https://doi.org/10.29309/TPMJ/2026.33.11.10485 www.theprofesional.com

ORIGINAL ARTICLE

The Analgesic effects of Gabapentin after Total Abdominal Hysterectomy.

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ABSTRACT… Objective: To assess the effectiveness of Gabapentin in reducing postoperative pain after total abdominal hysterectomy. **Study Design:** Cross-sectional Observational study. **Setting:** Department of Anesthesiology and Gynecology/ Obstetrics, Taj Medical Complex, Karachi, Pakistan. **Period:** September 15, 2024, to March 15, 2025. **Methods:** This study was conducted over six months using convenience sampling. It included 73 females between 35 and 65 years of age scheduled for elective total abdominal hysterectomy with or without salpingo-oophorectomy, and with American Society of Anesthesiologists I-II status. Patients received 1200 mg of Gabapentin orally two hours before surgery. Postoperative pain was assessed at multiple intervals up to 24 hours using the Visual Analog Scale (VAS). Side effects, such as nausea and respiratory issues, were also recorded. Data were analyzed with SPSS 23.0 using a paired-samples t-test to compare VAS pain scores, with $p<0.05$ set as the significance threshold. **Results:** The study found a mean age of 50.54 ± 8.06 years and a BMI of 31.13 ± 2.76 kg/m^2. Gabapentin provided effective pain relief in the first 4 hours (VAS: 0.30 ± 0.72 at 1 hour and 0.86 ± 1.15 at 4 hours), but pain increased significantly at 8 hours (2.38 ± 1.12) and peaked at 20 hours (5.12 ± 0.68). Heart rate rose from 82.61 ± 12.77 bpm at 1 hour to 92.60 ± 7.35 bpm at 20 hours, while systolic BP increased from 124.3 ± 11.71 mmHg to 134.05 ± 13.9 mmHg at 16 hours. Common side effects were headache (31, 42.5%) and nausea/vomiting (23, 31.5%), with no cases of respiratory depression. **Conclusion:** Gabapentin effectively reduced postoperative pain in the initial hours after total abdominal hysterectomy, but pain increased over time, suggesting the need for additional analgesics. It was generally well tolerated, with headache and nausea as the most common side effects.

Key words: Gabapentin, Postoperative Pain, Visual Analog Score.

Article Citation: Shahid N, Jamshad S, Rashid AM, Khan F, Kazim A. The Analgesic effects of Gabapentin after total Abdominal Hysterectomy. Professional Med J 2026; 33(11):2276-2283. https://doi.org/10.29309/TPMJ/2026.33.11.10485

INTRODUCTION

Hysterectomy is among the most frequently performed major surgeries in women. The laparoscopic technique is gaining popularity due to its benefits, including reduced postoperative pain, lower complication rates, faster recovery, and shorter hospital stays compared with open hysterectomy.[1,2] However, significant pain can still occur, especially in the early postoperative phase.[3,4] Recent literature has reviewed non-opioid pain management options for patients undergoing both vaginal and laparoscopic hysterectomy.[5]

Medicine is challenged with managing pain effectively while reducing opioid use. One strategy involves the combined use of non-opioid adjuvants for pain relief. Gabapentin, which binds to the α2δ subunit of voltage-dependent calcium channels, reduces calcium channel influx, thereby lowering excitatory neurotransmitter release and spinal sensitization.[6] Additionally, Gabapentin may stimulate the descending noradrenergic pain inhibition system, decrease microglial activation, and reduce the expression of pro-inflammatory cytokines.[6]

Administering Gabapentin in the perioperative period may lower both the occurrence and severity of postoperative pain for up to six months following otolaryngology, orthopedic, mastectomy, and abdominal or pelvic surgeries.[7] Professional guidelines recommend Gabapentin as part of a multimodal approach to pain management[8]; however, its effectiveness in this context has yielded mixed results, and standard practices vary across surgeries and hospitals nationwide.[9,10] Professional societies recommend using Gabapentin for effective acute pain management, as evidence suggests it helps reduce opioid needs.[8]

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Article received on: 17/03/2026
Date of revision: 02/05/2026
Accepted for publication: 27/05/2026

Systematic reviews and metaanalyses indicate that administering Gabapentin in the perioperative period reduces acute postoperative pain in humans undergoing surgeries, such as abdominal hysterectomy.[11,12] This has sparked interest in exploring Gabapentin's use in veterinary medicine. To assess a drug's analgesic effectiveness, it's essential to use reliable pain scoring systems. For cats, the Glasgow Composite Measure Pain Scale (rCMPS-F)[13] and the UNESP-Botucatu Multidimensional Composite Pain Scale (MCPS) have been recently employed.[14]

Gabapentin may lead to serious adverse effects such as suicidal thoughts, depression, Stevens-Johnson syndrome, anaphylaxis, angioedema, erythema multiforme, rhabdomyolysis, and withdrawal seizures or symptoms if stopped suddenly.[15] More commonly, Gabapentin may cause side effects like ataxia, dizziness, fatigue, drowsiness, fever, nystagmus, peripheral swelling, hostility, hyperactivity (in children), nausea, vomiting, tremors, weakness, double vision, diarrhea, dry mouth, infections, blurred vision, headaches, constipation, weight gain, unusual thoughts, memory loss, back pain, impotence, and depression. A study of adverse reactions reported to the FDA showed that Gabapentin, compared to duloxetine, was more frequently associated with withdrawal symptoms, auditory hallucinations, delusions, euphoria, ataxia, aggression, and substance use disorder.[16]

Effective postoperative pain control has been associated with improved outcomes, reduced opioid use, shorter hospital stays, and lower costs.[17,18] Multimodal analgesia is now the standard for managing postoperative pain, with gabapentinoids frequently included to help alleviate neuropathic pain.[19,20] Gabapentinoids, including Gabapentin and pregabalin, work by inhibiting central nervous system sensitization. Although Gabapentin and pregabalin share similar mechanisms and chemical structures, pregabalin is more potent and acts faster than Gabapentin.[21] Recently, high-quality evidence has confirmed the effectiveness and safety of gabapentinoids in managing neuropathic pain following spinal cord injury.[22,23]

Gabapentin, originally an anticonvulsant, has shown efficacy in managing neuropathic and postoperative pain by modulating calcium channels and reducing neuronal excitability. To evaluate the analgesic effects of Gabapentin on postoperative pain management in patients undergoing total abdominal hysterectomy, focusing on pain intensity, opioid consumption, and associated side effects during the early postoperative period. Therefore, this study aimed to assess improvements in gabapentin patient outcomes by enhancing overall pain control.

METHODS

This cross-sectional observational study was conducted at the Department of Anesthesiology and Gynecology/Obstetrics, Taj Medical Complex, Karachi, Pakistan, from September 15, 2024, till March 15, 2025, using a non-probability, convenience sampling technique, after obtaining ethical approval from the Ethical Review Committee of the concerned hospital. The study lasted about 6 months after the synopsis was approved. This study included 73 females between 35 to 65 years of age, admitted for elective total abdominal hysterectomy with or without salpingo-oophorectomy in the designated time period, and had ASA I-II (American Society of Anesthesiologists). Whereas, known allergy to opioids, asthmatic patients, who had systemic disease such as renal insufficiency, a history of peptic ulcer or bleeding diathesis, and who refused to participate, were excluded.

After obtaining ethical approval (Ref-HCM&D/656/2024, dated August 31st, 2024), patients were selected based on the inclusion criteria. Two hours before the hysterectomy, each patient was given 1200 mg of Gabapentin orally. During the surgery, a crystalloid infusion was administered via the parenteral route, and vital signs were continuously monitored before, during, and after the procedure. Postoperatively, patients were assessed for pain at multiple time points: immediately after surgery and at 1, 4, 8, 12, 16, 20, and 24 hours, using the Visual Analogue Scale (VAS) ranging from 0 (no pain) to 10 (worst pain). Side effects such as nausea, vomiting, respiratory depression, constipation, peripheral edema, headache, and diarrhea were also recorded.

Data was analyzed using SPSS version 23.0, with

quantitative variables presented as means and standard deviations, and qualitative variables as frequencies and percentages. A paired-samples t-test was used to test differences in heart rate, respiratory rate, blood pressure, and VAS pain scores at different time points, with p-values <0.05 considered statistically significant.

RESULTS

This study included 73 females using Gabapentin after hysterectomy and showed that the participants' mean age was 50.54 ± 8.06 years, with an average weight of 80.79 ± 10.39 kg and a mean height of 5.43 ± 0.14 feet. The mean BMI was 31.13 ± 2.76 kg/m^2, indicating a generally obese population. Baseline physiological parameters included a mean heart rate of 86.13 ± 9.04 beats/min, systolic blood pressure of 127.38 ± 12.77 mmHg, diastolic pressure of 77.72 ± 15.47 mmHg, and respiratory rate of 13.26 ± 1.85 breaths/min. Over the 24-hour postoperative period, heart rate increased gradually, from 82.61 ± 12.77 beats/min at 1 hour, peaking at 92.60 ± 7.35 beats/min at 20 hours, and then slightly declining to 88.50 ± 6.74 beats/min at 24 hours. Similarly, the respiratory rate increased over time, from 13.36 ± 1.82 breaths/min at 1 hour to 18.32 ± 21.53 breaths/min at 24 hours, with higher variability noted especially after 8 hours. Systolic blood pressure rose from 124.3 ± 11.71 mmHg at 1 hour to a maximum of 134.05 ± 13.9 mmHg at 16 hours, while diastolic pressure increased from 77.12 ± 13.64 mmHg at 1 hour to 85.72 ± 13.54 mmHg at 20 hours. Pain intensity, measured using the Visual Analog Scale (VAS), was minimal during the first four hours, with scores of 0.30 ± 0.72 at 1 hour and 0.86 ± 1.15 at 4 hours. Pain scores gradually increased, reaching 2.38 ± 1.12 at 8 hours and peaking at 5.12 ± 0.68 at 20 hours. A slight reduction was observed at 24 hours, with a mean VAS score of 4.83 ± 0.50 (Table-I).

The distribution of comorbidities, socioeconomic status, and side effects associated with Gabapentin use among the 73 female patients showed that most participants belonged to the middle socioeconomic class (49, 67.1%), followed by the low (16, 21.9%) and high (8, 11.0%) classes. Comorbidities such as hypertension were present in 46(63.0%) of patients, obesity in 25(34.2%), and diabetes in 19(26.0%). A history of other drug use was reported in 26(35.6%) of participants, while 8(11.0%) had a documented history of drug allergies. According to the American Society of Anesthesiologists (ASA) classification, 37 (50.7%) of the patients were classified as ASA II, 24 (32.9%) as ASA III, and 12 (16.4%) as ASA I. Regarding side effects, the most frequently reported adverse effect was headache, affecting 31(42.5%) of patients. Nausea and vomiting were experienced by 23 (31.5%) of the cohort, while diarrhea was reported in only 2 (2.7%). Importantly, no cases of respiratory depression were observed, as depicted in Table-II.

A comparison of heart and respiratory rates at various postoperative time points revealed significant temporal trends. The mean heart rate at 1 hour post-surgery was 82.61 ± 12.77 beats/min. Compared to this baseline, heart rate showed a progressive and statistically significant increase at later time points, including 8 hours (87.56 ± 7.86 bpm, $p < 0.001$), 12 hours (88.37 ± 7.03 bpm, $p < 0.001$), 16 hours (90.78 ± 10.60 bpm, $p < 0.001$), 20 hours (92.60 ± 7.35 bpm, $p < 0.001$), and 24 hours (88.50 ± 6.74 bpm, $p < 0.001$). However, the comparison between the 1-hour and 4-hour heart rates (80.71 ± 10.52 bpm) did not show a statistically significant difference ($p = 0.248$). For respiratory rate, the mean at 1 hour was 13.36 ± 1.82 breaths/minute. A substantial increase was noted by the 4-hour (13.02 ± 1.53 bpm, $p = 0.033$), while subsequent comparisons at 8, 12, 16, 20, and 24 hours showed higher mean values but were statistically insignificant ($p>0.05$), as depicted in Table-III.

The systolic blood pressure at 1 hour post-surgery was 124.3 ± 11.71 mmHg. No significant difference was observed at 4 hours (124.83 ± 9.53 mmHg; $p = 0.671$) and 12 hours (127.13 ± 12.94 mmHg; $p = 0.137$). However, significant increases were noted at 8 hours (129.47 ± 11.05 mmHg; $p < 0.001$), 16 hours (134.05 ± 13.9 mmHg; $p < 0.001$), 20 hours (133.69 ± 13.5 mmHg; $p < 0.001$), and 24 hours (131.09 ± 14.71 mmHg; $p = 0.003$), indicating a rising trend in systolic pressure over time. Similarly, diastolic blood pressure rose significantly at several time points compared to the 1-hour reading of 77.12 ± 13.64 mmHg. While the 4-hour value (76.61 ±

9.62 mmHg) showed no significant difference (p = 0.746), diastolic pressure was significantly elevated at 8 hours (82.97 ± 6.92 mmHg; p < 0.001), 12 hours (82.24 ± 12.64 mmHg; p = 0.022), 16 hours (85.30 ± 13.98 mmHg; p = 0.001), and 24 hours (81.90 ± 13.26 mmHg; p = 0.051). The mean VAS score at 1 hour was 0.30 ± 0.72, which significantly increased to 0.86 ± 1.15 at 4 hours, 2.38 ± 1.12 at 8 hours, 3.82 ± 1.07 at 12 hours, 4.82 ± 1.14 at 16 hours, and peaked at 5.12 ± 0.68 at 20 hours. After 24 hours, the score slightly decreased to 4.83 ± 0.50. All comparisons with the 1-hour baseline were highly significant (p < 0.001), as depicted in Table-IV.

TABLE-I

Demographic details and postoperative pain status in females using Gabapentin after abdominal hysterectomy (n=73).

Variables		Mean ± SD
Age (Years)		50.54±8.06
Weight (kg)		80.79 ±10.39
Height (Feet/Inches)		5.43±0.14
BMI (kg/m^2)		31.13±2.76
Heart Rate (beat/min)		86.13±9.04
Blood Pressure (mm of Hg)	Systolic	127.38±12.77
	Diastolic	77.72±15.47
Respiratory rate (breath/min)		13.26±1.85
Heart Rate (beat/min)	1 hour	82.61±12.77
	4 hour	80.71±10.52
	8 hour	87.56±7.86
	12 hour	88.37±7.03
	16 hour	90.78±10.60
	20 hour	92.60±7.35
	24 hour	88.50±6.74
Respiratory rate (breath/min)	1 hour	13.36±1.82
	4 hour	13.02±1.53
	8 hour	16.5 ±17.20
	12 hour	17.15±19.94
	16 hour	18.52±23.10
	20 hour	17.89±19.82
	24 hour	18.32±21.53
Blood Pressure (mm of Hg) Systolic	1 hour	124.3±11.71
	4 hour	124.83±9.53
	8 hour	129.47±11.05
	12 hour	127.13±12.94
	16 hour	134.05±13.9
	20 hour	133.69±13.5
	24 hour	131.09±14.71
Blood Pressure (mm of Hg) Diastolic	1 hour	77.12±13.64
	4 hour	76.61±9.62
	8 hour	82.97±6.92
	12 hour	82.24±12.64
	16 hour	85.30±13.98
	20 hour	85.72±13.54
	24 hour	81.90±13.26
VAS Score of Pain	1 hour	0.30±0.72
	4 hour	0.86±1.15
	8 hour	2.38±1.12
	12 hour	3.82±1.07
	16 hour	4.82±1.14
	20 hour	5.12±0.68
	24 hour	4.83 ±0.50

TABLE-II

The distribution of comorbidities and side effects associated with Gabapentin.

Variable		n	%
Socioeconomic Status	High	8	11.0
	Middle	49	67.1
	Low	16	21.9
Hypertension	Yes	46	63.0
	No	27	37.0
Obesity	Yes	25	34.2
	No	48	65.8
Diabetes	Yes	19	26.0
	No	54	74.0
Other Drug History	Yes	26	35.6
	No	47	64.4
Other Drug Allergy History	Yes	8	11.0
	No	65	89.0
ASA (American Society of Anesthesiologists) Status	I	12	16.4
	II	37	50.7
	III	24	32.9
Side effects Nausea/ Vomiting	Yes	23	31.5
	No	50	68.5
Diarrhea	Yes	2	2.7
	No	71	97.3
Headache	Yes	31	42.5
	No	42	57.5
Respiratory Depression	Yes	0	0.0
	No	73	100.0

DISCUSSION

Pain control following open hysterectomy has been a focus of research for many years. Due to Gabapentin's notable analgesic effects, it has frequently been administered for preemptive pain relief.[24] However, the link between gabapentin use and postoperative pain management after open hysterectomy remains debated. Therefore, this study aimed to evaluate the effectiveness of Gabapentin preemptive use in abdominal hysterectomy.

A systematic review and metaanalysis on women undergoing abdominal hysterectomy evaluated the effects of preemptive Gabapentin. The pooled data included 448 patients receiving Gabapentin and 443 in a control group.

TABLE-III

Comparison of Heart Rate and Respiratory Rate at different time intervals.

Variable		Mean ± SD	P-Value
Heart Rate (Beat/min)	1 hour	82.61±12.77	0.248
	4 hour	80.71±10.52	
	1 hour	82.61±12.77	<0.001
	8 hour	87.56±7.86	
	1 hour	82.61±12.77	<0.001
	12 hour	88.37±7.03	
	1 hour	82.61±12.77	<0.001
	16 hour	90.78±10.60	
	1 hour	82.61±12.77	<0.001
	20 hour	92.60±7.35	
	1 hour	82.61±12.77	<0.001
	24 hour	88.50±6.74	
Respiratory Rate (Breath/ min)	1 hour	13.36±1.82	0.033
	4 hour	13.02±1.53	
	1 hour	13.36±1.82	0.108
	8 hour	16.5 ±17.20	
	1 hour	13.36±1.82	0.103
	12 hour	17.15±19.94	
	1 hour	13.36±1.82	0.056
	16 hour	18.52±23.10	
	1 hour	13.36±1.82	0.051
	20 hour	17.89±19.82	
	1 hour	13.36±1.82	0.050
	24 hour	18.32±21.53	

Results showed a significant reduction in morphine use within 24 hours post-surgery, with doses dropping from 24.3-55.9 mg to 13.2-42.7 mg, and from 25.7-80 mg to 20.3-55 mg when Gabapentin was given before and after surgery. VAS pain scores also decreased. The gabapentin group experienced less nausea compared to the control group. Overall, preemptive Gabapentin effectively reduced postoperative pain, narcotic usage, and nausea and vomiting.[7] These findings were partially consistent with the present study results, which showed that nausea and vomiting were experienced by 23(31.5%) of the cohort. Initially, at 1 hour, the mean VAS score was very low (0.30 ± 0.72), reflecting minimal pain likely due to the preoperative Gabapentin. However, pain levels began to rise noticeably by 4 hours (0.86 ± 1.15), and this trend continued throughout the day, with a marked increase at 8 hours (2.38 ± 1.12) and 12 hours (3.82 ± 1.07), indicating the progressive onset of postoperative discomfort.

TABLE-IV

Comparison of blood pressure and VAS score of pain at different time intervals.

Variable			Mean ± SD	P-Value
Blood Pressure (mm of Hg)	Systolic	1 hour	124.3±11.71	0.671
		4 hour	124.83±9.53	
		1 hour	1243±11.71	<0.001
		8 hour	129.47±11.05	
		1 hour	124.3±11.71	0.137
		12 hour	127.13±12.94	
		1 hour	124.3±11.71	<0.001
		16 hour	134.05±13.9	
		1 hour	124.3±11.71	<0.001
		20 hour	133.69±13.5	
		1 hour	124.3±11.71	0.003
		24 hour	131.09±14.71	
	Diastolic	1 hour	77.12±13.64	0.746
		4 hour	76.61±9.62	
		1 hour	77.12±13.64	<0.001
		8 hour	82.97±6.92	
		1 hour	77.12±13.64	0.022
		12 hour	82.24±12.64	
		1 hour	77.12±13.64	0.001
		16 hour	85.30±13.98	
		1 hour	77.12±13.64	<0.001
		20 hour	85.72±13.54	
		1 hour	77.12±13.64	0.051
		24 hour	81.90±13.26	
VAS Score of Pain		1 hour	0.30±0.72	<0.001
		4 hour	0.86±1.15	
		1 hour	0.30±0.72	<0.001
		8 hour	2.38±1.12	
		1 hour	0.30±0.72	<0.001
		12 hour	3.82±1.07	
		1 hour	0.30±0.72	<0.001
		16 hour	4.82±1.14	
		1 hour	0.30±0.72	<0.001
		20 hour	5.12±0.68	
		1 hour	0.30±0.72	<0.001
		24 hour	4.83 ±0.50	

Similarly, another metaanalysis of randomized controlled trials compared Gabapentin and placebo in open hysterectomy, focusing on postoperative opioid use, pain scores, and adverse effects. Findings showed that patients receiving Gabapentin required significantly fewer opioids within 24 hours and reported lower pain scores on the VAS at 4, 12, and 24 hours post-surgery. Additionally, Gabapentin was associated with a lower incidence of nausea

and vomiting and higher patient satisfaction than placebo. Overall, Gabapentin effectively reduced opioid consumption, pain levels, and specific side effects after open hysterectomy.[24] These findings partially supported the present study and revealed that pain levels began to increase notably after 4 hours and continued to rise steadily through 8, 12, and 16 hours, indicating the progressive return of pain as the effect of anesthesia wore off. A slight decrease was observed at 24 hours (4.83 ± 0.50), suggesting the beginning of pain relief, possibly due to analgesic administration. As for side effects, headache (31/42.5%) was the most commonly reported, followed by nausea (23/31.5%), while diarrhea was reported in only 2 (2.7%). Importantly, no cases of respiratory depression were observed.

Likewise, respiratory depression has been observed in patients given preoperative Gabapentin, with older adults and those on multimodal pain management showing an elevated risk.[25,26] Older adults and individuals with additional medical conditions who were not included in other trials may be more prone to gabapentin-related side effects (such as drowsiness, ataxia, sedation, and dizziness). They may require adjusted, lower doses.[27,28] The present study was inconsistent with the above-cited studies. It revealed that 31 (42.5%) of the patients experienced headaches, 23 (31.5%) experienced nausea and vomiting, and only 2 (2.7%) reported diarrhea. Notably, respiratory depression was not observed in any case.

Interestingly, Verret et al. conducted a metaanalysis of 281 trials to evaluate the efficacy and safety of gabapentinoids in managing postoperative pain and reducing opioid use after surgery. Their findings indicated that perioperative gabapentinoids provide no clinically meaningful pain relief, do not help prevent chronic postoperative pain, and are associated with an increased risk of adverse effects.[29] Similarly, a study of spine surgery patients found that a preoperative dose of 900 mg gabapentin was associated with the lowest VAS pain scores, with no difference in adverse event rates across dosages. This suggests that, among the evaluated dosages, gabapentinoids do not carry a higher risk of side effects compared to other analgesics.[30] Nevertheless, caution remains warranted due to the potential for adverse effects such as sedation and respiratory depression, as reported in studies by Peene et al. and Waelkens et al.[31,32] These findings were inconsistent with the above-reported research. They showed that the pain began to increase noticeably after 4 hours and continued to rise steadily at 8, 12, and 16 hours, reflecting the diminishing effect of anesthesia and the onset of postoperative discomfort. A slight reduction in pain was observed at 24 hours (4.83 ± 0.50), likely due to the impact of pain management strategies. In terms of side effects, headache was the most commonly reported, followed by nausea and vomiting. No cases of respiratory depression were observed.

This study had a few limitations. This study's sample size was limited to 73 females, limiting the generalizability of the findings. Additionally, the absence of a control group makes it difficult to attribute all observed effects solely to Gabapentin. The reliance on subjective pain scores may introduce variability in pain assessment. Future studies should include larger, more diverse samples and a control group to better assess Gabapentin's effectiveness. Incorporating objective pain and recovery metrics, along with monitoring over extended postoperative periods, could provide a more comprehensive understanding of Gabapentin's impact on postsurgical recovery.

CONCLUSION

This study concluded that Gabapentin provided effective early postoperative pain relief in patients after abdominal hysterectomy, with minimal pain in the first few hours. However, pain intensity increased significantly over time, indicating the need for additional analgesic support. Heart rate, blood pressure, and respiratory rate also gradually increased over 24 hours. Gabapentin was generally well tolerated, with headache and nausea being the most common side effects. These findings suggest that Gabapentin may provide early postoperative pain relief but may require adjunctive analgesia for sustained pain control.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

SOURCE OF FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Nida Shahid:** Study conception, patient recruitment, drafting.
2	**Saira Jamshad:** Data collection.
3	**Asim Masroor Rashid:** Critical revisions.
4	**Farah Khan:** Data entry.
5	**Atia Kazim:** Data analysis.