

# Role of Low Dose Intravenous Ketamine for Postoperative Pain Relief Following Laparoscopic Cholecystectomy

Shanjida Kibria<sup>1</sup>, Sheikh Imran Alam<sup>1</sup>, Naushad Khan Shaon<sup>1</sup>, Md. Abdur Razzaque<sup>1</sup>, Md. Ashfaq Ahmad<sup>1</sup>, Ponam Saha<sup>1</sup>, Md Samir Asif<sup>1</sup>, Syed Golam Rabbi<sup>2</sup>, Dilip Kumar Bhowmick<sup>3</sup>

## Abstract

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**Background:** Laparoscopic cholecystectomy provides faster recovery but postoperative pain still remains a persistent challenge. Many patients experience visceral, somatic, or referred pain despite multimodal analgesic strategies, which are often limited by side effects and inconsistent efficacy. In this context, low-dose intravenous ketamine has emerged as a promising preemptive option, with the potential to reduce pain intensity, delay analgesic demand, and enhance overall recovery. The main objective of this study was to evaluate effectiveness of low dose intravenous ketamine for postoperative pain relief in laparoscopic cholecystectomy.

**Materials and methods:** This quasi-experimental study was carried out over one year at the Department of Anaesthesia, Analgesia and Intensive Care Medicine of Bangladesh Medical University, Dhaka, following ethical approval. A total of 90 patients aged 18–60 years undergoing laparoscopic cholecystectomy under general anesthesia were enrolled. Participants were divided into two groups. Group K who received low dose intravenous ketamine & Group NS received normal saline as placebo. Postoperative pain was assessed using the Visual Analogue Scale (VAS) at 0, 1, 2, 6, 12, and 24 hours. Rescue analgesia with IV pethidine (1 mg/kg) was given for VAS  $\geq 4$ . Outcomes included pain scores, time to first analgesic, total opioid requirement, haemodynamic parameters, and patient satisfaction.

**Result:** Postoperative pain intensity was significantly lower in the Group K at recovery ( $1.3 \pm 1.3$  vs.  $1.8 \pm 1.4$ ,  $p < 0.05$ ), at 1 hour ( $1.8 \pm 1.3$  vs.  $2.5 \pm 1.7$ ,  $p < 0.05$ ), and at 2 hours ( $2.0 \pm 1.4$  vs.  $5.1 \pm 1.6$ ,  $p < 0.05$ ), but differences diminished at later time points. Heart rate remained similar at most intervals, though significant differences were noted intraoperatively at 90 minutes ( $73.7 \pm 4.5$  vs.  $68.7 \pm 4.3$ ,  $p < 0.05$ ) and postoperatively at 1 hour ( $80.9 \pm 8.4$  vs.  $90.3 \pm 11.6$ ,  $p < 0.05$ ). Systolic blood pressure was stable pre and intraoperatively, but maintained significantly lower values at 1 hour ( $113.2 \pm 10.5$  vs.  $129.0 \pm 10.0$ ,  $p < 0.05$ ) and at 2 hours ( $111.9 \pm 10.6$  vs.  $130.7 \pm 12.6$ ,  $p < 0.05$ ) postoperatively in Group K. Diastolic and mean arterial pressures were similar both preoperatively and intraoperatively, yet Group K again showed significantly lower MAP values at 1 hour ( $79.4 \pm 9.0$  vs.  $2.7 \pm 11.7$ ,  $p < 0.05$ ) and at 2 hours ( $79.6 \pm 9.3$  vs.  $94.0 \pm 10.4$ ,  $p < 0.05$ ) postoperatively. Adverse effects did not differ significantly between groups. Group K showed, significantly prolonged the time to first analgesic demand, reduced total opioid consumption, and extended analgesia duration, although patient satisfaction scores were nearly identical across groups.

**Conclusion:** Low dose intravenous ketamine, reduces the postoperative pain scores, delayed first analgesic demand and reduced opioid consumption.

**Keywords:** Preemptive analgesia, Low dose ketamine, Post-operative pain management, Laparoscopic cholecystectomy, Opioid consumption

1. Resident, Department of Anaesthesia, Analgesia and Intensive Care Medicine, Bangladesh Medical University, Dhaka.
2. Indoor Medical Officer, Department of Medicine, Rajshahi Medical College, Rajshahi.
3. Professor, Department of Anaesthesia, Analgesia and Intensive Care Medicine, Bangladesh Medical University, Dhaka.

**Correspondence:**  
Shanjida Kibria  
Email: drshanjidakibria@gmail.com

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## Introduction

Laparoscopic cholecystectomy, a minimally invasive procedure for gallbladder removal, has become the gold standard in treating gallbladder-related disorders such as acute and chronic cholecystitis, symptomatic cholelithiasis, and biliary dyskinesia<sup>1,2</sup>. Since its introduction in the early 1990s, it has largely replaced open cholecystectomy due to its favourable outcomes in terms of recovery time, reduced postoperative pain, and enhanced patient satisfaction<sup>3</sup>. Gallstone disease affects approximately 5.4% of adults in Bangladesh with a notably higher prevalence among women (7.7%) compared to men (3.3%)<sup>4</sup>. Whereas in the United States it affects approximately 10-15% adults, with laparoscopic cholecystectomy performed in roughly 750,000 cases annually, making up about 90% of all cholecystectomies<sup>5,6</sup>. Despite the benefits of this procedure, postoperative pain remains a significant issue, manifesting in various forms including visceral, somatic, and referred pain. Visceral pain, the most prominent type, originates from internal organs and tends to peak within the first 24 hours post-surgery<sup>7</sup>. Somatic pain, arising from abdominal wall incisions, and referred pain in the shoulder from diaphragmatic irritation are also common and can persist for days<sup>8</sup>. While many patients experience moderate pain, studies show that 30% report severe pain in the initial 48 hours, often requiring strong analgesics for effective relief<sup>9</sup>. To manage such types of diverse pain effectively, several analgesic methods and medications are employed, including non-opioid analgesics and local anaesthetic infiltration<sup>10</sup>. However, limitations of traditional analgesics include side effects, the potential for opioid dependence, and ineffectiveness in some patients<sup>11,12</sup>. This has driven interest in alternative strategies, particularly preemptive analgesia, which involves administering analgesics before surgical stimuli to prevent central sensitisation and reduce the risk of postoperative pain<sup>13</sup>. Ketamine, an N-Methyl – D – aspartate (NMDA) receptor antagonist, has shown promise as a pre-emptive analgesic for acute pain by blocking pain pathways and reducing opioid consumption<sup>14</sup>. Previous study showed, ketamine at a dose of 0.5 mg/kg can provide strong and effective analgesia<sup>15</sup>. Although some common adverse effects including

dizziness, tachycardia, mild hypertension, hallucination are also seen with this dose<sup>15</sup>. In the present study, 0.3 mg/kg ketamine was used to balance the advantages and side effects. Given ketamine's opioid-sparing properties and ability to reduce postoperative pain intensity, there is a growing hypothesis that low dose intravenous ketamine may be especially beneficial in laparoscopic cholecystectomy. Studies indicate that ketamine administration before surgery can delay the time to the first analgesic request, stabilize haemodynamic, and potentially exert anti-inflammatory effects, further enhancing postoperative recovery<sup>16,17</sup>. This research aimed to explore these potential benefits, examining whether low dose intravenous ketamine can serve as a viable strategy to manage postoperative pain following laparoscopic cholecystectomy.

## Methods

This quasi-experimental study was carried out between September, 2024 to October, 2025 in the general surgery operation theatre under the supervision of the Department of Anaesthesia, Analgesia and Intensive care medicine at Bangladesh Medical University (BMU), Dhaka. Patients aged from 18 years to 60 years with ASA status I & II undergoing elective laparoscopic cholecystectomy under general anaesthesia were included. Patients who had choledocholithiasis, currently having opiate, any sedative, NSAIDs and sleep aid drug, history of hypersensitivity to study drugs, patients with psychiatric disease, cardiac comorbidities, severe respiratory, renal, hepatic disease, and those whose laparoscopic cholecystectomy were changed to an open procedure were excluded from this study.

Prior to the commencement of this study, the thesis protocol was approved by the IRB, Bangladesh Medical University. Informed written consent was obtained from the patient after explaining every ethical issue regarding the study. A total of 90 adult patients were enrolled during the study period. They were divided into two groups: Group K included 45 patients who received ketamine, and Group NS included 45 patients who received normal saline as placebo.

Detailed socio demographic information (age, sex, weight etc.) were collected. Preoperative variables such as ASA class, Pre-induction haemodynamic parameters (heart rate, blood pressure) and planned surgery were documented. All patients underwent a pre anaesthetic checkup the day before surgery. The patients were explained about general anaesthesia in detail during the preanaesthetic visit. Before surgery patients were made familiar with VAS.

### Study Procedures

All patients were kept nil per oral for 8 hours before surgery. Baseline non-invasive blood pressure (NIBP), heart rate (HR), electrocardiography (ECG), pulse oximetry (SpO<sub>2</sub>), respiratory rate (RR) and end tidal carbon dioxide (ETCO<sub>2</sub>) were recorded using a multiparameter monitor during the surgery. Ventilator settings were checked and adjusted according to patient parameters. Safety features such as circuit integrity, alarm systems and oxygen supply were ensured prior to induction. A wide bore intravenous (IV) cannula was secured in all patients before induction. All patients received pantoprazole 40mg IV as premedication. After preoxygenation for 3-5 minutes with 100% oxygen, general anaesthesia was induced using intravenous fentanyl 2 µg/kg followed by intravenous propofol 2 mg/kg (until loss of verbal commands). A single intravenous bolus of ketamine at a dose of 0.3 mg/kg diluted with normal saline to make 2 ml, was administered to patients assigned to Group K, whereas 2 ml of normal saline as placebo was administered to patients assigned to Group NS. Tracheal intubation was facilitated by intravenous suxamethonium 2 mg/kg and correct placement of the cuffed endotracheal tube was confirmed with capnography and bilateral chest auscultation. The tube was then secured appropriately, and the eyes were protected with adhesive tape.

Intraoperatively, anaesthesia was maintained with 30% oxygen in 70% nitrous oxide, and isoflurane was used at a minimum alveolar concentration of 1. Volume controlled ventilation was provided with a tidal volume of 6-8 ml/kg inspiratory/expiratory ratio of 1:2 and the respiratory rate was adjusted to maintain an end tidal carbon dioxide concentration of 35 mmHg. The neuromuscular blocker vecuronium bromide was administered at a dose of 0.1 mg/kg as

a bolus, followed by 0.04 mg/kg for maintenance. Standard monitoring included ECG, HR, NIBP, SpO<sub>2</sub>, RR, ETCO<sub>2</sub>, and ventilator alarms to ensure patient safety.

At the end of surgery, intravenous ondansetron 0.1mg/kg was administered as prophylaxis against postoperative nausea and vomiting. All patients received 15 mg/kg paracetamol IV before completion of surgery. The residual neuromuscular blockade was antagonized with a mixture of IV neostigmine 0.05 mg/kg and atropine 0.02 mg/kg IV once spontaneous respiratory efforts were adequate. Tracheal extubation was performed after patients regained consciousness, demonstrated purposeful movement and achieved stable haemodynamic. Perioperative complications, including oral secretions, nausea, and vomiting, were managed promptly. Patients were then transferred to the post anaesthesia care unit for continued monitoring. This study was conducted in a double-blind manner. The patients were unaware of their Group allocation and both injectates were prepared in identical syringes. Postoperative assessor who evaluated the outcomes was also blinded to the Group allocation.

All patients were kept under observation in the post-anaesthesia care unit (PACU) for 6 hours before being moved to the ward. In the PACU, pain intensity using visual analogue scale (VAS) and haemodynamic parameters (HR, SBP, DBP, MAP) were documented. Pain scores were evaluated using the VAS on arrival to the PACU and then at 1, 2, 6, 12 and 24 hours postoperatively by face-to-face interview / with the help of my colleague /over telephone. If VAS score was 4 or more, 1mg/kg of IV pethidine was administered. Total dose of opioid administered in the first 24 hours postoperatively was recorded. The time for requirement of the first dose of opioid as rescue analgesia was also recorded. Haemodynamic parameters (HR, SBP, DBP, MAP) were recorded in 1hour, 2hours, 6hours, 12hours, 24hours. Patient satisfaction was recorded on a 5-point Likert scale after 24 hours.

Data collection was performed by an independent assessor who was not involved in Group allocation or intervention. A preformed standardized

questionnaire was used for data collection, ensuring consistency. All collected information was stored securely in separate data record forms. Once all data had been collected, statistical analysis was performed to compare the outcomes between two groups (Group K and Group NS). This included comparing intensity of pain by using VAS score, time of first analgesic requirement, total opioid consumption, haemodynamic parameters and patient satisfaction.

**Study measures**

**Visual analogue scale (VAS)**

Visual analogue scales (VAS) are unidimensional pain rating scales used ubiquitously to measure the sensory component of pain. The most commonly used VAS consists of a horizontal 10 cm line ranging from “no pain” to “unbearable/worst pain,” on which subjects are asked to make a mark representing their level of perceived pain intensity. The scale is scored by measuring the distance from the “no pain” end to the patient’s mark.<sup>18</sup>

**Patient satisfaction**

Assessment of the level of patient satisfaction on the anaesthetic and analgesic care of the patient on a 1- 5 Likert scale. (Very dissatisfied-1, dissatisfied-2, neutral-3, satisfied-4, very satisfied 5).<sup>19</sup>

**Statistical analysis:**

All the collected data was compiled on a master chart. The statistical analysis was carried out using the Statistical Package for Social Sciences version 29 for Windows (SPSS Inc. Chicago, Illinois, USA). Qualitative Variables of this study are expressed as percentage. Quantitative variables were expressed as Mean ± SD. Comparison was calculated by Chi-square test for the categorical variables and unpaired t-test and repeated measure ANOVA for the continuous variables. p-values <0.05 was considered as statistically significant.

**Results**

Total ninety ASA class I-II patients scheduled for laparoscopic cholecystectomy, were allocated into two groups. Group K received ketamine while Group NS received normal saline as placebo. No participants were excluded from this study due to lost in follow up or conversion to open surgery. Table ‘1’ shows the demographic characteristics of the studied groups.

Both groups were comparable at baseline in terms of age, sex distribution, body mass index, and ASA score. No statistically significant differences were observed.

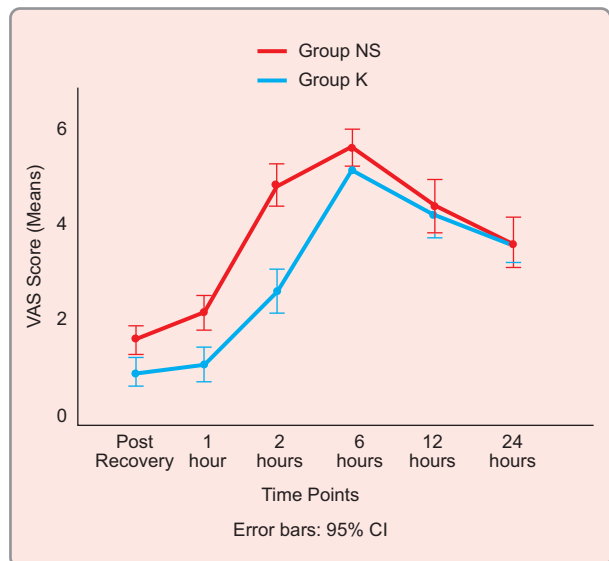
**Table I:** Demographic characteristics of the studied groups (n = 90)

Variables	Group K n = 45	Group NS n = 45	p-value
Age (in years)	33.6±5.4	34.3±6.0	0.30
Sex			
Male	20 (44%)	18 (40%)	0.67
Female	25 (56%)	27 (60%)	
BMI (kg/m <sup>2</sup> )	30.6±4.0	30.0±4.5	0.25
ASA score			
I	10(22%)	18(40%)	0.10
II	35(78%)	27(60%)	

Values are expressed as Mean ± SD and total number within parenthesis percentage (%) over column in total. Values were analysed by unpaired t-test for continuous variable and chi-square test for categorical variable. P<0.05 is considered statistically significant

Hypertension was similar in both groups (22.2% vs. 15.5%). Diabetes mellitus was more frequent in Group K (44.4%) compared to Group NS (26.7%), while bronchial asthma /COPD was slightly higher In Group NS (17.8%) than in Group K (11.1%). Overall, Group K had more metabolic comorbidity than Group NS.

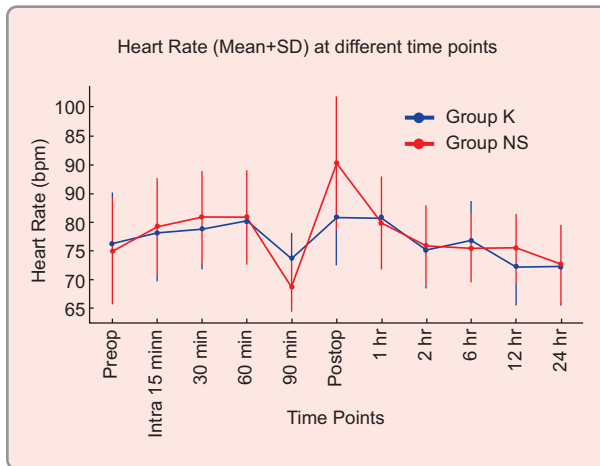
Figure 1 depicted that post recovery VAS was (1.3±1.3 vs. 1.8 ± 1.4). At 1 hour (1.8±1.3 vs. 2.5±1.7)



**Figure 1:** Changes in postoperative pain intensity (VAS score) at different time points

and at 2 hours (2.0±1.4 vs. 5.1±1.6) following operation, VAS scores were significantly lower in Group K compared to Group NS. But VAS at 6 hours (5.8±1.0 vs., 5.9±1.4) 12 hours, (4.8±0.9 vs. 4.6±1.5.), and 24 hours (4.2±0.6 vs. 4.0±1.4) were not statistically significant between groups.

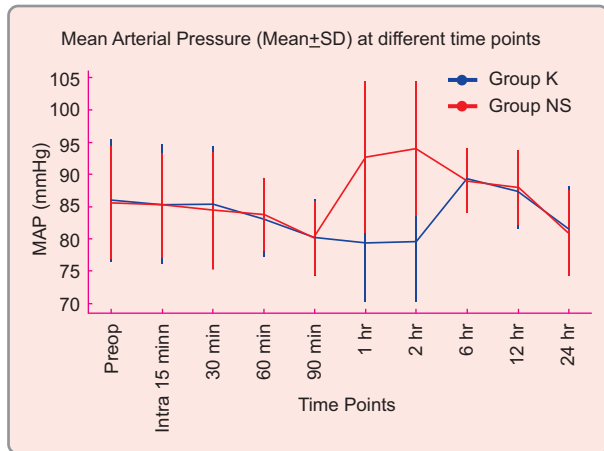
Figure 2 shows preoperative heart rates were similar between groups (76.3±8.8vs.75.0±9.2) bpm. At 15 minutes (78.2±8.4 vs. 79.2±8.4) bpm, 30 minutes (78.9±7.0 vs. 80.9±8.2) bpm and at 60 minutes (80.3±6.8 vs. 80.9 ±8.2) bpm, no significant differences were observed. At 90 minutes, a marked variation was noted, with heart rates lower in Group NS (73.7 ±4.5 vs. 68.7±4.3) bpm. Postoperative heart rates at 2 hours (80.8±7.0 vs. 79.9±8.0) bpm, 6 hours (75.3± 6.8 vs.75.9± 6.9) bpm,12 hours (76.9±6.8 vs75.5 ± 6.0) bpm, and 24hours (72.3±6.7 vs.72.7±6.8) bpm were not statistically significant between groups. But at 1 hour following operation, heart rate was significantly lower in Group K compared to Group NS (80.9±8.4 vs. 90.3± 11.6) bpm. Repeated measure ANOVA was also done. Within subject effects (Time trend) was significant (p value <0.001) and between subject effects (p value 0.004) was also statistically significant.



**Figure 2:** Time dependent changes in heart rate in two studied groups

Preoperative mean arterial pressure was comparable between two groups (86.0±9.5vs.85.0±8.8) mmHg. At 15 minutes, MAP remained nearly identical (85.4±9.2 vs. 85.2 ±8.1) mmHg, with similar trends at 30 minutes (85.4±9.0 vs. 84.4±9.2) mmHg at 6 hours

(89.3±4.7 vs. 89.0±5.0) mmHg, 12 hours (87.4±5.9 vs. 87.9±5.8) mmHg, and 24 hours, (81.4±6.7 vs. 80.9±6.7) mmHg were not statistically significant between groups. But at 1 hour (79.4±9.0 vs. 92.7±11.7) mmHg and 2 hours (79.6±9.3 vs. 94.0±10.4) mmHg following operation, mean arterial pressure was significantly lower in Group K compared to Group NS. Repeated measure ANOVA was also done. Within subject effects (Time trend) was significant (p value <0.001), between subject effects (p value 0.49) was statistically non-significant. (Figure 3)



**Figure 3:** Comparison of mean arterial pressure at different time points in the studied groups

Table II demonstrated that incidence of nausea and vomiting in Group K (35.6%) and in Group NS (31.15%). Certain side effects including hallucination (11.1% vs 8.9%), sedation (55.6% vs 44.4%). Cardiovascular changes such as tachycardia (46.7% vs 42.2%) and hypertension (62.2% vs 66.7%) were not statistically significant between groups.

**Table II:** Adverse effects in the postoperative period (n = 90)

Variables	Group K n = 45	Group NS n = 45	p-value
Nausea and vomiting	16(35.6%)	14(31.1%)	0.80
Hallucination	5(11.1%)	4(8.9%)	1.00
Sedation	25(55.6%)	20(44.4%)	0.40
Tachycardia	21(46.7%)	19(42.2%)	0.80
Hypertension	28(62.2%)	30(66.7%)	0.80

Values are presented as absolute numbers (within parenthesis percentage over column total) values were analysed by chi-square test, Fisher's exact test. P<0.05 is considered statistically significant.

Table III demonstrates that the duration of surgery did not differ significantly between the groups (53.9±12.6 vs. 54.6±7.4). In contrast, other analgesic-related parameters showed significant differences. Group K exhibited a longer time to first analgesic request (5.7±0.9 vs. 2.8±0.6), prolonged duration of analgesia (4.5±3.5 vs. 2.7±1.1), and reduced total opioid consumption (120.6±20.1 vs. 178.3±28.4) compared with Group NS, indicating a distinct analgesic benefit in Group K.

**Table III:** Comparison of clinical variables between groups (N = 90)

Variables	Group K n = 45	Group NS n = 45	p-value
Duration of Surgery (min)	53.9±12.6	54.6±7.4	0.70
Time to First Analgesic Demand (hours)	5.7±0.9	2.8±0.6	<0.05
Duration of Analgesia (hours)	4.5±3.5	2.7±1.1	<0.05
Total opioid Consumption(mg)	120.6±20.1	178.3±28.4	<0.05

Values are presented as absolute numbers (within parenthesis percentage over column total) values were analysed by chi-square test, Fisher’s exact test. P<0.05 is considered statistically significant.

Table IV illustrates the patient satisfaction scores. Across all categories, (very dissatisfied, dissatisfied, neutral, satisfied and very satisfied) the results were not statistically significant between groups.

**Table IV:** Assessment of patient satisfaction scores using Likert scale (N = 90)

Likert Scale	Group K n = 45	Group NS n = 45	P-value
Very dissatisfied	2 (4.4%)	3(6.7%)	0.90
Dissatisfied	14(31.1%)	15(33.3%)	
Neutral	20(44.4%)	17(37.8%)	
Satisfied	9(20%)	10(22.2%)	
Very satisfied	0(0%)	0(0%)	

**Discussion**

Adequate postoperative pain control plays a significant role in surgical outcome as it affects

postoperative mobility, duration of hospital stay, patient satisfaction and overall clinical outcome<sup>15</sup>. Postsurgical pain severity may also be influenced by patient factors including gender, age and anxiety<sup>20</sup>. Total ninety ASA class I-II patients scheduled for laparoscopic cholecystectomy, were allocated into two groups. Group K received ketamine while Group NS received normal saline.

In this study, baseline demographic variables including age, sex, BMI, and ASA score showed statistically nonsignificant differences between Group K and Group NS (p > 0.05), ensuring both cohorts were comparable for subsequent outcome analysis. When compared with other published data, the mean age in this study was somewhat lower than that reported by Maruf, Ershad and Nazrina<sup>21</sup> and by Sudersan, Thangavelu and Segaran<sup>22</sup>. Gender distribution in this study was balanced, consistent with Jain, Nazir and Mustafi<sup>15</sup>, who noted 11 males vs. 10 and 14 females vs. 15, and with Maruf, Ershad and Nazrina<sup>21</sup>, who observed 10 males vs. 11 and 20 females vs. 19. Similar patterns were seen in Sudersan, Thangavelu and Segaran<sup>22</sup>, although with a higher proportion of females (12 males vs. 7 and 14 females vs. 19).

The mean BMI of this study was higher than that reported by Sudersan, Thangavelu and Segaran<sup>22</sup>, who documented lower average BMI(p= 0.316). Regarding ASA scores, predominantly ASA II patients observed, differing from Maruf, Ershad and Nazrina<sup>21</sup>, who reported 22 vs. 23 for ASA I and 8 vs. 7 for ASA II, as well as from Sudersan, Thangavelu and Segaran<sup>22</sup>, who found 20 vs. 11 for ASA I and 6 vs. 15 for ASA II, suggesting variation in the preoperative risk profile across studies.

Comorbidities in this study such as hypertension, diabetes mellitus, and bronchial asthma/COPD showed statistically nonsignificant differences between the Group K and Group NS (p=0.40), confirming that both groups were comparable in terms of baseline clinical status. These findings align with previous reports, where Pereira et al.<sup>17</sup> observed no significant variation in the prevalence of hypertension (p=0.552) or chronic respiratory diseases (p=0.684) between study groups. According

to KarimSaadati et al.<sup>23</sup> and Pereira et al.<sup>17</sup>, there was no meaningful difference in the proportion of patients with diabetes mellitus across study cohorts ( $p=0.460$ ;  $p=0.446$ ).

Postoperative pain intensity in this study, measured by VAS scores, was significantly lower in the Group K during recovery and in the early postoperative period, with statistical significance noted at recovery, 1 hour, and 2 hours ( $p < 0.05$ ), while no significant differences were observed at 6, 12, and 24 hours ( $p=0.30$ ;  $p=0.40$  and  $p=0.20$ ). Jain, Nazir and Mustafi<sup>15</sup> reported low VAS scores in both groups, showing statistical significance at 1 hour ( $p=0.056$ ). But at 2 hours ( $p=0.13$ ), at 6 hours ( $p=0.623$ ), at 12 hours ( $p=0.207$ ) and at 24 hours ( $p=0.137$ ) VAS was statistically nonsignificant. Kundra et al.<sup>24</sup> observed higher pain scores overall, with VAS at 1 hour (2.9 vs. 3.4) and persisting differences up to 24 hours (3.6 vs. 3.7). Maruf, Ershad and Nazrina<sup>21</sup> found reduced scores in the ketamine group at 0 hour ( $p=0.027$ ) and in later time points, at 6 hours ( $p=0.046$ ), at 12 hours ( $p=0.041$ ) and at 24 hours ( $p=0.045$ ) which may be due to variation in drug dose, surgical invasiveness and patients' response. Sudersan, Thangavelu and Segaran (2024) demonstrated the clearest early analgesic benefit, with VAS at 1 hour ( $p<0.001$ ) and at 2 hours ( $p<0.001$ ) and at 6 hours ( $p<0.001$ ), confirming ketamine's strong analgesic effect in early postoperative period.

Heart rate remained similar between the two groups in the preoperative and early intraoperative periods in this study, with no statistically significant differences up to 60 minutes, while a significant divergence was observed at 90 minutes intraoperatively and at 1 hour postoperatively ( $p < 0.05$ ), after which the values stabilized without notable group variation. These findings are in line with Jain, Nazir and Mustafi<sup>15</sup>, who also reported nearly identical preoperative heart rates (75 vs. 77) bpm, and with Sudersan, Thangavelu and Segaran<sup>22</sup>, who found close intraoperative readings across multiple time points and was statistically significant

( $p<0.001$ ). Kundra et al.<sup>24</sup> documented higher preoperative rates (86 vs. 90.7) bpm and more pronounced postoperative variations, including 79.9 bpm vs. 77.3 bpm at 1 hour, 83 bpm vs. 82.9 bpm at 2 hours, 78.25 bpm vs. 86.8 bpm at 6 hours, 80.45 bpm vs. 83.5 bpm at 12 hours, and 82.1 bpm vs. 80.45 bpm at 24 hours, indicating greater fluctuations in their cohort compared to this study which may be due to variation in drug dose and patients body physiology, variation in demographic factors and patients comorbidities.

In this study, systolic blood pressure was comparable between the groups in the preoperative and intraoperative phases up to 90 minutes, with  $p$  values remaining statistically nonsignificant, while in the postoperative period, significantly higher values were observed in the Group NS at 1 and 2 hours ( $p<0.05$ ), which may be due to pain related sympathetic activation. Though differences at 6, 12, and 24 hours were statistically nonsignificant ( $p=0.70$ ;  $p=0.10$ ; and  $p=0.50$ ). Talebi et al.<sup>16</sup> reported a preoperative SBP followed by intraoperative values of at 15 minutes, at 30 minutes, and at 60 minutes, showing close similarity between groups and was statistically nonsignificant ( $p=0.58$ ).

In this study, diastolic blood pressure remained comparable between groups during the preoperative and intraoperative phases, with no significant differences observed at 15, 30, 60, or 90 minutes, while in the postoperative period, a statistically significant rise was noted in Group NS at 1 hour ( $p < 0.05$ ), but all other time points showed no significant variation. Talebi et al.<sup>16</sup> documented stable DBP trends, reporting preoperative values followed by intraoperative readings at 15, 30, 60 minutes indicating close haemodynamic similarity between groups across most intervals and was statistically significant ( $p=0.004$ ).

Mean arterial pressure was comparable between groups at baseline ( $p=0.42$ ) and throughout the intraoperative period in this study, with no significant differences at 15, 30, 60, or 90 minutes ( $p=0.91$ ;  $p=0.60$ ;  $p=0.68$  and  $p=1.00$ ), may be due to uniform

suppression of sympathetic activity by anaesthetic drugs, while in the postoperative period a marked elevation was observed in the Group NS at 1 and 2 hours ( $p < 0.05$ ) which reflected sympathetic activation driven by pain. After which MAP stabilized with no further significant differences. Talebi et al.<sup>16</sup> similarly reported stable intraoperative MAP values and was statistically significant ( $p < 0.001$ ). Likewise, Sudersan, Thangavelu and Segaran<sup>22</sup> observed preoperative MAP values of 93.5 mmHg vs. 93 mmHg, with postoperative readings showed 90 mmHg vs. 91 mmHg at 1 hour and 91 mmHg vs. 87 mmHg at 2 hours, further supporting the trend of haemodynamic stability across groups.

In this study, adverse effects such as nausea and vomiting, hallucination, sedation, tachycardia, and hypertension showed no statistically significant differences between Group K and Group NS ( $p > 0.05$ ), with both groups experiencing comparable rates of these events. This pattern differs from Jain, Nazir and Mustafi<sup>15</sup>, who reported equal nausea and vomiting cases (5 vs. 5) and no hallucinations in either group. Kundra et al.<sup>24</sup> found nausea and vomiting in 15% patients across both groups, with hallucinations observed only in the ketamine group (10% vs. 0%). Maruf, Ershad and Nazrina<sup>21</sup> reported nausea in 10% vs. 13.3%, vomiting in 10% vs. 6.7%, delirium in 16.7% vs. 13.3%, and hallucinations in 10% vs. 6.7%, indicating more variation across adverse outcomes compared to the balanced findings of this study.

In this study, the duration of surgery was comparable between groups with statistically nonsignificant difference ( $p = 0.70$ ), a finding consistent with Jain, Nazir and Mustafi<sup>15</sup>, who reported ( $p = 0.155$ ), and Maruf, Ershad and Nazrina<sup>21</sup>, who found ( $p = 0.783$ ). The time to first analgesic demand in this cohort was significantly prolonged in Group K ( $p < 0.05$ ), aligning with Sudersan, Thangavelu and Segaran<sup>22</sup>, who reported ( $p = 0.001$ ), and Maruf, Ershad and Nazrina<sup>21</sup>, who observed ( $p = 0.021$ ). The duration of analgesia was significantly longer in Group K ( $p < 0.05$ ), a finding supported by Jain, Nazir and

Mustafi<sup>15</sup>, who reported  $16.58 \pm 6.57$  minutes compared to  $1.76 \pm 2.04$  minutes ( $p = 0$ ). Regarding total analgesic consumption, these results showed a marked reduction in Group K ( $p < 0.05$ ), which echoes Jouguelet-Lacoste et al.<sup>25</sup>, who demonstrated a 40% reduction with IV ketamine, though Jain, Nazir and Mustafi<sup>15</sup> found smaller, nonsignificant differences ( $132.0 \pm 7.61$  mg vs.  $150.0 \pm 51.08$  mg,  $p = 0.208$ ).

Patient satisfaction scores assessed using a Likert scale in this study showed statistically nonsignificant differences between Group K and Group NS ( $p = 0.90$ ), with most participants reporting neutral to satisfied responses, while very few were dissatisfied, and none rated themselves as very satisfied. This contrasts with Ahern et al.<sup>26</sup>, who reported markedly higher satisfaction, with 85% of patients stating they would be willing to receive the same medication again, highlighting a stronger positive perception of ketamine use in their cohort compared to the more balanced distribution observed in this finding.

The findings of this study align well with previously published evidence, showing the beneficial role of low-dose intravenous ketamine in postoperative pain management following laparoscopic cholecystectomy. By demonstrating consistent trends across demographic, haemodynamic, analgesic, and patient-centered outcomes, these results add meaningful support to its use as a safe and effective adjuvant in multimodal analgesia.

## Conclusion

Under the condition of present study, it can be concluded that low dose intravenous ketamine reduces the postoperative pain scores, delays first analgesic demand and reduces pethidine consumption. Long-term follow-up is needed to assess the sustained analgesic benefits and safety profile of low-dose intravenous ketamine.

## Declaration:

Ethics approval: The study was approved by the IRB, BMU (Reg. no.5272; BSMMU/2024/11013).

**Author Contributions:**

Conception and development of the idea: SK, DKB

Writing: SK, SGR

Data analysis: SK, MSA, SIA,

Data collection: MAA, PS, MSA, NKS, MAR

Review and Editing: SK, DKB

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