



Original Research

Comparison of the Efficacy of Peri-Operative Use of Bupivacaine with Corticosteroids Versus Bupivacaine Alone in Lumbar Disc Disease Surgery

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ABSTRACT

Objectives: To compare the efficacy of peri-operative use of bupivacaine with corticosteroids versus bupivacaine alone in lumbar disc disease surgery.

Materials and Methods: This randomized controlled study at PIMS Hospital (Nov 2023–May 2024) involved 76 patients (ages 25–65) undergoing lumbar disc surgery. Patients with prior surgery, epidural steroids, spinal trauma, or rheumatoid arthritis were excluded. Group A received Gelfoam soaked in 10 mL of 0.25% bupivacaine + 2 mL dexamethasone, while Group B received Gelfoam with 10 mL of 0.25% bupivacaine only. Efficacy was assessed over 24 hours.

Results: Patients in Group A and B had mean ages of 43.08 ± 10.50 and 42.11 ± 10.22 years, respectively. The majority of the 45 patients (59.21%) were in the 25–45 age range. The male-to-female ratio was 2.16:1, with 52 (68.42%) of the 76 cases being male and 24 (31.58%) being female. The mean baseline VAS score was 6.61 ± 1.03 . The mean baseline VAS score in group A (corticosteroid and bupivacaine) was 6.47 ± 1.01 and the mean pre-therapy VAS score in group B (bupivacaine alone) was 6.74 ± 1.06 . The efficacy of using bupivacaine and corticosteroids during lumbar disc disease surgery was found to be 30 (78.95%) as compared to 20 (52.63%) in the bupivacaine group only, with a 0.016 p-value.

Conclusion: The study concluded that the efficacy of peri-operative use of corticosteroid and bupivacaine is higher as compared to bupivacaine alone in lumbar disc disease surgery.

Keywords: Lumbar disc herniation, Corticosteroid, Bupivacaine.Efficacy.

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INTRODUCTION

A rupture in the outer annulus fibrosus (fibrous ring) of an intervertebral disc causes the soft, center component nucleus pulposus to protrude past the torn outer rings, resulting in spinal disc herniation, a medical disorder that affects the spine. Despite the possibility of straining, trauma, and lifting accidents, age-related degradation of the annulus is the most frequent cause of disc herniation. Tears are almost always poster-o-lateral because the posterior longitudinal ligament prevents disc herniation in the midline.¹ The release of inflammatory chemical mediators may be facilitated by this disc ring rupture, even if there is no compression of the nerve roots. This could cause severe pain.²

In the lower back, lumbar disc herniations most commonly happen between the fifth and sacrum or between the 4th and 5th lumbar vertebral bodies. The perineal nerve can transmit symptoms to the foot and/or toe, as well as the lower back, thighs buttocks, genital/anal area, and other areas. Sciatica nerve damage is the most common nerve that causes sciatica symptoms. Additionally, injury to the femoral nerve can result in burning sensations in the hips and legs, tingling, or numbness in one or both legs or even the foot.^{3,4}

Compression and the inflammatory process that the herniation triggers are typically the causes of leg and lower back pain after lumbar disc herniation.⁵ Although the prolapsed disc and the mechanical strain on the nerve roots can be removed surgically, the inflammatory response may persist beyond the procedure.⁶ Therefore, postoperative pain may result from inflammatory inflammation of sensory nerve roots or dorsal root ganglia. For almost 20 years, epidural steroids have been used to reduce pain following lumbar discectomy.⁷ According to recent studies, the early stages of postoperative pain can be effectively reduced by administering intraoperative epidural steroids.^{7,8} Steroids are also administered intravenously, with satisfactory

outcomes.⁹

According to reports, pre-operative (preemptive) local anesthetic injections administered to the site of the incision are particularly useful in minimizing pain that occurs during both rest and movement.¹⁰ Good analgesia for the surrounding tissue of the wound may be provided by long-term, efficient local anesthetic infiltration. Bupivacaine is the most frequently used local anesthetic. Bupivacaine has been found to provide efficient postoperative pain relief following spinal surgery, either alone or in conjunction with methylprednisolone.¹¹ Compared to administering opioids directly, the effects of epidural opioids are prolonged when gel foam soaked in opioids is used in the epidural area.¹² In lumbar disc disease surgery, the combined peri-operative corticosteroid and bupivacaine group showed 72.0% efficacy, whereas the bupivacaine group alone showed 44.0%.¹³

As there is not any local study in the literature, that has assessed the results of the use of peri-operative Bupivacaine and corticosteroids in lumbar disc disease surgery, so, the the purpose of my research is to compare the effectiveness of peri-operative corticosteroid and bupivacaine versus bupivacaine alone in lumbar disc disease surgery. The result of my study will not only modify the treatment of this problem but also set baseline data both at the national and international levels. Additionally, a more effective approach can be regularly used in our general practice to lower the morbidity rate of our population.

MATERIALS & METHODS

Study Design and Study Setting

This randomized controlled trial, conducted in the Neurosurgery Department at PIMS Hospital, Islamabad, from 17th November 2023 to 16th May 2024, utilized a calculated sample size of 76 patients (38 per group) utilizing non-probability

consecutive sampling, with a 95% confidence level, 80% research power, and expected efficacy rates of 44.0% for bupivacaine alone and 72.0% for peri-operative corticosteroid plus bupivacaine.

SAMPLE SELECTION

Inclusion Criteria

Patients aged 25-65 years of both genders with lumbar prolapsed intervertebral disc (per operational definition) undergoing surgery, with symptoms lasting more than 3 months.

Exclusion Criteria

Patients with a history of lumbar disc surgery, spinal trauma, lumbar epidural steroid injection, rheumatoid arthritis, active malignancy, or pregnancy were excluded.

DATA COLLECTION PROCEDURE

Following institutional ethical review committee approval, 76 patients (38 in each group) who met the inclusion criteria and were admitted to the inpatient neurosurgery department of PIMS Hospital in Islamabad were chosen. All selected cases were given the chance to choose a slip from the total number of mixed-up slips (half-slips with the letter "A" and other half-slips with the letter "B") after providing their informed consent and they were assigned to the appropriate group. Following hemostasis and before final closure, the surgeon inserted two absorbable gelatin sponge pieces soaked in the study drug into the epidural space above the paraspinal area, above the nerve roots. Participants in Group A received gel foam soaked in 10 mL of 0.25% bupivacaine and 2 mL of dexamethasone. Gelfoam that had been soaked in 10 milliliters of 0.25% bupivacaine was given to patients in group B. According to the operational definition, the researcher monitored each patient for a full day to determine efficacy (yes/no). Patients who did not follow up were not included.

All data including the demographic data (age, gender, BMI, diabetes mellitus, place of living, baseline VAS score, and efficacy) was documented on a proforma that was specifically designed (Annexure-I).

STATISTICAL ANALYSIS

SPSS version 25.0 was utilized to conduct the statistical analysis. The mean and standard deviation were displayed for age, the length of symptoms, BMI, and the initial VAS score. Gender, diabetes mellitus (yes/no), residence (urban/rural), and efficacy (yes/no) were presented as frequency and percentage. Efficacy between both groups was analyzed by chi-square test and p-value less than ≤ 0.05 was taken as significant.

Stratification was done for gender, age, duration of symptoms, baseline VAS score, BMI, diabetes mellitus (Yes/No), and place of living (rural/urban). A p-value of less than 0.05 was considered significant in the post-stratification chi-square test.

RESULTS

Age Distribution

The Mean age in this research was 42.76 ± 10.31 years, with a range of 25 to 65 years. Patients in group A were 43.08 ± 10.50 years old on average, whereas those in group B were 42.11 ± 10.22 years old. Most of the 45 patients (59.21%) were in the 25–45 age range, as indicated in Table 1.

Gender Distribution

The male to female ratio was 2.16:1, with 52 (68.4%) of the 76 patients being male and 24 (31.5%) being female.

Duration of Symptoms

The symptoms lasted an average of 5.13 ± 1.51 months. Table 2 shows that the mean symptom duration was 4.76 ± 1.44 months in group B and

5.50 ± 1.50 months in group A.

Table 1: Age distribution for both groups (n=76).

Age (Years)	Group A (n=38)		Group B (n=38)		Total (n=76)	
	No. of Patients	%age	No. of Patients	%age	No. of Patients	%age
25-45	23	60.53	22	57.89	45	59.21
46-65	15	39.47	16	42.11	31	40.79
Mean ± SD	43.08 ± 10.50		42.11 ± 10.22		42.76 ± 10.31	

Body Mass Index (BMI) Distribution

Mean BMI was 29.04 ± 2.76 kg/m² (Table 4).

Table 2: Gender distribution for both groups.

Gender	No. of Patients	Percentage (%)	Male: Female Ratio
Male	52	68.4%	2.16: 1
Female	24	31.6%	
Total	76	100%	

Table 3: Patient distribution according to symptoms duration.

Duration of symptoms (In Months)	Group A (n=38)		Group B (n=38)		Total (n=76)	
	No. of Patients	%age	No. of Patients	%age	No. of Patients	%age
4-6 months	29	76.32	34	89.47	63	82.89
>6 months	09	23.68	04	10.53	13	17.11
Mean ± SD	5.50 ± 1.50		4.76 ± 1.44		5.13 ± 1.51	

Table 4: Patient distribution based on BMI.

BMI (kg/m ²)	Group A (n=38)		Group B (n=38)		Total (n=76)	
	No. of Patients	%age	No. of Patients	%age	No. of Patients	%age
≤27	13	34.21	11	28.95	24	31.58
>27	25	65.79	27	71.05	52	68.42
Mean ± SD	29.08 ± 3.06		29.00 ± 2.46		29.04 ± 2.76	

Diabetes Mellitus Status

Table 5: Distribution of patients according to DM.

DM	Group A (n=38)		Group B (n=38)		Total (n=76)	
	No. of Patients	%age	No. of Patients	%age	No. of Patients	%age
Yes	11	28.95	15	39.47	26	34.21
No	27	71.05	23	60.53	50	65.79

Baseline Pain Scores (VAS)

The mean baseline VAS score was 6.61 ± 1.03. The mean baseline VAS score in group A (corticosteroid and bupivacaine) was 6.47 ± 1.01 and the mean pre-therapy VAS score in group B (bupivacaine alone) was 6.74 ± 1.0 as shown in Table 6.

Comparison of Treatment Efficacy Between Groups

The efficacy of peri-operative Bupivacaine and corticosteroids in the lumbar disc disease surgery was found to be 30 (78.95%) as compared to 20

(52.63%) in the bupivacaine group only group, with a p-value of 0.016.

Table 6: Patient distribution according to baseline pain score.

Baseline Pain Score	Group A (n=38)		Group B (n=38)		Total (n=76)	
	No. of Patients	%age	No. of Patients	%age	No. of Patients	%age
≤6	22	57.89	17	44.74	39	51.32
>6	16	42.11	21	55.26	37	48.68
Mean±SD	6.47 ± 1.01		6.74 ± 1.06		6.61 ± 1.03	

Stratification of Efficacy by Age

Table 8 presents the stratification of treatment efficacy based on age groups in both Groups A and B, each with 38 participants. Among patients aged **25–45 years**, There was a statistically significant difference in efficacy between group A (17 patients) and group B (13 patients) ($P = 0.0022$). Whereas among patients aged 46–65 years, efficacy was shown in 13 individuals in group A and seven in group B, with no significant difference ($P = 0.2287$). These findings suggest that treatment efficacy was significantly better in younger patients (**25–45 years**) Group A in contrast to Group B. Whereas in older patients (**46–65 years**), There were no statistically significant variations in the groups' efficacy.

Table 7: Comparison of Treatment Efficacy Between Groups.

Treatment Group	No. of Patients with Efficacy	Percentage (%)	p-value
Bupivacaine + Corticosteroids (Group A)	30	78.95%	0.016
Bupivacaine Alone (Group B)	20	52.63%	
Total	50	65.79%	

Table 8: Efficacy stratification by age.

Age (years)	Group A (n=38) Efficacy		Group B (n=38) Efficacy		P value
	Yes	No	Yes	No	
25 – 45	17	06	13	09	0.0022
46 – 65	13	02	07	09	0.2287

Table 9: Efficacy stratification according to gender.

Gender	Group A (n=38) Efficacy		Group B (n=38) Efficacy		P-value
	Yes	No	Yes	No	
Male	21	05	14	12	0.0351
Female	09	03	06	06	0.0065

Stratification of Efficacy by Gender

Table 9 presents the stratification of treatment efficacy based on gender in both Groups A and B, each with 38 participants. Among **male** patients, efficacy, with a statistically significant difference ($P = 0.0351$) between the 14 patients in Group B and the 21 patients in Group A. Similarly, among **female** patients, six patients in group B demonstrated efficacy, in contrast to nine in group A also showing a statistically significant

difference ($P = 0.0065$). According to these findings, both males and females in Group A experienced much greater treatment efficacy than those in Group B, with the difference being more noticeable for males.

Stratification of Efficacy by Duration of Symptoms

Table 10 presents the stratification of treatment efficacy regarding the duration of symptoms in

Groups A and B, each with 38 participants. Among patients with symptoms lasting **4–6 months**, 22 patients and 18 patients in Groups A and B respectively showed efficacy, with a statistical significant difference ($P = 0.0006$). However, among those with symptoms lasting **more than 6 months**, there was no discernible difference in the efficacy of the two patients in Group B and the eight patients in Group A ($P = 0.3781$). These findings suggest that treatment efficacy was significantly better in Group A for patients with symptom duration of **4–6 months**, however, there was no statistically significant difference in efficacy between the groups for those whose symptoms persisted for more than six months.

Stratification of Efficacy by BMI

Table 11 presents the stratification of treatment efficacy based on **BMI (kg/m^2)** in 38 individuals each in Groups A and B. Among patients with a **BMI ≤ 27** , There was no discernible difference in the efficacy of the 10 and 6 patients in Groups A and B respectively ($P = 0.7743$). However, among those with a **BMI > 27** , Efficacy was observed in 14 patients in group B and 20 in group A, with a P value = 0.0002, indicating a statistically significant difference. These findings suggest that while a BMI ≤ 27 did not significantly impact treatment efficacy, a higher BMI (> 27) was associated with a significant difference in efficacy, favoring Group A.

Table 11: Efficacy stratification based on body mass index.

BMI (kg/m^2)	Group A (n=38) Efficacy		Group B (n=38) Efficacy		P value
	Yes	No	Yes	No	
≤ 27	10	03	06	05	0.7743
> 27	20	05	14	13	0.0002

Stratification of Efficacy by Residence (Urban/Rural)

Table 10: Efficacy stratification according to symptom duration.

Duration of symptoms	Group A (n=38) Efficacy		Group B (n=38) Efficacy		P Value
	Yes	No	Yes	No	
4-6 months	22	07	18	16	0.0006
>6 months	08	01	02	02	0.3781

Table 12 presents the stratification of treatment efficacy based on the place of living in both Groups A and B, each with 38 participants. Among rural residents, Efficacy was observed in 10 patients in Group B and 16 in Group A, with not a significant variation (P value = 0.6384). However, among urban residents, A statistically significant difference ($P = 0.0001$) was noted, with effectiveness found in 10 patients in Group B and 14 patients in Group A. These results suggest that while the place of living had little impact on treatment response in rural patients, a significant difference in efficacy was observed among urban patients, favoring Group A.

Table 12: Stratification of efficacy according to residence.

Place of Living	Group A (n=38) Efficacy		Group B (n=38) Efficacy		P Value
	Yes	No	Yes	No	
Rural	16	05	10	09	0.6384
Urban	14	03	10	09	0.0001

Stratification of Efficacy by Diabetes Mellitus

Table 13 presents the stratification of treatment efficacy concerning diabetes mellitus (DM) in both Groups A and B, each with 38 participants. Among patients with DM, efficacy was observed in 8 patients in Group B and 9 in Group A, with no discernible difference ($P = 0.4351$). However, with

21 patients in Group A and 12 in Group B, there was a statistically significant difference ($P = 0.0006$) in the effectiveness of treatment between non-diabetic patients. These findings suggest that treatment efficacy was significantly better in non-diabetic patients, particularly in Group A, while diabetes was associated with a reduced and statistically insignificant difference in treatment. Response.

Stratification of Efficacy by Baseline Pain Score

Table 15 presents the stratification of treatment efficacy based on baseline pain scores in **Groups A and B**, each with 38 participants. Among those with a baseline pain score of ≤ 6 , efficacy was observed in nine patients in Group B and seventeen in Group A; there was no discernible difference ($P = 0.4005$). However, for those with a pain score > 6 , efficacy was observed in 13 and 11 patients in Group A and B respectively with

$P = 0.0001$, indicating a statistically significant difference. This suggests that while higher baseline pain scores were linked to decreased efficacy in Group B, treatment efficacy was more consistent in Group A.

DISCUSSION

Debilitating pain and discomfort may result from a herniation of the lumbar disc. Lumbar discectomy is the primary surgical procedure for treating a herniated disc in the absence of spondylolisthesis. Two Medicare patients out of every 1000 will have a lumbar laminectomy, either with or without a discectomy.¹⁴ Radicular pain can persist in certain patients even after discectomy. After discectomy, several surgeons use intraoperative epidural steroids over the exposed dura and/or nerve root to reduce postoperative

Table 14: Efficacy stratification concerning DM.

DM	Group A (n=38) Efficacy		Group B (n=38) Efficacy		P Value
	Yes	No	Yes	No	
Yes	09	02	08	07	0.4351
No	21	06	12	11	0.0006

Table 15: Efficacy stratification in relation to baseline pain score.

Baseline Pain Score	Group A (n=38) Efficacy		Group B (n=38) Efficacy		P-value
	Yes	No	Yes	No	
≤ 6	17	05	09	08	0.4005
> 6	13	03	11	10	0.0001

discomfort. The usage of intraoperative epidural steroids varies greatly among surgeons. According to a 2009 study conducted in Canada, Epidural steroids were commonly used after surgery by 49% of surgeons.¹⁵ Two reviews on the use of epidural steroids following lumbar spine discectomy focused primarily on functional outcomes, including postoperative hospital stay and pain relief.^{16,17}

This study compares the efficacy of bupivacaine plus corticosteroid and bupivacaine used during lumbar disc surgery. With a range of 25 to 65 years, the study's mean age was 42.76 ± 10.31 years. Patients in group A were 43.08 ± 10.50 years old on average, whereas those in group B were 42.11 ± 10.22 years old. 45 patients, or the majority, were between the ages of 25 and 45 (59.21%). 52 (68.42%) of the 76 patients were men, and 24 (31.58%) were women,

giving a male-to-female ratio of 2.16:1. The effectiveness of peri-operative corticosteroid plus bupivacaine in lumbar disc disease surgery was 30 (78.95%) in my study, whereas the bupivacaine group alone was 20 (52.63%), with a p-value of 0.016. During lumbar disc disease surgery, the combined peri-operative Bupivacaine with corticosteroid group showed 72.0% efficacy, while the bupivacaine group alone showed 44.0%.¹³

In comparison to a placebo group, A study discovered that following lumbar laminectomy, wound infiltration with 30 mL of 0.375% bupivacaine greatly reduced postoperative pain. In contrast to just 11 out of 24 patients who got bupivacaine, all 21 placebo users needed analgesics within the first nine hours after surgery ($P < 0.001$).¹⁸ In another trial, after lumbar discectomy, a 10-ml injection of 0.5% bupivacaine into the incision led to a longer duration of analgesia and lower pain scores.¹⁹ Before wound closure following lumbar laminectomy, a different study examined the infusion of 0.25% bupivacaine and 0.25% ropivacaine into the skin and paraspinal muscle. The mean time to first demand for rescue analgesia was found to be considerably longer in the bupivacaine group than in the ropivacaine or control groups.²⁰ When ropivacaine was continuously injected into wounds in lumbar arthrodesis patients, It was linked to reduced pain thresholds and a lower need for analgesics than a placebo.²¹ A similar experiment of wound injection using 20 milliliters of bupivacaine (0.25%) demonstrated similar better postoperative pain relief in patients undergoing lumbar spine laminectomy as compared to a placebo.²²

It is known that corticosteroids work as analgesics by binding to glucocorticoid receptors on various cells.²³ Since it impacts the solitary Schwann cell sheath that covers the nociceptor C fibers.²⁴ They work through potassium channels rather than blocking the Na channels found along the unmyelinated fibers.²⁵ Thus, dexamethasone and bupivacaine both act on nociceptor fibers, but

through two distinct ways. Blocking C fibers will prevent pain from being transmitted, resulting in a preventative analgesic effect.

Mack et al,²⁶ claimed that in patients undergoing microsurgery for lumbar laminectomy, Steroid infiltration or local anesthetics by themselves do not reduce post-operative discomfort and the need for opioids. In their investigation, they administered 0.25% bupivacaine in a 15 ml volume intravenously to the paraspinal muscles and ketorolac on the wound site.

Yorukoglu et al,²⁷ compared bupivacaine infusion on the wound site along with low-dose intrathecal and epidural morphine to relieve pain during lumbar disc surgeries. They discovered that the morphine group had a lower meperidine requirement during the first six hours after surgery, while all groups had a similar meperidine requirement during the first twenty-four hours. The fact that the control group (20%) required more analgesics indicated that using intravenous PCA to extend the analgesia over the first 24 hours could result in a less expensive treatment choice. Out of all the groups, the bupivacaine-methylprednisolone group required less morphine.

Glasser et al,²⁸ gave the first group IV Depo-Medrol® 250 mg and IV Depo-Medrol® 160mg before and after the procedure. Additionally, 30 mL of 0.25% bupivacaine was administered to the paravertebral muscles and subcutaneously. After that, they applied an autologous fat graft to the damaged nerve that had been soaked in 80 mg of methylprednisolone. 32 patients participated in the trial. Just before the procedure, they gave the second group's paravertebral muscles and subcutaneous tissue 30 milliliters of 0.25% bupivacaine, and before the skin incision, they gave the control group's subcutaneous tissue 10 milliliters of 0.5% lidocaine. The postoperative pain levels of the study group patients were evaluated at 24-hour, one-week, and one-month intervals throughout

the postoperative period, and individuals in the control group received a placebo. While no palliation was possible for patients receiving a placebo, 44% of patients receiving systemic corticosteroids plus local bupivacaine experienced full palliation after the post-operative 24-hour period, compared to 14% of patients receiving bupivacaine alone. After a month, there was no discernible difference between the groups. However, they found that patients who received a combination of corticosteroids and bupivacaine had better levels of patient satisfaction.

While the duration of meaningful relief varies, a recent systematic review found that dexamethasone in combination with local anesthetic considerably lowers the VAS score and analgesic use.²⁹ Epidural steroids act to prolong the analgesic impact of local anesthetics and minimize postoperative pain by reducing inflammation at the nerve roots. In perioperative lumbar spine surgery, several randomized experiments have demonstrated the benefits of locally injected epidural methylprednisolone.³⁰⁻³² However, the analgesic efficacy of dexamethasone as a laminectomy surgery adjuvant to epidural levobupivacaine has not been studied before.

Chadduk et al,³³ applied fat tissue soaked in 40 mg methylprednisolone to the wound site after injecting 0.25% bupivacaine or 40 mL saline to the paravertebral muscle during the closure of the wound. The study involved 50 participants. When the Visual Analogue Score (VAS) and four-point pain measurements were utilized to assess patients' pain regimens at 3, 12, and 24 hours, no significant differences were seen. The fact that the participants in the control group received methylprednisolone supports the notion that administering steroids to the epidural area is essential for treating post-operative pain.

Similar outcomes were noted in a trial in which bupivacaine and methylprednisolone were injected at the surgical site during an open discectomy.³⁰ In a study comparing bupivacaine + An autogenous fat piece soaked in

methylprednisolone on the nerve root after the procedure, bupivacaine by itself was found to be insufficient in reducing postoperative pain following lumbar decompression.³¹ Perioperative corticosteroids, such as 250 mg intravenous solumedrol, 160 mg of depomedrol intramuscularly, and an 80 mg depomedrol-soaked free fat transplant applied to the dural sac, were found to improve recovery time and hospital stay for microscopic disc surgery.³²

CONCLUSION

This study concluded that the efficacy of the use of corticosteroids and bupivacaine during surgery is higher as compared to bupivacaine alone in lumbar disc disease surgery. So, we recommend that perioperative use of bupivacain and corticosteroids should be used in every patient who will undergo lumbar disc disease surgery to reduce post-operative pain.

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Additional Information

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AUTHOR CONTRIBUTIONS

S. No.	Author's Full Name	Intellectual Contribution to Paper in Terms of
1	Amer Zaman & Bilal Ahmad	Study design, Methodology, and Paper writing.
2	Nafees Ahmad Khan & Ibrahim	Data Calculation and Data Analysis.
3	Ibrahim & Amer Zaman	Interpretation of Results.
4	Bilal Ahmad	Statistical Analysis.

5	Nazia Afzal & Syed Arif Hussain	Literature Review and Quality Insurer.
6	Nazia Afzal & Amer Zaman	Study design, Methodology, and Paper writing.