



Correlation of Various Comorbid Factors and Cytokine Biomarker Study on Lumbar Degenerative Disorders

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ABSTRACT

Globally, disc degenerative disorders are the primary cause of lower back pain (LBP). The purpose of this study was to determine the relationship between cytokinin biomarkers and age, sociodemographic, and occupational characteristics in Lumbar Degenerative Disease patients. It was a prospective study carried out at Rajahmundry, GSL Medical College in collaboration with Department of orthopedic. The study was carried out in December 2021 to January 2023. For the study, every comorbid factor was taken into account. Prior to therapy, serum samples were obtained and subjected to multiplex assays to measure the levels of interleukin (IL)-1 β , IL-2, IL-4, IL-6, IL-8, IL-10, IL-12p70, and IL-13. When using Logistic Regression Analysis (LRA), P values less than 0.05 were deemed statistically significant. There were 112 members in all, with a 1:1.2 male to female ratio. Subjects with LBP had considerably greater levels of IL-6 than did the control group. Socioeconomic status and LBP were significantly correlated (OR=0.986, 95% CI: 0.931-1.124, P=0.0423). LBP is high (54.4%) among individuals who sit constantly for more than eight hours, according to the amount of time spent sitting. IL-6 levels were observed to positively correlate with age, BMI, and the duration of symptoms. **Conclusion:** the current clinical study's conclusions represent the outcomes of the initial analysis of circulating cytokine levels. All age groups and socioeconomic classes have LBP often. Long periods of inactivity and obesity are significant risk factors. Although it (QOL) was not examined in this study, LBP has an impact on life quality. It is advised to do extensive, community-based research with a sizable sample size.

Keywords: Lower back pain, Cytokinin, Interleukin, Biomarkers

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INTRODUCTION

Age is a major risk factor for the development of neurological disorders (ND) worldwide. As a result of the epidemiological shift, the burden is rising quickly in India as well. Despite not being lethal, non-communicable diseases account for a sizable portion of both communicable and non-communicable infections in India, according to data that is currently available. Thus, the Indian government incorporated ND in a number of social initiatives pertaining to health [1]. Disc Degenerative Disorders (DDD) are a highly common clinical disorder that can affect people of any age and are the primary cause of lower back pain (LBP) worldwide [2]. The non-medical populace is drawn to LBP numbers because more than half of all people report having this problem at some point in their lives [3-4]. The financial loss resulting from lower productivity and lost wages is another important aspect of lower back pain. The majority of Indians are rural dwellers who rely on the building, agricultural, and other industries. Thus, there are variations in the prevalence of LBP. LBP ranks among the top 10 causes of Years Lived with Disability (YLWD), which is consistent with the worldwide situation among Indians [5]. From a clinical perspective, LBP is a complex combination of several illnesses with a variable response to therapy. Physical examination is rarely diagnostic for LBP because the condition is triggered by various triggers with comparable clinical presentations. Intervertebral disc herniation (DH), spinal stenosis (SS), and degenerative disc degeneration are among the most typical diagnosis for low back pain (LBP). India is one of the most populous countries in the world, home to 18% of all people. However, there is a significant lack of evidence, particularly from this region, about LBP. Furthermore, Indians' lifestyles have changed significantly over the past ten years as a result of financial gains and technological advancements. In addition to them, LBP is typically regarded

as a decoration for older adults who fall into the upper income bracket [1, 5]. and this in mind, a study was carried out in a tertiary healthcare setting to determine the relationship between age, sociodemographic, and vocational characteristics and lower back pain. This could encourage preventive actions among the general public. Additionally, the professionals' approach to treatment will be simple.

MATERIAL AND METHODS

It was a prospective study carried out at the GSL Medical College in Rajahmundry's anatomy department and in collaboration with department of orthopedic. The study was carried out in December 2021 to January 2023. The Institutional Ethics Committee approved the study protocol. It was obtained via the subjects' informed permission. The participants in this study were adults over the age of 18, both genders, and diagnosed with LBP who were outpatients at this Medical College hospital. This study excluded people who were uncooperative, did not have low back pain (LBP), were on immunosuppressive or steroid therapy, had spine surgery, were receiving or had received physiotherapy, had cancer, had known vertebral fractures, had experienced trauma, or were unconscious. This is a post-secondary medical educational setting that offers several undergraduate and graduate programs. The patients who visited the orthopaedic department for medical issues were assessed and looked over. The World Health Organization (WHO) classifies discomfort between the buttock and the lower edge of the ribcage as lower back pain (LBP). At the time of the clinical presentation of the subjects, blood samples were taken for the serum study. The study included those who, according to procedure, were confirmed to be LBP. A thorough clinical history was gathered after the study subject was recruited. Every result was documented in the study proforma. The study was described in detail in the native tongue. Participants could ask questions if they had any. Following the resolution of any remaining questions, the participants' sociodemographic information was documented using the Modified Kuppaswamy scale [6]. The National Institutes of Health (NIH) website was used to calculate the participant's Body Mass Index (BMI), which was then separated into four categories based on their height in centimeters and weight in kilograms [7]. Factors including the nature of the work, the posture in which one sits, the length of time one spends sitting still, stress connected to one's employment, if one must perform outside work as part of the job, frequency of eating, and food consumption were also noted in this study. Multiplex electrochemiluminescence immunoassays (MD, USA) that are commercially available were used to test the serum levels of cytokines. The assay was carried out in compliance with the manufacturer's instructions. To assess IL-1 β , IL-2, IL-4, IL-6, IL-8, IL-10, IL-12p70, and IL-13, duplicate samples were tested. Samples were diluted 1:2 in Diluent 2 (MSD) for the cytokine multiplex. 50 μ l was added, and the mixture was incubated at 4 $^{\circ}$ C for a whole night. After the first incubation, each well received 25 μ l of detector antibody after the plates were cleaned with 0.05 percent Tween in phosphate buffered saline. After two hours of incubation at room temperature, the plates were cleaned once more and scanned using a 2 \times read buffer utilizing an MSD SECTOR Imager 2400 plate reader. For every test, the lower and upper limits of detection (LLOD and ULOD, respectively) were calculated, and the percentage of samples with concentrations at or above the LLOD (% detected) is given.

Statistical Analysis

Data were analysed using SPSS version 21. It was presented by mean \pm SD for continuous variables and percentage for categorical data. Logistic Regression Analysis (LRA) was applied and $P < 0.05$ were considered to be statistically significant.

RESULTS

The study involved 112 individuals in total; 50 (44.64%) were women and 52 (55.35%) were men. Ratio of men to women was 1:1.2. The group with the highest age, consisting of participants who were >68 years old (22.32%; 25), was followed by 58-67 (18.75%; 21), 17.86% (20) in 38-47 and 48-57 years old (showing 19 (16.96%), 12.5% (14) in 28-27 years old and lowest (11.6%; 13) in 18-27 years old (Table 1). The mean age of the group was 48.3 years. Age and LBP did not shown to be correlated in LRA (OR=0.923, 95% CI: 1.2-2.9, $P=0.62$).

Table 1 Age wise distribution of the study participants; n (%)

Age (Years)	Male (%)	Female (%)	Total (%)
18-27	08 (7.2)	05 (4.4)	13 (11.6)
28-37	08 (7.2)	06 (5.3)	14 (12.5)
38-47	12 (10.7)	08 (7.1)	20 (17.86)
48-57	10 (8.96)	09 (8.0)	19 (16.96)
58-67	11 (9.85)	10 (8.9)	21 (18.75)
≥ 68	13 (11.62)	12 (10.7)	25 (22.32)
Total	62 (55.35)	50 (44.64)	112 (100)

Upon analyzing the BMI, the obesity group had the highest percentage of participants (37.5%; 42) with

LBP, followed by the overweight (25.89%; 29), normal weight (16.96%; 19), and underweight (19.6%; 22) groups (Table 2). The study participants' average weight was 56.2 kg, and the LRA showed no correlation between LBP and BMI (OR=0.968, 95% CI: 2.1-3.6, P=0.820).

Table 2 BMI of the study participants; n (%)

BMI	Male (%)	Female (%)	Total (%)
Underweight (<18.5)	12 (10.7)	10 (8.9)	22 (19.6)
Normal weight (18.5-24.9)	12 (10.7)	07 (6.25)	19 (16.96)
Overweight (25-29.9)	15 (13.4)	14 (12.5)	29 (25.89)
Obesity (≥ 30)	23 (20.5)	19 (16.9)	42 (37.5)
Total	62 (55.35)	50 (44.64)	112 (100)

Of the study participants, 22.32% (25) reported eating at home, while the majority (62.4%; 70) reported eating outside. The study found a significant correlation between socioeconomic level and LBP (OR=0.986, 95% CI: 0.931-1.124, P=0.0423). The majority of respondents were upper class (31.25%) in terms of income, followed by upper middle class (22.32%), lower middle class (18.11%), middle class (17.85%), and lower class (8.92%). The incidence of low back pain (LBP) is shown to be higher in individuals with sitting jobs, including shop owners (25%) and skilled workers (40.17%), unskilled workers (28.57%), and clerks. Startling findings revealed that the group under study lacked experience. Semi-professionals (20.53%) and unemployed people (18.75%) came next (Table 3).

Table 3 Various demographic factors of the study participants

Parameter	N	%
Eating mode		
Outside	70	62.4
In house	25	22.32
Family income		
Upper class	35	31.25
Upper middle class	25	22.32
Middle class	18	18.11
Lower middle class	20	17.85
Lower class	10	8.92
Occupation		
Student	12	10.71
Professional	20	17.85
Semi-professional	23	20.53
Clerical, Shop owner	28	25
Skilled worker	45	40.17
Unskilled worker	32	28.57
Unemployed	21	18.75

The study participants were split into two groups: those who continuously sat for more than eight hours and those who did so for less than eight hours. The majority of research participants 55.4% sit for longer than eight hours. Workplace stress was reported by 69.64% of respondents, and outside work related stress was reported by 64.28%.

Table-4 Lower and upper limits of detection (LLOD and ULOD, respectively) for measured biochemical factors in serum samples (pg/ml)

Biochemical factor	LLOD (pg/ml)	ULOD (pg/ml)	% Detection
IL-1β	0.062	428	8%
IL-2	0.051	1453	52%
IL-4	0.024	188	26%
IL-6	0.073	498	100%
IL-8	0.068	766	98%
IL-10	0.052	332	99%
IL-12p70	0.072	1452	39%
IL-13	0.50	472	45%

Percentage detected (% detected) is the percentage of samples with concentrations at or above LLOD. Nearly all samples (>98% identified) had measurable levels of IL-6, IL-8, and IL-10 (Table 4). Based on imaging analysis of the disease severity grade, serum levels of IL-6 were similar across severity classes and no significant variations were observed in these biochemical parameters. Relatively few samples (9–59% identified) had measurable levels of IL-1β, IL-2, IL-4, IL-12p70, and IL-13 (Table 4). Subjects with LBP had

considerably lower levels of IL-2, and their levels of IL-6 were statistically higher. The study compares the demographics and comorbidities of several diagnostic groupings. Between DH and Other diagnoses, there were no appreciable variations in the gender distribution or BMI. Nonetheless, notable distinctions were noted in the age of the subjects and the length of their symptoms among the diagnostic categories. Compared to DH participants (10 months; $p < 0.0002$), those with LBP due to other diagnosis had a higher mean age and a longer mean duration of symptoms (12 months). Participants with SS or DDD were shown to have considerably greater levels of IL-6 than participants with DH, even after adjusting for the effects of age, gender, and OA history. The participants with other diagnosis had mean blood IL-6 levels of 0.74 ± 0.116 pg/ml, which was 57% greater than the levels found in DH subjects (0.47 ± 0.060 pg/ml; $p < 0.02$).

DISCUSSION

LBP is the leading cause of YLWD worldwide and one of the major public health concerns [1, 2, 5]. The results showed that the prevalence of LBP varied from 6.2% to 92%, and that it is increasing at a faster rate, particularly in low- and middle-income nations [2]. Although the majority of LBP cases resolve on their own, 5 to 10% may develop chronic LBP [8]. The participants in this study were 112 (100%) LBP people. Males made up 55.35% of the total (62) and the male to female ratio was 1:1.2. Thus, the group that suffers is the male population. On the other hand, reports from the community that showed a high frequency of LBP among women were also available [9, 10]. The research did not, however, provide an explanation for the significant incidence of women. This could be due to a combination of genetic, psychological, and sex hormones. People with LBP were enlisted in the current study. Men were shown to have higher rates of lower back pain (LBP) than women because they are more likely to engage in outdoor activities. The two age groups most frequently at risk of DDDs are adults and children. because there is a significant compromise in the consumption of nutrient-dense foods in the highest age group. Thus, this is a very delicate group. Due to middle age's high level of productive work activity, DDDs are highly likely to occur. The largest percentage of participants in the current study (22.32%) were over 68, with 58–67 years old (18.75%) coming in second. (Table 1). The literature indicates that there is a risk of LBP for young Indians [20]. Therefore, it is imperative that children are also informed of the main preventive strategies. Overweight and obesity are major global public health concerns, and their prevalence is rising. One of the risk factors for LBP is obesity. Increasing weight on the lumbar vertebrae may cause mechanical pressure on the spine, and inflammatory changes in obese people ultimately lead to low back pain [11]. Moreover, a rise in body weight causes disc degeneration, inflammatory changes in the spine, and wears and stress on the spinal structures [12]. According to Table 2, the prevalence of LBP in overweight and obese participants in this study was 37.5% and 25.89%, respectively. These results indicate that there is a positive correlation between LBP and BMI. In addition to applying mechanical pressure to the spinal area, pain is also caused by the increased production of cytokines such IL 6 and $TNF\alpha$ [13]. Strong correlation has been found in the literature to exist between a high BMI and a higher prevalence of low back pain [14]. Based on the correlation between gender and BMI and LBP in this study, the incidence of being overweight is about identical for both genders. In contrast, the obese category has a significant frequency of low birth weight in men (20.53%) and females (16.96%), respectively (Table 2). Obesity and female sex hormones are important contributors to musculoskeletal discomfort, which in turn causes lower back pain (LBP). However, additional factors like physical activity, lifestyle choices, cultural influences, and Lumbar Disc Herniation (LDH) provide a better explanation for this gender gap [15, 16]. With the exception of LDH, there was no discernible gender difference in this study because all participants are employed and participated in household duties. In this study, 61.59% of LBP participants fell into the overweight and obesity group; in the Bansal et al. article [17], that number was 55.7%. Those with high BMI are known to have high pain intensity LBP in addition to high prevalence [14, 17]. The degree of pain was not measured in this study. For all living things, eating is the most vital action. Humans engage in this daily, however the frequency and volume of our consumption vary. There is a significant shift among Indians, therefore the source and consumption pattern are crucial [18]. In this study, 62.4% (70) of the participants reported eating out. According to research, over 35% of individuals consume junk food (JF) multiple times per week, which raises daily energy intake by 13% [18]. The biggest risk associated with JF, the global epidemic, and the primary cause of LBP is obesity. Upon inquiry from the research team, every participant disclosed their usage of JF. According to this study, the incidence of LBP rises with income, reaching 31.25% in the top class and 8.92% in the poor class (Table 3). The relationship between income and LBP is not linear. When someone's financial situation changes, they typically develop a sedentary lifestyle and alter their eating habits as well. Consumption of JFs and beverages with a high sugar content increases with income. For LBP, these lifestyle adjustments are crucial. The incidence was significantly lower in the low-income group since they had to work harder throughout their lives. There is a danger of developing LBP even if we do not work. In this study, the percentage of unemployed people was 18.75% (Table 3). Another risk factor for LBP is

prolonged sitting; in this study, 40.17% (45) of skilled workers reported experiencing LBP as a result of prolonged sitting (Table 3). This is a tertiary care hospital that enrolls close to 4000 students in various undergraduate and graduate medical programs. Twelve of these LBP medical students participated in this study (Table 3). According to a recent survey, 14.3% of medical students had LBP [17]. 53.4% was the result of another Australian study [19]. The disparity in operational definitions of LBP accounts for the variation in prevalence. Because of the updated curriculum, psychological stress is the most significant element among the medical students in this study. The literature reported similar findings [20]. However, a Saudi study noted that LBP in medical students is not caused by stress. Nonetheless, medical professionals reported feeling dissatisfied with their jobs [21]. Medical experts were not involved in this study. The research's strengths its first epidemiological study from this area and adequate sampling of several population categories are these. Circulating IL-6 levels and pain levels have been linked in chronic pain [22]. Sowa et al. showed correlations between pain and pain-related function and serum levels of neuropeptide Y or chondroitin sulfate 846 in patients with isolated back pain without radiculopathy [23]. Since cytokines and chemokines are important in neuropathic pain, the link between inflammatory mediators and pain is not limited to LBP [24]. It should come as no surprise that patients with additional conditions linked to neuropathic pain also have systemic cytokine increases. While TNF- α and IL-8 levels were not observed to differ between knee OA patients and control participants, patients with knee OA were reported to have considerably higher serum levels of IL-6 and IL-10 than controls [25]. When compared to other individuals experiencing joint discomfort, people with RA also exhibit higher systemic IL-6 [26]. Additionally, elevated serum levels of IL-6 have been linked to aging. numerous investigations conducted on healthy older persons have demonstrated that, in the absence of disease or acute infection, levels of numerous cytokines, including TNF- α and IL-6, rise with age. While there is a correlation between elevated inflammatory markers and age, the exact cause of these markers is still unknown. However, some potential causes include visceral obesity, reduced sex steroid hormones, smoking, melancholy, and aging-related periodontal diseases [27].

CONCLUSION

This study indicates that LBP is prevalent across all age and socioeconomic levels. Long periods of continuous sitting and obesity are significant risk factors. Individuals with LBP had considerably greater serum levels of IL-6. After adjusting for the effects of age, gender, and OA history, people with LBP due to SS or DDD had significantly greater levels of IL-6 than participants with DH. This research implies that circulating cytokines are involved in disc diseases like DDD and SS on a larger scale. In individuals with LBP, positive relationships were observed between IL-6 levels and age, BMI, and the duration of symptoms. The Quality of Life (QOL) is impacted by LBP. However, this was not examined in this research. This is the research's shortcoming. It is advised to do extensive, community-based research with a sizable sample size.

DECLARATIONS

CONFLICT OF INTEREST

The authors declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

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