. In conclusion, the results of the present work confirmed that (1) Serum hs CRP is significantly higher in the patients with extrusion vs. bulging of lumbar disk herniation and (2) The proposed cut-off point can be used as a handy primary tool (comparing with more time-consuming, expensive and sophisticated computer tomography or MRI) for predicting the severity of herniation.

REFERENCES

- Ackerman, W.E. III and J.M. Zhang, 2006. Serum hs-CRP as a useful marker for predicting the efficacy of lumbar epidural steroid injections on pain relief in patients with lumbar disc herniations. *J. Ky. Med. Assoc.*, 104: 295-299.
- Baradaran, A. and H. Nasri, 2005. Association of serum c-reactive protein (CRP) with some nutritional parameters of maintenance hemodialysis patients. *Pak. J. Nutr.*, 4: 175-182.
- Chao, Z., Z. Yue, C. Tong-Wei, W. Jian, H. Yong and P. Yong, 2007. Microendoscopic discectomy, a less traumatic procedure for lumbar disk herniation. *Chin. J. Traumatol.*, 10: 311-314.
- Doita, M., T. Kanatani, T. Ozaki, N. Matsui, M. Kurosaka and S. Yoshiya, 2001. Influence of macrophage infiltration of herniated disc tissue on the production of matrix metalloproteinases leading to disc resorption. *Spine*, 26: 1522-1527.
- Fardon, D.F. and P.C. Milette, 2001. Nomenclature and classification of lumbar disc pathology. Recommendations of the combined task forces of the North American spine society, American society of spine radiology, and american society of neuroradiology. *Spine*, 26: E93-E113.
- Foglar, C. and R.W. Lindsey, 1998. C-reactive protein in orthopedics. *Orthopedics*, 21: 687-691.
- Gabay, C. and I. Kushner, 1999. Acute-phase proteins and other systemic responses to inflammation. *N. Engl. J. Med.*, 340: 448-454.
- Gronblad, M., J. Virri, S. Seitsalo, A. Habtemariam and E. Karaharju, 2000. Inflammatory cells, motor weakness, and straight leg raising in transligamentous disc herniations. *Spine*, 25: 2803-2807.

- Haaga, J.R., D. Boll, V.S. Dogra, M. Forsting, R.C. Gilkeson, K.H. Ha and M. Sundaram, 2008. CT and MRI of the Whole Body. 5th Edn., Mosby, USA., ISBN-13: 978-0323053754, pp: 767-768.
- Kawaguchi, S., T. Yamashita, K. Yokogushi, T. Murakami, O. Ohwada and N. Sato, 2001. Immunophenotypic analysis of the inflammatory infiltrates in herniated intervertebral discs. *Spine*, 26: 1209-1214.
- Kawaguchi, S., T. Yamashita, G. Katahira, H. Yokozawa, T. Torigoe and N. Sato, 2002. Chemokine profile of herniated intervertebral discs infiltrated with monocytes and macrophages. *Spine*, 27: 1511-1516.
- Le Gars, L., D. Borderie, G. Kaplan and F. Berenbaum, 2000. Systemic inflammatory response with plasma C-reactive protein elevation in disk-related lumbosciatic syndrome. *Joint. Bone. Spine.*, 67: 452-425.
- Moore, R.J., 2006. The vertebral endplate: Disc degeneration, disc regeneration. *Eur. Spine J.*, 15: S333-S337.
- Nasri, H., S. Shirani and A. Baradaran, 2006. Association of platelet count and mean platelet volume with serum C-reactive protein in regular hemodialysis patients. *Asian J. Cell Biol.*, 1: 59-64.
- Pouriesa, M., R.F. Fouladi and S. Mesbahi, 2013. Disproportion of end plates and the lumbar intervertebral disc herniation. *Spine J.*, 13: 402-407.
- Sugimori, K., Y. Kawaguchi, M. Morita, I. Kitajima and T. Kimura, 2003. High-sensitivity analysis of serum C-reactive protein in young patients with lumbar disc herniation. *J. Bone. Joint. Surg. Br.*, 85: 1151-1154.
- Thompson, D., M.B. Pepys and S.P. Wood, 1999. The physiological structure of human C-reactive protein and its complex with phosphocholine. *Structure*, 7: 169-177.
- Virri, J., M. Gronblad, S. Seitsalo, A. Habtemariam, E. Kaapa and E. Karaharju, 2001. Comparison of the prevalence of inflammatory cells in subtypes of disc herniations and associations with straight leg raising. *Spine*, 26: 2311-2315.
- Woertgen, C., R.D. Rothoerl and A. Brawanski, 2000. Influence of macrophage infiltration of herniated lumbar disc tissue on outcome after lumbar disc surgery. *Spine*, 25: 871-875.
- Zhang, C., Y. Zhou, T.W. Chu, J. Wang, W.D. Wang and Y. Hao, 2006. Traumatic responses following microendoscopic discectomy: Clinical analysis of 44 patients. *Zhonghua Yi Xue Za Zhi.*, 86: 3039-3042 [Article in Chinese].