J Med Sci 2025;45 (6):223-228
DOI: 10.4103/jmedsci.jmedsci_60_25

ORIGINAL ARTICLE

Effect of Hyperventilation Prior to CO_2 Insufflation in Laparoscopic Cholecystectomy: A Randomized Controlled Trial

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Background: Carbon dioxide (CO_2) insufflation during laparoscopic surgery may result in hemodynamic and ventilatory side effects, due to hypercarbia and elevated intra-abdominal pressure. Several techniques have been developed and evaluated to reduce these adverse effects. **Aim:** The aim of the study was to compare hemodynamic changes after controlled hyperventilation prior to CO_2 insufflation during laparoscopic cholecystectomy. **Methods:** Thirty patients scheduled for laparoscopic cholecystectomy were randomly divided into two groups. Group 1 patients were ventilated with a tidal volume (TV) of 8 mL/kg, 15 min before CO_2 insufflation. The respiratory rate (RR) was adjusted to maintain an end-tidal CO_2 ($EtCO_2$) of 31–35 mmHg. In Group 2 patients, the lungs were ventilated with a TV of 8 mL/kg 15 min before CO_2 insufflation. The RR was adjusted to maintain an $EtCO_2$ of 36–40 mmHg. Hemodynamic parameters were compared between the two groups. **Results:** It was observed that the mean value of mean arterial pressure (MAP) was higher in group 2 (94.80 ± 6.372, 89.87 ± 4.779) in comparison to group 1 (87.07 ± 4.818, 86.27 ± 4.217) at 5 min and 10 min after insufflation. The differences were statistically significant ($P = 0.001$ and $P = 0.037$, respectively). There was a statistically significant difference in the mean heart rate at 5 min after insufflation in group 1 (73.80 ± 6.483) and group 2 (82.00 ± 8.375) ($P = 0.006$). **Conclusion:** Hyperventilation before CO_2 insufflation is a simple and effective measure for decreasing the effect of pneumoperitoneum. It can be used in limited-resource settings.

Key words: Anesthesia, cholecystectomy, general, hemodynamics, hyperventilation, insufflation, laparoscopic

INTRODUCTION

Laparoscopic procedures have become an integral aspect of modern operating theatres, with the majority of surgeries performed using minimally invasive techniques.[1] These approaches offer a range of advantages, including reduced postoperative pain, quicker mobilization, shorter hospital stay, decreased morbidity rates, and alleviation of financial strain in patients.[2,3]

Laparoscopic procedures are commonly performed in high-risk patients, such as the elderly, overweight patients, and those with preexisting conditions such as cardiovascular and lung diseases.[4,5] Therefore, heightened vigilance throughout the procedure is essential for ensuring appropriate management. Although laparoscopic surgery is associated with a lower risk of cardiovascular mortality than open surgery, understanding its specific hemodynamic and ventilatory effects that may increase the risk of cardiovascular and pulmonary complications is critical.[6,7]

Carbon dioxide (CO_2) insufflation during laparoscopic surgery can induce significant hemodynamic and ventilatory side effects due to hypercarbia and elevated intra-abdominal pressure.[8,9] Hemodynamic effects include increased afterload, decreased preload, and reduced cardiac output, while ventilatory effects manifest as increased airway pressure, hypercarbia, and decreased pulmonary compliance.[10] Various strategies have been developed and evaluated based on the underlying pathophysiological mechanisms to mitigate these adverse

Received: March 25, 2025; Revised: June 25, 2025;
Accepted: July 16, 2025; Published: August 22, 2025
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How to cite this article: Nigam S, Shukla U, Gupta R, Yadav U, Saxena A, Mukherjee M. Effect of hyperventilation prior to CO_2 insufflation in laparoscopic cholecystectomy: A randomized controlled trial. J Med Sci 2025;45:223-8.

effects. A few of these techniques use low intra-abdominal gas pressures, reduced gas insufflation rates, warmed gas, and gasless laparoscopy to target the gas insufflation process with varying degrees of success.

Herein, we hypothesized that hyperventilation before CO_2 insufflation during laparoscopic surgery might enhance hemodynamic stability immediately following insufflation. This study aimed to compare hemodynamic changes observed after controlled hyperventilation prior to CO_2 insufflation during laparoscopic cholecystectomy.

MATERIALS AND METHODS

This study was carried out after receiving approval from the institutional ethical committee (ethical clearance no: 97/2023-24, dated August 22, 2023) and adhered to the principles outlined in the 2013 Helsinki Declaration. Written informed consent was obtained from the participants in a designed proforma. Our study is registered with the Clinical Trials Registry of India (CTRI) under registration number CTRI/2024/02/062535. Assuming a true difference in mean arterial pressure (MAP) of 3.71 units between the test and reference groups, with a pooled standard deviation of 5.68 units, a sample size of 11 participants per group (a total of 22 for equal group sizes) was calculated to achieve 80% power at a 5% significance level. To ensure robustness, we selected a sample size of 30.

Thirty patients aged between 20 and 50 years, classified as American Society of Anesthesiologists (ASA) Class I or II, of either sex, and scheduled for laparoscopic cholecystectomy under general anesthesia, were included in the study. Participants who refused to participate, pregnant females, obese patients (body mass index [BMI] >29 kg/m^2), or smokers were excluded. Computer-generated random numbers were used to assign patients to two groups, each consisting of 15 patients. Before providing written informed consent, each patient received a comprehensive explanation of the procedure. An anesthesiologist, who was not involved in data collection, opened the envelope containing computer-generated random sequence numbers and revealed the group assignments in the procedure area. The data recorder was not present in the ventilatory settings, ensuring they were unaware of the assigned group.

On the day before surgery, each patient was assessed by an attending anesthesiologist during a preoperative visit in the evening. The patients were administered oral pantoprazole (20 mg) and alprazolam (0.25 mg) tablets the night before surgery to minimize anxiety on the day of the procedure. Prior to surgery, all patients were required to fast for 8 h for meals and 2 h for clear fluids. Upon arrival in the operating room, ASA standard monitors were attached to monitor various aspects of patient care throughout the intraoperative and postoperative periods, such as noninvasive blood pressure, heart rate (HR), electrocardiography, peripheral pulse oximetry, and capnography (end-tidal CO_2: $EtCO_2$). Bispectral index (BIS) electrodes were positioned to track the depth of anesthesia, aiming to maintain an intraoperative BIS value of 40–60. Peripheral vascular access was obtained using an 18-gauge intravenous cannula, and Lactated Ringer's solution was administered.

Furthermore, patients were premedicated with intravenous injections of glycopyrrolate (5 μg/kg), midazolam (0.05 mg/kg), and fentanyl (2 μg/kg). Preoxygenation was performed with 100% oxygen for 3 min, followed by anesthesia induction with intravenous propofol (2 mg/kg), with loss of verbal command as the endpoint. To facilitate direct laryngoscopy and intubation, intravenous vecuronium (0.1 mg/kg) was administered. Endotracheal intubation was performed with a tube size of 7.0–7.5 mm I.D. in female patients and 8.0–8.5 mm I.D. in male patients. Controlled ventilation was maintained intraoperatively using 65% N_2O, 35% O_2, and isoflurane (0.4%–1%) to ensure a BIS value of 40 − 60. Supplemental neuromuscular blockage was achieved with a divided dose of 0.02 mg/kg of injection vecuronium. Following intubation, all patients in group 1 were ventilated with a tidal volume (TV) of 8 mL/kg for 15 min before CO_2 insufflation. The respiratory rate (RR) was adjusted to maintain an $EtCO_2$ of 31–35 mmHg, representing a drop of ≥ 5 mmHg from the baseline. In Group 2, patients were similarly ventilated with a TV of 8 mL/kg for 15 min before CO_2 insufflation, with the RR adjusted to maintain an $EtCO_2$ of 36–40 mmHg. All the patients were positioned in the supine position with a slight head-up and left tilt. Insufflation for pneumoperitoneum is done at a rate of 4 l/min, and pressure was maintained at 12 mmHg in all the patients.

In both groups, systolic blood pressure (SBP), diastolic blood pressure (DBP), MAP, HR, and SpO_2 were recorded at baseline, 5 min before CO_2 insufflation, and at 5, 15, and 30 min after CO_2 insufflation, as well as 5 min after desufflation of the pneumoperitoneum. Fall in MAP of more than 20% was considered hypotension and managed with injection mephentermine in a bolus dose of 6 mg. Following surgery, any residual neuromuscular blockade was reversed using intravenous neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg). All patients were extubated once awake and responsive to commands and were then shifted to the postoperative room for further observation.

Statistical analysis

Data are presented as mean ± standard deviation and percentages (%). Quantitative factors were statistically analyzed and compared within groups using the paired *t*-test, and between groups using the unpaired *t*-test. Qualitative factors were statistically analyzed and compared using Fisher's exact test or the Chi-square test. Statistical significance was set at $P \leq 0.05$. Statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, New York, USA).

RESULTS

Thirty patients scheduled for laparoscopic cholecystectomy were randomly divided into two groups, each consisting of 15 patients. None of the patients were excluded from our study [Figure 1]. This prospective, randomized, single-blind clinical study aimed to assess the hemodynamic changes after controlled hyperventilation prior to CO_2 insufflation during laparoscopic cholecystectomy. The primary outcomes of the study were alterations in HR, SBP, DBP, MAP, and SpO_2 between the two groups.

Demographic data, including age, sex, BMI, and ASA physical status, were comparable among study groups, as summarized in Table 1. The depth of anesthesia was measured using BIS monitoring in both groups before the insufflation of CO_2. The mean BIS value for Group 1 (49.0 ± 3.047) was similar to that of Group 2 (48.80 ± 4.427; P = 0.886) [Figure 2].

The mean SBP was measured at baseline; 5 min prior to insufflation; and at 5, 10, and 15 min after insufflation, as well as 5 min after desufflation. Intergroup comparison revealed significant differences at 5 and 10 min after insufflation (P < 0.001 and 0.009, respectively) [Table 2]. For the mean DBP, the difference between the groups was statistically significant at 5 min after insufflation (P = 0.035) [Figure 3]. Furthermore, MAP was noted for each group, revealing the mean MAP was higher in Group 2 (94.80 ± 6.372 at 5 min, 89.87 ± 4.779 at 10 min) compared to Group 1 (87.07 ± 4.818 at 5 min, 86.27 ± 4.217 at 10 min) following insufflation [Table 3 and Figure 4]. These differences were statistically significant (P = 0.001 and 0.037, respectively). There were no episodes of hypotension or hypertension in any patient.

The mean HR was also measured in both groups, showing a statistically significant difference at 5 min after insufflation: Group 1 (73.80 ± 6.483) and Group 2 (82.00 ± 8.375), with a P = 0.006 [Table 4]. No significant difference in SpO_2 levels was observed between the groups.

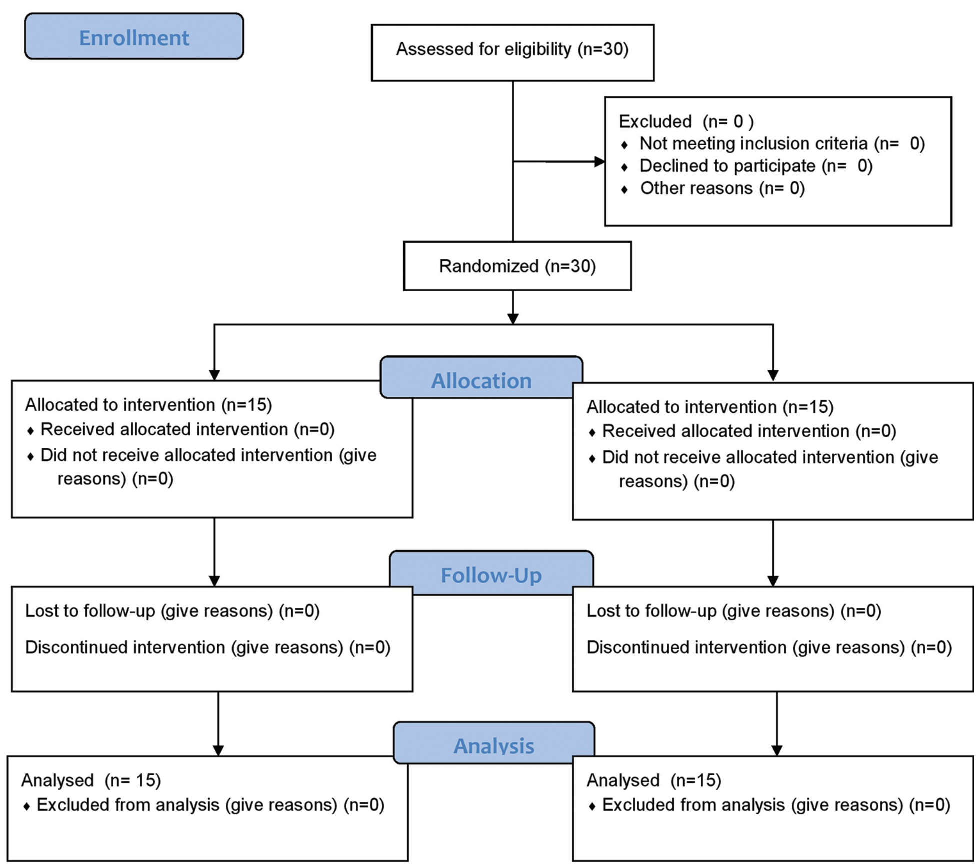

Figure 1: Consort flow diagram

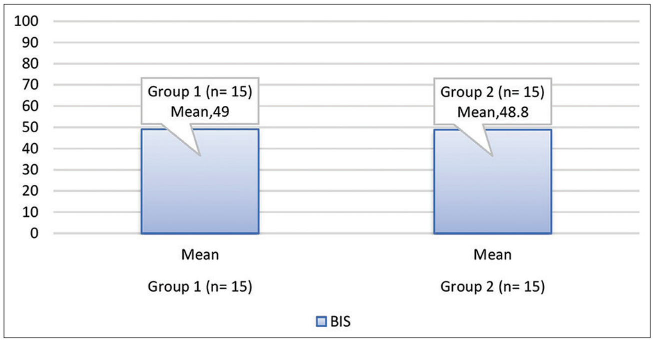

Figure 2: Bispectral index value in the groups

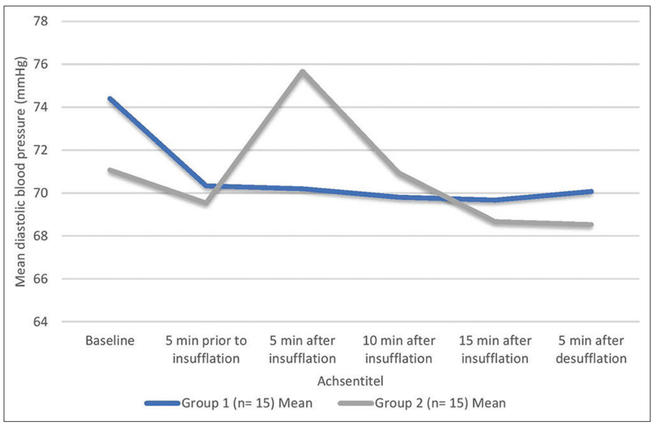

Figure 3: Comparison of diastolic blood pressure between two groups

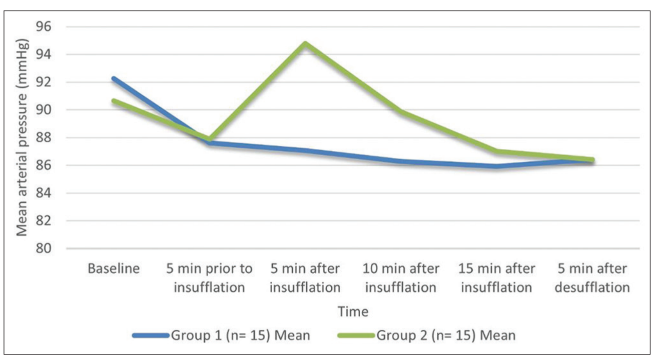

Figure 4: Comparison of mean arterial pressure between two groups

Table 1: Demographic data of patients in study groups

Parameters	Group 1 (*n*=15)	Group 2 (*n*=15)	*t* and χ^2	*P*
Age (years)	34.20±8.368	37.93±8.746	−1.195	0.097
Sex				
Male	6	5	0.142	0.706
Female	9	10		
BMI	22.53±1.885	22.47±1.959	0.095	0.536
ASA PS				
I	9	10	0.142	0.531
II	6	5		

Data expressed in numbers analyzed by Chi-square test. Data expressed in mean±SD is analyzed by unpaired *t*-test. BMI=Body mass index; ASA PS=American Society of Anesthesiologists physical status; SD=Standard deviation; *n*=Number of patients in group

Table 2: Comparison of systolic blood pressure between the groups

SBP	Group 1 (*n*=15)	Group 2 (*n*=15)	*P*
Baseline	127.87±8.951	129.73±7.564	0.542
5 min prior to insufflation	122.27±7.658	124.33±7.518	0.462
5 min after insufflation	120.87±6.523	133.53±8.383	<0.001
10 min after insufflation	119.73±7.096	127.93±8.697	0.009
15 min after insufflation	119.33±6.789	123.93±9.293	0.133
5 min after desufflation	119.20±6.614	122.33±8.015	0.253

Data are expressed as mean±SD and analyzed by unpaired *t*-test. SBP=Systolic blood pressure; SD=Standard deviation

Table 3: Comparison of mean arterial pressure between the groups

MAP	Group 1 (*n*=15), mean±SD	Group 2 (*n*=15), mean±SD	*t*	*P*
Baseline	92.27±5.788	90.67±4.402	0.852	0.401
5 min prior to insufflation	87.60±4.595	87.87±6.289	−0.133	0.895
5 min after insufflation	87.07±4.818	94.80±6.372	−3.749	0.001
10 min after insufflation	86.27±4.217	89.87±4.779	−2.188	0.037
15 min after insufflation	85.93±3.936	87.00±4.899	−0.657	0.516
5 min after desufflation	86.40±4.611	86.40±4.469	0.000	1.000

Data are expressed as mean±standard deviation and analyzed by unpaired *t*-test. MAP=Mean arterial pressure; SD=Standard deviation

DISCUSSION

Laparoscopic surgery offers several advantages over laparotomy, which requires a large abdominal wall incision. These benefits include reduced surgical trauma, less postoperative pain, cleaner surgical field of view, faster recovery of bowel function, and decreased abdominal adhesions. Thus, laparoscopic surgery is often the preferred option for abdominal procedures.[11]

Increased intra-abdominal pressure due to CO_2 pneumoperitoneum during laparoscopic procedures reduces lung compliance, leading to significant alterations in hemodynamic parameters.[12] CO_2 absorption may cause a sudden increase in partial pressure of Carbon dioxide ($PaCO_2$), which can induce a variety of pathophysiological alterations. This triggers stress reactions that are characterized by

Table 4: Comparison of heart rate between the groups

HR	Group 1 (*n*=15), mean±SD	Group 2 (*n*=15), mean±SD	*t*	*P*
Baseline	77.53±8.034	77.87±8.692	−0.109	0.914
5 min prior to insufflation	73.8±6.795	78.2±9.807	−1.428	0.164
5 min after insufflation	73.8±6.483	82±8.375	−2.999	0.006
10 min after insufflation	72.67±6.422	77.73±8.066	−1.903	0.067
15 min after insufflation	72.4±6.445	76.67±7.584	−1.660	0.108
5 min after desufflation	71.73±5.970	74.53±6.479	−1.231	0.229

HR=Heart rate; SD=Standard deviation

catecholamine release and an activated sympathetic nervous system.[13] The intraoperative use of muscle relaxants enhances abdominal capacity, allowing a larger volume of CO_2 at lower abdominal pressures. As a result, this approach improves the surgical field exposure and mitigates the adverse effects of pneumoperitoneum.[14]

CO_2 insufflation for pneumoperitoneum creation leads to a rapid increase in $PaCO_2$ and a reduction in lung capacity and functional residual capacity due to the pushed-up diaphragm. Sudden hypercapnia induces several hemodynamic changes.[15] Hypocapnia before and during laparoscopic cholecystectomy has been suggested as a potential strategy for mitigating the adverse hemodynamic effects of CO_2 insufflation. In our study, greater hemodynamic stability was observed in patients who were hyperventilated prior to CO_2 insufflation. The mean MAP was significantly higher in Group 2 (94.80 ± 6.372, 89.87 ± 4.779) compared to Group 1 (87.07 ± 4.818, 86.27 ± 4.217) at 5 min and 10 min after insufflation, with a statistically significant difference (P = 0.001 and 0.037, respectively). In addition, there was a significant difference in mean HR at 5 min after insufflation in Group 1 (73.80 ± 6.483) and Group 2 (0.006), with $P = 0.006$.

The results of the present study align with those of El–Tahan *et al*. (2012),[16] who reported that hypocapnia induced before and during pneumoperitoneum resulted in significantly lower arterial blood pressures, lower $PaCO_2$ and $EtCO_2$ values, a higher Pa-$EtCO_2$, increased RR ($P < 0.001$), and a decreased requirement for additional fentanyl and labetalol doses compared to the control group. Their findings led to the conclusion that hypocapnia, when employed prior to and during CO_2 insufflation, effectively reduces blood pressure spikes following CO_2 pneumoperitoneum during laparoscopic cholecystectomy anesthesia.

In another study, Maharjan and Shrestha[17] evaluated the impact of hyperventilation on hemodynamic, partial pressure of CO_2, and acid-base balance in patients undergoing laparoscopic procedures. The control group was ventilated with a TV of 10 mL/kg and an RR of 12/min, while the study group was ventilated with the same TV and an RR of 15/min. $EtCO_2$, $PaCO_2$, pH, and bicarbonate levels were measured before, during, and after CO_2 pneumoperitoneum, whereas hemodynamic variables, including HR and MAP, were documented and analyzed. A linear increase in $EtCO_2$ and $PaCO_2$ was observed in the control group, with measurements at higher normal levels ($EtCO_2$ 33.3 ± 3.20, 37.93 ± 3.95, and 43.20 ± 3.40; $PaCO_2$ 30.08 ± 2.35, 34.80 ± 4.01, and 41.94 ± 3.66 mmHg before, during, and after pneumoperitoneum, respectively). In contrast, the study group exhibited lower normal levels of these parameters ($EtCO_2$ 33.33 ± 4.11, 28.00 ± 4.10, and 36.73 ± 2.49 mmHg and $PaCO_2$ 31.80 ± 2.73, 29.36 ± 3.16, and 35.15 ± 1.32 mmHg before, during, and after pneumoperitoneum, respectively). Significant differences were noted between the groups during and after pneumoperitoneum induction. Although the pH and bicarbonate levels remained within normal ranges, the control group showed a declining propensity towards acidosis. To avoid the negative effects of hypercarbia and acidosis, it was concluded that a 10%–15% increase in minute volume is advantageous during CO_2 pneumoperitoneum. These results were consistent with those of the present study.

In another investigation, Tan *et al*.[8] demonstrated that during pelvic laparoscopy, the lungs experienced a rapid 30% increase in CO_2 elimination, which quickly stabilized. This increase was manageable through hyperventilation, with a corresponding 30% rise in minute ventilation, compensating for elevated CO_2 levels.

Several methods have been explored to reduce the effect of pneumoperitoneum during laparoscopic surgery. Jee *et al*.[18] investigated the potential of intravenous magnesium sulfate to mitigate hemodynamic stress responses to pneumoperitoneum by modulating the neurohumoral responses during laparoscopic cholecystectomy. Preoperative administration of magnesium sulfate attenuated the rise in arterial pressure, likely due to the decreased release of catecholamines, vasopressin, or both. Meanwhile, Chen *et al*.[19] examined the effect of the right stellate ganglion block on hemodynamic and stress responses during CO_2 pneumoperitoneum. The findings suggested that the right stellate ganglion block can lower blood catecholamine levels, thereby promoting hemodynamic stability and preventing cardiovascular complications in elderly patients. However, further research is required to validate these results.

These results have the potential to enhance perioperative outcomes in both critically ill and cardiac patients. Moreover, by minimizing intraoperative opioid usage, they can promote faster and smoother postoperative recovery.

CONCLUSION

Hyperventilation before CO_2 insufflation is a simple and effective measure for decreasing the effects of pneumoperitoneum. This approach can be applied in resource-limited settings.

Limitations

This study was conducted at a single centre with a small sample size. In addition, $PaCO_2$ levels were not measured. Future research should explore the impact of pneumoperitoneum on intracranial and cerebral perfusion pressures.

Data availability statement

The data that supports the findings of this study are available from the corresponding author, [Dr. Urvashi Yadav], upon reasonable request.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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