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Efficacy of Intrathecal Dexmedetomidine on Post-operative Pain Relief in General Surgical Cases

Muhammad Salman Maqbool, Fahad Zubair, Kainat Irshad, Hozaifa Iqbal

Abstract

Objectives: To compare the efficacy of intrathecal bupivacaine combined with dexmedetomidine versus bupivacaine alone in providing postoperative analgesia for patients undergoing general surgical procedures under spinal anesthesia.

Study design and setting: A single-blind interventional study was conducted by the Anesthesiology Department at Farooq Hospital (ASMC), Rawalpindi, from January 16th to December 25, 2024.

Methodology: After ethical approval from the Research Advisory Committee of Akhtar Saeed Medical College, Rawalpindi,60 patients (placed in ASA classes I-III) undergoing elective general surgical cases in spinal block were enrolled and randomized into two groups (by lottery method). Group A received intrathecal 1.5 mL hyperbaric bupivacaine 0.75% (15 mg) alone, while Group B received the same dose of bupivacaine with 5microgram dexmedetomidine. Standard ASA monitoring, preloading with isotonic crystalloids, and spinal anaesthesia at the L3–L4 level were employed using a 26-G spinal needle. Hemodynamic parameters, adverse effects and need for rescue analgesia were documented. Statistical analysis done by SPSS v26(with $p<0.05$ as significant).

Results: Demographic parameters (age, weight, BMI) were comparable between groups. Mean postoperative analgesia duration was significantly longer in the dexmedetomidine group (20.18 ± 3.48 h) compared to group B (11.78 ±1.64 h, $p < 0.05$). The dexmedetomidine group required fewer rescue opioid doses, reflecting an opioid-sparing effect.

Conclusions: Intrathecal dexmedetomidine to bupivacaine in spinal anaesthesia for general surgical cases significantly prolongs the postoperative analgesia period.

Keywords: Bupivacaine, Bromage scale, Dexmedetomidine, Lumbar puncture, Postoperative rescue analgesia

How to cite this Article:
Maqbool MS, Zubair F, Irshad K, Iqbal H. Efficacy of Intrathecal Dexmedetomidine on Post-operative Pain Relief in General Surgical Cases. J Bahria Uni Med Dental Coll. 2026;16(1):74-80 DOI: https://doi.org/10.51985/JBUMDC2025705

INTRODUCTION

Spinal anaesthesia is one of the most frequently used anaesthetic approaches applied during surgery, and it provides surgical anaesthesia for lower abdominal, urological, cesarean sections, and orthopaedic surgeries, compared to general anaesthesia. It is a type of regional block in which a local anaesthetic drug is administered in the subarachnoid space.

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Received: 03-09-2025
1st Revision: 27-10-2025
2nd Revision: 29-11-2025
Accepted: 15-12-2025

Spinal anaesthesia results in a block of autonomic, motor, and sensory function in the lower body.[1] General contraindications to spinal anaesthesia include the patient's refusal, coagulopathy, infection at the site of drug administration, stenotic valvular disease and increased intracranial pressure.[1] Most common injection site is either L3-4 or L4-5 interspace, and the local anaesthetic agent most commonly employed is bupivacaine; others include lidocaine, procaine, tetracaine and ropivacaine.[2]

Bupivacaine is an amide-type local anaesthetic that works by blocking voltage-gated sodium channels that propagate action potentials in nerve terminals.[2]Bupivacaine may be used alone, or other drugs can be added as adjuvants, like sufentanil, dexmedetomidine, fentanyl, epinephrine, morphine, midazolam, dexamethasone and clonidine, are added to enhance the duration of block density and for postoperative analgesia.[2]The commonly used agent as an adjunct is dexmedetomidine.[3]Dexmedetomidine is a new drug that has specificity in the targets: presynaptic alpha-2 adrenoreceptors located in the dorsal horn of the spinal cord, which causes analgesia by means of changing the intensity of synthesis of neurotransmitters.[3]

Dexmedetomidine is also administered as premedication and as an accessory in routine general anaesthesia regimen,

it acts by binding to adrenoceptors at the locus ceruleus level, and it works as an analgesic, anxiolytic and as a sedative agent.[4] These effects may be the effect of either systemic absorption/ vascular redistribution to higher brain areas, or as a result of cephalad migration in intrathecal dexmedetomidine adjuvant use.[5] Thus, dexmedetomidine administration intravenously or intrathecally prolongs spinal anaesthesia and enhances postoperative analgesia.[6]

The effectiveness of Dexmedetomidine has been noted to provide relief of postoperative pain when combined with Bupivacaine in general surgical patients. Its use with Bupivacaine also curtails the possibility of neurotoxicity.[5] It causes dose-related sedation, anxiolysis, and analgesia (spinal and supraspinal sites) with no respiratory depression, alpha-2 agonists are found to decrease anaesthetic needs, and due to their sympatholytic action, they provide hemodynamic stability during the intraoperative period.[4]The Dexmedetomidine has been further evaluated in the context of sedation and treating delirium in ventilated patients in intensive care units, as well as for procedural sedation and as an adjunct infusion during general anaesthesia, which controls emergence agitation and prevents postoperative delirium and cognitive dysfunction.[7] In a study conducted by Ayesha Shahid and colleagues in monitoring hemodynamic stability(pulse, blood pressure) for up to five minutes following endotracheal intubation, comparing lignocaine with dexmedetomidine, they noted intravenous dexmedetomidine superiority in comparison to lignocaine in the prevention of laryngoscopy pressor response.[8]

In another randomized controlled trial by Ayesha and colleagues in parturients undergoing cesarean delivery using bupivacaine 0.5% 12mg alone and with dexmedetomidine 4ug observed onset of pain postoperatively they noted that mean onset of pain in dexmedetomidine group was 364±35.6 minutes in comparison to 179 minutes in plain bupivacaine group. They concluded that dexmedetomidine as adjuvant had better efficacy in controlling postoperative pain in first six hours.[9]

Dexmedetomidine also has good analgesia with the least drug interaction. Administration of dexmedetomidine decreases the risk of shivering in postoperative anaesthetized patients. A study by Riaz, Iqbal & Salman Haider has found that this combination improves pain relief, prolongs analgesic effect, decreases opioid intake, and increases patient satisfaction. One of the main advantages of dexmedetomidine is it can increase analgesic duration. Only patients receiving bupivacaine usually need rescue analgesics at about 7 hours post-subarachnoid block. But after the addition of dexmedetomidine, the analgesic duration increases considerably, usually lasting 9 hours or longer.[10]

The postoperative pain is a major surgical complication, which can lead to morbidity, longer hospital stays, financial burden, and various complications, including respiratory in addition to psychological complications. In a study on postoperative pain outcome after surgery, they inferred that almost half of the patients suffered moderate to severe intensity of pain with a high rate of opioid consumption.[11]

The safety profile of this combination is also excellent. Notably, dexmedetomidine does not result in a higher rate of side effects like hypotension or bradycardia; furthermore, patients administered dexmedetomidine have a lower rate of side effects. Neonatal outcomes of health are unchanged, further attesting to the safety of this combination for surgical patients [8,9,10]

Clinical trials uniformly show that the addition of dexmedetomidine extends postoperative analgesic duration by about 2 to 3 hours, postpones the first demand for rescue analgesics, and dramatically minimizes pain score intensity as well as total opioid use over the initial 24 hours following surgery.[4] The reason why it is effective is that its mechanism of action as a selective alpha-2-adrenergic agonist increases spinal analgesia by blocking pain transmission at the dorsal horn and amplifying the action of local anaesthetics. At therapeutic doses (usually 5 microgram), intrathecal dexmedetomidine also possesses an excellent safety profile with low chances of hemodynamic instability or side effects like nausea, vomiting, or shivering. But higher doses have the risk of causing transient bradycardia or hypotension. A second significant advantage of dexmedetomidine is its opioid-sparing activity. Patients receiving this combination receive fewer rescue doses of opioids after the operation than those in the bupivacaine-alone group.[3,4] This decrease in opioid intake serves to reduce opioid-related side effects and results in better overall recovery. Additionally, maternal satisfaction is greater in the dexmedetomidine group with sustained pain relief and less need for supplementary analgesics. The enhanced comfort and less use of opioids allow for a generally improved postoperative course.[3]

It is imperative from the above discussion that adequate control of post-operative surgical pain is a cornerstone in patient management. The rationale for the study conducted was combining dexmedetomidine with bupivacaine intrathecally, to assess its effectiveness on improving the quality of analgesia post-operatively in patients undergoing general surgical procedures without openly increasing adverse effects, in comparison to Bupivacaine alone. As fewer studies have been conducted involving general surgical procedures (under sub-arachnoid block), this study combines orthopaedic, urological, gynaecological and infra-umbilical general surgical procedures in a teaching private hospital. Primary outcomes included postoperative analgesia duration and opioid requirement; secondary outcomes evaluated hemodynamic stability and incidence of adverse effects. This study will assess a method to improve post-operative analgesia following a subarachnoid block.

METHODOLOGY

The Research Advisory Committee and Institutional Review Board, Akhter Saeed Medical College, Private Limited, Rawalpindi Campus, Main Murree Expressway, Bahria Golf City, Rawalpindi, endorsement was taken vide letter number (RAC-14-6-23),15th June 23, for this study. Statistical Kingdom calculator was used for calculation of sample size using t-distribution; with a margin of error; 0.04, a confidence level; 0.96 (Z-score of 2.29), and a standard deviation of 0.29, resulting in 60 patients. A total of 60 patients, planned for elective infra-umbilical surgical procedures randomly divided into 2 groups by employing computer-generated divisions within the electively placed surgical case lists, were divided(n=30) in each study group. Participants were broadly informed about the study and provided consent in written form before registration. The study duration was ten months and was convened at Farooq Hospital, Rawalpindi, from 16th Jan 2024 to 25th December 2024. The inclusion criteria of this single-blind interventional study were piloted with random sampling methodology for both genders, for elective surgery under sub-arachnoid block incorporating departments of surgery/ urology/orthopaedics and gynaecological patients (aged 28 to 55 years), and belonging to ASA class I and II or ASA III(medically controlled co-morbid states) were included in accordance with the foregoing conducted studies.[9,10,12] The exclusion criteria included, as per various study guidelines included patients with cardiac disease, liver and kidney disease, coagulopathy, emergency procedures and those who did not give consent.[9,10] Proper preoperative informed verbal consent was done before the surgery, and written informed consent was obtained after explaining the procedure to the patient. Patients were also informed about the procedure to be performed, the technique being employed, and the risks and possible benefits, in clear terms so that they could make a better decision regarding participation in research. In both groups, patients were prepared as per ASA guidelines. Patients were unaware of the group allocation. In both groups, patients were prepared as per ASA guidelines.[12] However, after being taken into the main operating theatre, emergency drugs were prepared, monitors were attached (electrocardiograph, capnograph, pulse oximetry and non-invasive blood pressure), an intravenous large-bore line was inserted, and patients were preloaded with crystalloid solutions, which was followed by a spinal block at L3–L4 interspace with a 26-G Quincke spinal needle in both groups. A consultant anesthesiologist performing spinal block also participated in the research, was not aware of group allocation, whereas another senior registrar anesthesiologist prepared medication to be placed intrathecally and was not part of the research outcome and also did randomization of research patients into 2 groups, thus endorsing unbiased handling of the study. In group A, 1.5 mL hyperbaric bupivacaine 0.75% 15 mg was used, and in group B, 1.5 mL hyperbaric bupivacaine 0.75% 15 mg plus 5 microgram dexmedetomidine medication was used in the study. In both research groups, hemodynamic parameters (systolic, diastolic, heart rate, SpO2) were recorded preoperatively and every 5 minutes for 50 minutes post-block. Adverse hemodynamic effects (hypotension, bradycardia), use of anti-cholinergic and vasopressors noted. The hemodynamic monitoring was continued, and the need for rescue analgesia was documented in the Post-Anaesthesia Care Unit. Hypotension was defined as systolic blood pressure of less than 90 mmHg and treated by phenylephrine 50 microgram increments. Bradycardia was defined as a heart rate of less than 50 beats per minute, and was treated with atropine 0.01 mg/kg. Supplemental oxygen was given via face mask to all patients to maintain O2 saturation of about 98%. Sedation scores in Group A, but specifically in B, were noted because of the sedative properties of dexmedetomidine in the intraoperative and postoperative period. All the patient data was noted on the anaesthesia proforma, and the confidentiality of the patients was ensured. The Paired sample t-test was used with a confidence interval of 95% (to seek significance) for analysis of the study variables in both groups, with a p-value greater than 0.05. SPSS v.26 was used for statistical analysis.

RESULTS

The average age in years of bupivacaine patients (group A) is 42.12 ± 13.40, and that of the patients taking bupivacaine with dexmedetomidine (group B) is 42.70 ± 11.09. The average weight of bupivacaine patients was 75.32 ± 7.43 as compared to 73.51 ± 6.85 in patients using bupivacaine plus dexmedetomidine. The average Body Mass Index (BMI) between the patients of group A was 24.13 ± 3.11, and the mean BMI that corresponded to the patients of group B was 23.87 ± 2.84. The average postoperative analgesia in the bupivacaine group was 12.57 ± 2.53 as compared to the average postoperative analgesia in the bupivacaine plus dexmedetomidine group of 20.18 ± 3.48. Zero per cent are the Bupivacaine patients were diagnosed with bradycardia, although non-bradycardia individuals were hundred percent (100%) whereas bupivacaine plus dexmedetomidine patients, owing to bradycardia were 16.7, and non-bradycardia individuals were 85.5. In bupivacaine, 5.4 of patients had hypotension and 93.7 had no hypotension whereas in the case of bupivacaine plus dexmedetomidine, the same was 25% and 75 % respectively. Among the patients of bupivacaine, 90.6 % did not have nausea and 9.4 % had nausea, but with bupivacaine plus dexmedetomidine, 6.4 had nausea and 93.7 were without nausea. In bupivacaine, 6.4 per cent of the patients vomited as compared to 93.7 percent of the patients vomited although in dexmedetomidine plus bupivacaine, there were 3.1 percent and 96.9 percent of the patients who vomited. The ASA grades are depicted in Table 1. The analgesic medications used postoperatively are shown in Table 2. Statistical analysis revealed that there was a marked improvement in relative frequency of

bradycardia in the Bupivacaine plus Dexmedetomidine group 2, when compared to the Bupivacaine alone group 1 with a "p-value of 0.026* and the Lavene test was applied for analysis of variances and the p-value was less than .05(0.228*) showed a significant statistical difference between variances as presented in Table 3. The hemodynamic variables of both groups are presented graphically in Figure 1.

DISCUSSION

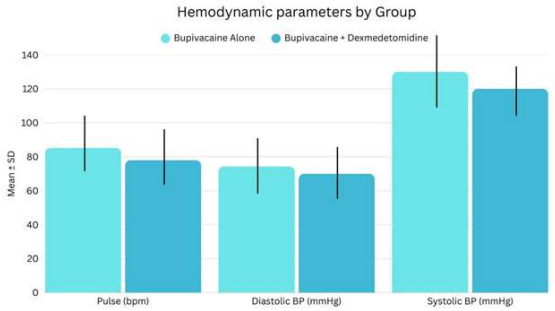
The addition of adjuvants to local anesthetics has gained significant attention these include fentanyl, midazolam, ketamine, etc. but have shorter durations of analgesia, higher incidence of side effects such as pruritus, nausea, vomiting, and respiratory depression, and less consistent prolongation of sensory and motor block in comparison to dexmedetomidine.[13,14,15] A combination that has emerged with promising results is dexmedetomidine combined with bupivacaine, compared to bupivacaine alone.[3] This combination offers a range of clinical benefits as the current research studied postoperative pain following the use of a combination of dexmedetomidine and bupivacaine in spinal anesthesia in general surgical procedures. Dexmedetomidine is an extremely selective agonist, alpha-2-receptor with the property of being sedative, anxiolytic/analgesic. It has been demonstrated that when used as an adjuvant agent to local anesthetics in spinal anesthesia, dexmedetomidine enhances the action of the block by exerting effects both centrally and on the spinal cord as it holds potential in ensuring the best opioid-sparing effects which remain an important subject regarding perioperative care.[4] Bupivacaine, a long-acting amide local anesthetic, is commonly used for spinal anesthesia due to its effective sensory and motor blockade. However, its duration of analgesia, although longer than some other

Table 1: Demographic data (n=30)

Variables		Group A	Group B
ASA classes (frequency/percentage)	Class-1	20/75%	28/62%
	Class-2	9/22%	10/35%
	Class-3	1/2.5%	2/3%

Table 2: Postoperative analgesics data. (n=30)

		Group-A	Group-B
Post op analgesic Used N /%	Opioids	6 / 20%	3 /10%
	NSAIDS	24/80%	27/90%



local anesthetics, is still limited in the context of postoperative pain control.[2] The foundation for combining dexmedetomidine with bupivacaine in our study centers on prolonging and improving the quality of analgesia without significantly increasing adverse effects.

Clinical studies comparing the combination of dexmedetomidine and bupivacaine with bupivacaine alone consistently reveal that the addition of dexmedetomidine leads to a significant prolongation of postoperative analgesia.[1] Patients who receive this combination generally experience a longer duration of pain relief, often double the duration provided by bupivacaine alone. This extension in analgesia means that patients require their first dose of rescue analgesics much later in the postoperative period, ultimately reducing the frequency and total dose of opioid or other analgesic medications administered. Reducing opioid consumption is particularly beneficial in the current medical landscape, where minimizing opioid-related side effects and dependency is a priority, as in our study, fewer patients needed opioids in group B.

When considering patients' postoperative experience, those who receive dexmedetomidine in addition to bupivacaine report significantly lower pain scores across various postoperative time points. This consistent reduction in pain directly correlates with improved patient comfort and potentially quicker overall recovery, and reduces complications such as deep vein thrombosis or pulmonary issues. The lower pain scores and delayed need for additional analgesics contribute to higher satisfaction levels among patients receiving the combination therapy.

From a hemodynamic perspective, concerns often arise regarding the addition of potent adjuvants like

Table 3: Independent Sample t-test results. (n=30)

Variables			Group A	Group B
Bradycardia		Yes Count	0	5(0.026*)
		No Count	32	27
Post-operative analgesia duration	Levene's Test	variances assumed / not assumed	1.482	0.228*

*p < 0.05 is considered statistically significant.
**Calculated by the Independent Sample t-test

dexmedetomidine, given its sympatholytic effects that can potentially lead to bradycardia or hypotension. However, most clinical trials using standard intrathecal doses of dexmedetomidine, typically between 3 and 5 micrograms, demonstrate that while there may be mild decreases in heart rate and blood pressure, these changes are generally clinically insignificant and easily managed. The hemodynamic stability with this combination remains comparable to that observed with bupivacaine alone, which underscores its safety profile for use in a broad patient population.[4,8,9]

Nevertheless, a mild increase in sedation is a noted side effect of dexmedetomidine. This sedative effect is generally well-tolerated and not problematic for most patients; in fact, for some, it may be considered beneficial as it can alleviate perioperative anxiety and contribute to a smoother induction of anaesthesia. Importantly, the incidence of severe adverse effects such as respiratory depression or neurological complications has not been demonstrated to increase with the addition of intrathecal dexmedetomidine. Moreover, the combination has been found to reduce the occurrence of postoperative shivering, nausea, and vomiting the common complications of spinal anaesthesia, which further enhanced patient comfort.[1] From a practical clinical perspective, the dexmedetomidine-bupivacaine combination represents a cost-effective strategy to manage postoperative pain, reducing the reliance on systemic analgesics such as opioids or nonsteroidal anti-inflammatory drugs (NSAIDs), which have their own side effect profiles.[2] The longer duration of analgesia may also translate into shorter stays in recovery units and better allocation of healthcare resources. A meta-analysis study done on (randomized controlled trials), which used dexmedetomidine as an adjuvant to local anaesthetic agents, inferred that motor and sensory block duration was prolonged, along with post-operative analgesia duration. However, there was no significant statistical difference in the incidence of hypotension; they noted that bradycardia per-operatively was transient in nature and easily reversible with intravenous atropine.[16] Patients who receive this combination generally experience a longer duration of pain relief, often double the duration provided by bupivacaine alone.[17] These results were similar to our conducted study. Bradycardia incidence was higher with dexmedetomidine as stated in our study, whereas no significant differences were observed in nausea, vomiting, or other adverse effects, and all hemodynamic (blood pressure) changes were clinically manageable in both groups. As stated earlier that optimal post-operative pain control plays a role in faster recovery. In this context a study done by Thaku SK and colleagues noted that dexmedetomidine markedly extended post-operative analgesic duration. Additionally, extent of intrathecal sensory and motor block was not affected by dexmedetomidine in their study. Furthermore, more hemodynamic stability was not compromised with dexmedetomidine as adjunct.[18]Usage of dexmedetomidine together with bupivacaine increases the length of the postoperative analgesia and lowers opioid usage. In their study, the combination group had a mean analgesia time of 19.18 hours, whereas the single agent bupivacaine used in the other group had a mean analgesia time of 11.78 hours ($p < 0.05$). Patients in the dexmedetomidine group needed less opioid medication within the first 24 hours as well (20.69 mg vs. 10.88 mg in the bupivacaine-only group, $p < 0.05$). In spite of these advantages, the incidences of bradycardia and hypotension were more in the dexmedetomidine comparison group.[18]

In a triple-blind randomized study, assessing the analgesic effect of 0.5% bupivacaine noted that patients' pain perception on a numerical rating scale, duration of analgesic effect and post-op analgesics used. They noted that use of bupivacaine didn't have a superior analgesic value in comparison to placebo in regulating post-operative acute pain.[19]Similar results were inferred in our study. A systematic review study on sub-arachnoid dexmedetomidine as an adjuvant in elective surgical cases. They noted post-op analgesia duration, adverse effects(bradycardia, hypotension, post-op shivering, and nausea pointed out that post-op analgesic duration was prolonged, and had a lower visual analogue scale, nausea and shivering in comparison to placebo.[20]As regards recent advancement in use of centrally acting alpha-2 agonists(dexmedetomidine) in various other clinical settings, such as in the Emergency Department, a study done by Kevin Baumgartner and colleagues pointed out that dexmedetomidine can be used in selected clinical scenarios, as the hemodynamic effects(bradycardia, hypotension) do require medical treatment infrequently.[21]In another recent efficacy study of bupivacaine alone and with dexmedetomidine local wound infiltration at the end of abdominal surgeries after general anaesthesia, showed a marked useful difference in post-operative analgesia effect with the use of the latter combination.[22] A study done by Zulfiqar Ahmed and colleagues to assess clinical effects of dexmedetomidine across regional and general anaesthesia regimens as well as procedural sedation pointed out that it's highly efficacious in reducing general opioid requirement post-operatively, as well as having a stable hemodynamic effect(pulse and blood pressure) and thus good recovery outcome. Their study results were similar to ours, with less opioid requirement post-operatively.[23]

Another randomized, placebo-controlled study tested 60 patients with similar results, i.e. a considerable reduction in the postoperative morphine requirement in those administered with bupivacaine than in those who received ropivacaine ($p = 0.03$). The patients treated with bupivacaine were exposed to less pain during incision and less vomiting in the first six hours after surgery, along with a lower total number of pharmacological analgesia demands.[24]

Apart from prolonging analgesia, the dexmedetomidine-bupivacaine combination has been shown to hasten the onset

of both sensory and motor blockade. This faster onset can be highly advantageous in operative settings by allowing surgical procedures to commence sooner with adequate anaesthesia. In addition, the quality of the block is generally enhanced, displaying a more profound and reliable sensory and motor effect. This enhancement contributes to better intraoperative conditions and reduced patient discomfort during positioning or surgical manipulation.[25]

In summary, the evidence firmly supports the conclusion that the combination of dexmedetomidine and bupivacaine in spinal anaesthesia offers superior postoperative analgesia compared to bupivacaine alone. This superiority is reflected in a significantly prolonged duration of pain relief, faster onset and improved quality of sensory and motor blocks, lower pain scores, reduced need for rescue analgesics, and high patient satisfaction. The safety profile of the combination is acceptable, with stable hemodynamics and only mild sedation and other minor side effects reported. This makes dexmedetomidine an excellent adjunct to bupivacaine in providing enhanced postoperative analgesia in patients undergoing a variety of general surgical procedures under spinal anesthesia and be a valuable addition to multimodal analgesic strategies in surgical care.

Limitations of the study included a smaller sample size, and additional research is needed to confirm the results of our findings.

CONCLUSION

Dexmedetomidine, when added to bupivacaine as an adjuvant in Spinal anaesthesia in general surgical cases, increases the post-op duration of analgesia in comparison to bupivacaine alone.

Conflicts of interest: Nil

Source of Funding: Nil

Acknowledgement: Nil

Authors Contribution:
Muhammad Salman Maqbool: Concept & Design of Study, Drafting, Revisiting Critically, Data Collection & Analysis, Final Approval of version
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