



Effect of Instilling 1 Liter Normal Saline into The Peritoneal Cavity after Laparoscopic Cholecystectomy on Post-Op Pain Relief: A Comparative Analysis

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ABSTRACT

Background: In Pakistan, gall bladder related diseases like cholelithiasis impacts 10% to 15% of adults. Pain control measures remain vital in patients' outcome improvement and the decreased use of analgesics after surgery. A locally adapted solution that will decrease pain and utilize fewer analgesics will be more helpful in limited access setting such as Pakistan where these additional resources in pain management may not be easily available. **Aim:** This research aims to explore the effects of saline instillation on pain relief by making comparison between postoperative pain levels and analgesic consumption patients who receive saline instillation and those who do not. **Methodology:** This comparative study aimed to assess the efficacy of intraperitoneal 1 liter normal saline instillation for pain management after laparoscopic cholecystectomy. Data were collected from February to September 2024 at a tertiary care hospital in Punjab, Pakistan, involving 70 patients (35 males, 35 females) undergoing elective cholecystectomy. Group A (Control) received standard surgery, while Group B received saline instillation. Pain intensity was measured using the VAS scale, and statistical analysis was performed using SPSS. **Results and Conclusion:** This study examined the effects of 1-liter normal saline instillation after laparoscopic cholecystectomy on postoperative pain and opioid use. Results showed that saline significantly reduced pain (mean score: 2.83 vs. 6.06) and analgesic consumption (50.29 mg vs. 91.14 mg) compared to the control group, offering better pain relief and lower medication usage.

INTRODUCTION

Background

Pain is a considerable problem during the postoperative period, especially after many minimally invasive surgeries such as laparoscopic cholecystectomy, frequently used for the treatment of gallbladder disorders. In Pakistan, gall bladder related diseases like cholelithiasis impacts 10% to 15% of adults¹. Laparoscopic cholecystectomy has displaced open surgery as the reference treatment of symptomatic gallstones since it has reduced invasiveness, shorter postoperative recovery time and fewer complications. Nevertheless, postoperative pain persists being a major concern that prolong patient's hospital stay, results in a high rate of analgesia use, and slow recovery².

To reduce the postoperative pain, efforts such as instillation of fluid like normal saline within the peritoneal cavity has been used³. Such technique decreases pain since it prevents the peritoneum from becoming irritated and reducing the inflammation response. Although evidence indicates significant advantages, its effectiveness remains uncertain due to a lack of data regarding postoperative pain control with laparoscopic surgery from the Pakistani context.

Postoperative Pain in Laparoscopic Surgeries

Laparoscopic cholecystectomy that involves the removal of gall bladders through small incisions has received

widespread acceptance since its practice is not much invasive⁴. Nevertheless, this is not an advantage because after the operation, many patients suffer from severe pain, which negatively influences the recovery progress⁵. Pain following the surgery is classified as visceral pain from gallbladder bed and parietal pain from the incision. The severity of this pain depends on some conditions like peritoneal inflammation, CO₂ residual pneumoperitoneum, and operative injury. A cross-sectional survey of patients from Pakistan documented moderate to severe pain that has been measured between 4 to 7 VAS (Visual Analogue Scale) in Pakistani patients after LS⁶.

Pain control measures remain vital in patients' outcome improvement and the decreased use of analgesics after surgery. Rajput⁷ showed that failure to adequately manage patients' pain may create extended hospitalizations, delayed ambulation, and higher rates of persistent pain. Furthermore, failure to adequately control pain leads to increased use of opioid analgesics with predictable side effects including nausea, vomiting and respiratory compromise⁸.

The Role of Saline Instillation in Pain Management

Intraperitoneal instillation with normal saline solution is a recent innovation that seeks to minimize pain intensity after the surgery is conducted via laparoscopy. Pillai⁹ claimed that saline forms a protective layer between the diaphragm and residual CO₂ largely cause shoulder pain after laparoscopy. In addition, saline may also assist in the decrease pain by decreasing the concentration of such mediators of inflammation. Intraperitoneal saline installation application as a pain relief approach in under-studied in Pakistan. Modern therapies of pain involve the use of NSAIDs (non-steroidal anti-inflammatory drugs) and opioids as the principal treatments, both of which present adverse effects such as gastrointestinal irritation and opioid dependency, respectively¹⁰. A locally adapted solution that will decrease pain and utilize fewer analgesics will be more helpful in limited access setting such as Pakistan where these additional resources in pain management may not be easily available.

Laparoscopic Cholecystectomy in Pakistan: Current Practices and Challenges

Gallbladder diseases, including gallstones affect Pakistanis with an overall prevalence rate of gallstone being 9% in women and 5% in men¹¹. Although the technique itself has been defined, further developments need to be achieved in the field of management of patients after surgery and, in particular, in the management of pain. However, opioids have negative side effects including their addictive properties, which make the treatment expensive to the healthcare system. Furthermore, the operating procedures have improved over the years, most of the health care centers in Pakistan

are challenged with inadequate equipment, few staff and poor pain control policy. Such reasons call for new strategies which could include the instillation of saline, which might prove to be cheaper, accessible and effective means towards managing postoperative pains.

Significance of the Study

Since gallbladder diseases are highly common in Pakistan and laparoscopic cholecystectomy is commonly performed, an efficient postoperative pain control protocol is important. This research assumes considerable importance especially in a resource poor country like Pakistan because the care given to the patients after the surgery has impacts on the patient outcomes, the resources used in the operation of the healthcare facilities and the costs incurred.

Objectives of the Study

This research aims to explore the effects of saline instillation on pain relief by making comparison between postoperative pain levels and analgesic consumption patients who receive saline instillation and those who do not. Following are the objectives of the research:

- To demonstrate if there is a prominent variation in postoperative pain levels (VAS scores) between the experimental group (saline instillation) and the control group (no saline instillation) after laparoscopic cholecystectomy.
- To make comparison between two groups with analgesic consumption to evaluate whether saline installation overcomes the need for pain medication

METHODOLOGY

Study Design

This research was designed in a comparative manner to compare the efficacy of intraperitoneal instillation of 1 liter of normal saline on the management of pain after laparoscopic cholecystectomy. The study involved two groups of patients: a group of patients who was given standard postoperative care (control group), while the other set was given Laparoscopic cholecystectomy with the instillation of 1 liter of normal saline into the peritoneal cavity post-surgery (experimental group). Data were documented over eight months of the year 2024, and the particular month in which data was collected is February- September, 2024 in a tertiary care hospital in Punjab, Pakistan.

Study Population and Sampling

A sample of 70 patients (35 males and 35 females) undergoing elective laparoscopic cholecystectomy because of symptomatic gallstone disease were recruited into the study. The sample size was sufficient to detect variations in postoperative pain levels between the groups. Group A (Control Group) were those who undergo standard laparoscopic cholecystectomy without saline instillation while Group B (Experiment Group)

was those patients who were given Laparoscopic cholecystectomy with the instillation of 1 liter of normal saline into the peritoneal cavity post-surgery.

Inclusion and Exclusion Criteria

Table 1

The inclusion and exclusion criteria for the research given below to make sure the appropriate participants selection:

Inclusion Criteria	Exclusion Criteria
Patients aged 18 to 65 years	Conversion to open cholecystectomy
Electively undergoing laparoscopic cholecystectomy	History of chronic pain or regular opioid use
	Allergy to saline or local anesthetics
	Pregnant or lactating
	Intra-abdominal infections or peritonitis

Data Collection

Data of this study was collected from February 2024 to September 2024 to get a more systematic and comprehensive assessment of the medical patients' recovery. Information on all cases was collected systematically with an aim of identifying several variables that would enhance a strong analysis. To keep anonymity, each participant's Patient ID was documented. There was also evidence of group allocation as the researcher separated the two groups into control and experimental groups for evaluation. It was also recorded that whether the patients got saline instillation or not because this defined the assessment of the performance of the intervention¹².

Evaluation of pain relief after the surgery was conducted using the Visual Analogue Scale (VAS) at 4 hours of surgery. Self-reported intensity by VAS is a validated approach as it measured pain intensity using the scales that range from 0 (no pain) to 10 (worst possible pain)¹³. This approach not only gave the level of pain at various time intervals but also the actual effects of the treatment on the patient in a short-term basis and a long-term basis. This measure enabled the researcher to compare the efficacy of saline instillation in the reduction of the requirement for supplemental analgesic administration. Age was measured in years; gender as male or female; the duration of the surgery in minutes; and the number of days of the hospital stay while further demographic data was obtained to support the outcomes and to test for correlations with postoperative results. The presence of these variables enabled one to evaluate the key factors in relation to pain and its treatment¹⁴.

In total, 70 patients that qualified to the set criteria were randomly assigned to the two groups after receiving a detailed description of the study, and giving consent. All surgeries were carried out by consultants in the surgical unit II in the specified hospital, to ensure the research has uniformity in terms of qualified surgeons for the sampled patient population.

Statistical Analysis

Statistical analysis was done on SPSS software. Age, gender, duration of surgery and stay in the hospital were assessed using descriptive statistics such as means and standard deviations. Independent t-tests were used to determine the differences in the primary outcomes VAS scores and mean analgesic consumption between the two groups. When making comparisons, the statistical significance was set at $p < 0.05$ ¹⁵.

Ethical Considerations

The study was done ethically with permission from the Ethical Review Board of the hospital. Each patient was offered written informed consent before participating in the study. The objectives of the study were clearly explained to the participants as well as any significant risk and benefit was conveyed. All patients' identities were removed from the study to ensure that their privacy and confidentiality were strongly observed.

RESEARCH FINDINGS AND RESULTS

Table 2

Demographic Analysis

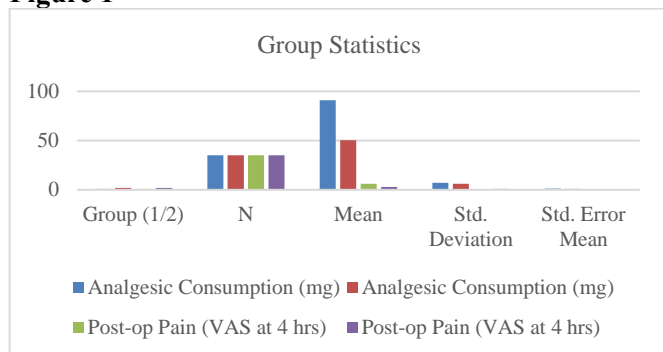
Gender					
Valid		Frequency	Percent	Valid Percent	Cumulative Percent
	male	35	50.0	50.0	50.0
	female	35	50.0	50.0	100.0
	Total	70	100.0	100.0	

The participant's gender distribution was kept balanced, with males (50%) and females (50%). This equal representation means that findings associated with postoperative pain relief and, consequently, analgesic consumption will not be skewed in any way by gender; thus, can be generalized¹⁶. The inclusion of an equal male and female participants, this research assessed reliably how the saline instillation intervention impacts postoperative outcomes throughout the gender. This contributes to an extensive pain management understanding in laparoscopic cholecystectomy patients.

Table 3

Group Statistics

Group Statistics					
	Group (I/2)	N	Mean	Std. Deviation	Std. Error Mean
Analgesic Consumption (mg)	1	35	91.14	7.080	1.197
	2	35	50.29	6.295	1.064
Post-op Pain (VAS at 4 hrs)	1	35	6.06	.765	.129
	2	35	2.83	.785	.133

Figure 1

It has been demonstrated from the group statistics that there are significant variations in both analgesic consumption and postoperative pain levels between Group 1 and Group 2. For analgesic consumption, the control group, which did not receive saline instillation, had a mean consumption of 91.14 mg (SD = 7.080), while the experimental group, which received saline

instillation, reported a substantially lower mean of 50.29 mg (SD = 6.295). It implies that the saline interventions were efficient in overcoming the analgesics amount required postoperatively.

Regarding postoperative pain assessed at 4 hours using the Visual Analogue Scale (VAS), the control group experienced a mean pain score of 6.06 (SD = 0.765), whereas the experimental group reported a significantly lower mean pain score of 2.83 (SD = 0.785). Such results are supported by the confidence intervals with the mean difference of analgesic consumptions at 95% Confidence Interval was found to be 37.662 to 44.053 and for the pain scores was found to be 2.859 to 3.598. These findings eminence the clinical application of the saline instillation in patients' relief from postoperative pain and therefore, need of fewer analgesics, making the procedure notably beneficial for improving the recovery process.

Table4*Independent Samples Test*

Independent Samples Test										
		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Analgesic Consumption (mg)	Equal variances assumed	1.687	.198	25.515	68	.000	40.857	1.601	37.662	44.053
	Equal variances not assumed			25.515	67.081	.000	40.857	1.601	37.661	44.053
Post-op Pain (VAS at 4 hrs)	Equal variances assumed	.445	.507	17.424	68	.000	3.229	.185	2.859	3.598
	Equal variances not assumed			17.424	67.952	.000	3.229	.185	2.859	3.598

The Independent Samples Test results offer compelling evidence of the efficacy of saline instillation in the management of postoperative results. For analgesic consumption, Levene's Test indicated equal variances ($F = 1.687$, $p = 0.198$), which allows us to interpret the t-test results confidently. The t-test yielded a t-value of 25.515 with 68 degrees of freedom and a p-value of 0.000, indicating a statistically significant difference in analgesic consumption between the two groups. Such mean differences (i.e. 40.857 mg) indicates that the group who received saline (experiment group) consumed significantly less analgesic medication in comparison with the control group. Same as, for measured postoperative pain at 4 hours, the conducted Levene's Test indicated equal variances ($F = 0.445$, $p = 0.507$).

The t-test results showed a t-value of 17.424 with 68 degrees of freedom and a p-value of 0.000. This means that a significance declined in pain scores confirmed in the experiment group. The mean differences (3.229) on the VAS mirrors a significant decline in the levels of pain among patients who received saline installation. The confidence interval reinforces such results, with confidence interval (95%) for the mean differences in analgesic consumption that range from 37.662 to 44.053 mg while the pain scores from 2.859 to 3.598. the research findings show the clinical importance of saline instillation in overcoming postoperative pain and analgesic needs. This makes it a useful approach to enhance recovery after laparoscopic cholecystectomy.

Table 5
Independent Samples Effect Sizes

Independent Samples Effect Sizes					
		Standardizer ^a	Point Estimate	95% Confidence Interval	
				Lower	Upper
Analgesic Consumption (mg)	Cohen's d	6.699	6.099	4.970	7.219
	Hedges' correction	6.774	6.032	4.914	7.140
	Glass's delta	6.295	6.491	4.880	8.091
Post-op Pain (VAS at 4 hrs)	Cohen's d	.775	4.165	3.319	5.001
	Hedges' correction	.784	4.119	3.282	4.946
	Glass's delta	.785	4.111	3.025	5.184

The denominator used in estimating the effect sizes

Cohen's d uses the pooled standard deviation.

Hedges' correction uses the pooled standard deviation, plus a correction factor.

Glass's delta uses the sample standard deviation of the control group.

The effect sizes derived from the Independent Samples analysis offers a differences magnitude between the experiment and control group. For analgesic consumption, the effect size measured by Cohen's d is 6.699, which indicates a very large effect. The 95% Confidence Interval for Cohen's d ranges from 6.099 to 7.219, further confirming the strength of this effect. Hedges' correction yields a similar point estimate of 6.774, emphasizing the consistency of the finding, while Glass's delta at 6.295 supports the interpretation of a substantial reduction in analgesic needs due to saline instillation. In terms of postoperative pain assessed at 4 hours, Cohen's d is reported at 0.775, indicating a moderate to large effect size. The confidence interval for this measure ranged from 3.319 to 5.001, which indicates that saline instillation helps in decreasing pain significantly in the experimental group. Hedges' correction and Glass's delta offers comparable values of

0.784 and 0.785, respectively – this validates the intervention effectiveness.

These effect sizes underscore the clinical relevance of saline instillation in decreasing not only the amount of analgesic administered but also the level of postoperative pain; thus, its implementation is considered a useful effort in enhancing client outcome after laparoscopic cholecystectomy. The highly significant findings for frequency of analgesic consumption support the effectiveness of this technique to have a genuine large impact on clinical pain management habits.

Descriptive Statistics

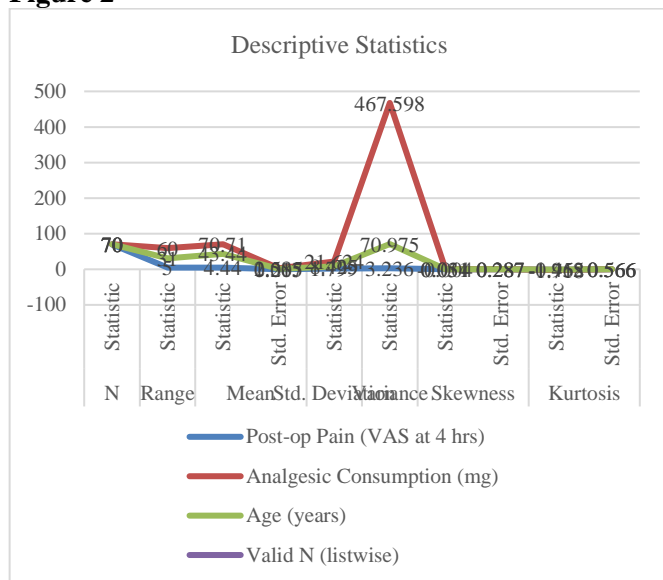
The descriptive statistics offers extensive key variables overview that focuses on postoperative pain, age and analgesic consumption. For postoperative pain assessed at 4 hours using the Visual Analogue Scale (VAS), the sample comprised 70 participants. The pain scores ranged from a minimum of 1 to a maximum of 6, resulting in a mean score of 4.44 (SD = 0.215), indicating a moderate level of pain experienced by patients. The variance of 1.799 suggests some variability in pain levels among participants, while the skewness of -0.004 indicates a nearly symmetrical distribution of pain scores. The kurtosis value of -1.452 signifies a platykurtic distribution, suggesting a flatter peak than a normal distribution. In terms of analgesic consumption, also with 70 participants, the range of consumption varied widely from 10 mg to 70 mg, yielding a mean of 70.71 mg (SD = 2.585). The high variance of 21.624 highlights significant differences in analgesic use among patients, which may be influenced by their individual pain experiences. The skewness of 0.034 suggests that the distribution is relatively normal, while the kurtosis of -1.718 indicates a slightly flatter distribution than normal.

Regarding age, the participants' ages ranged from 18 to 49 years, with a mean age of 43.44 years (SD = 1.007). The variance of 8.425 reflects some diversity in the age of the patients, while the skewness of 0.051 indicates a symmetrical distribution of ages. The kurtosis of -0.965 suggests a distribution that is less peaked than normal.

Table 6

Descriptive Statistics										
	N	Range	Mean	Std. Deviation	Variance	Skewness	Kurtosis			
	Statistic	Statistic	Statistic	Std. Error	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
Post-op Pain (VAS at 4 hrs)	70	5	4.44	.215	1.799	3.236	-.004	.287	-1.452	.566
Analgesic Consumption (mg)	70	60	70.71	2.585	21.624	467.598	.034	.287	-1.718	.566
Age (years)	70	31	43.44	1.007	8.425	70.975	.051	.287	-.965	.566
Valid N (listwise)	70									

Figure 2



DISCUSSION

Objective 1: Significant Difference in Postoperative Pain Levels

This research postulates that there is a significant disparity in postoperative pain levels between the experimental group (saline instillation) and the control group (no saline instillation). In the control group, their total mean VAS for pain measured was 6.06, while the experimental group who underwent saline instillation tested. In line with the research findings, Kepenekian¹⁷ and Amer-Cuenca¹⁸ asserted that interventions enhancing peritoneal cavity stimulation are effective for overcoming pain relief. In particular, Adlan¹⁹ pointed out a decrease in the mean pain scores after the administering of saline in a group of Laparoscopic surgery. However, the current study differs from some of similar studies such as Stamenkovic²⁰ that stressed on saline instillation as a useful technique and recommends it as an option to the normal pain control measures. Furthermore, while it is common for prior research adopted different surgical procedure while the current research focused on laparoscopic cholecystectomy to determine other differences in pain management efforts in this manner.

Objective 2: Comparison of Analgesic Consumption

This research achieves the second objective by revealing that the experimental group consumed less of analgesic medication, with a mean of 50.29 mg compared to 91.14 mg in the control group. With, a Cohen's d of 6.699, saline instillation reduces the patients' requirement for pain medicine significantly. These findings correspond with the study by Bai²¹ that showed that those patients, who received local anesthetics or saline instillation, had lower doses of analgesics, which led to the change in pain management practices. Moreover, unlike Fakhri²² who investigated several methods of surgery, the studied work analyzes only laparoscopic cholecystectomy and

compares the most suitable analgesics for this particular intervention, which is crucial to determine concrete demands on the analgesia in this method. The level of detail is useful in expanding the current body of knowledge and establishing the possibility for saline instillation to be utilized routinely in surgical recovery. The findings also contradicted the research findings of Stamenkovic²³ who noted that there could be minimal differences in the overall use of analgesics in specific patients. In contrast, it found significantly stronger evidence for the effect of saline instillation on the requirement of an analgesic. Although the results concern pain and amount of administered analgesics, the results likely imply, that intervention's effectiveness may not vary significantly with demographic factors such as age and gender. However, no correlation analyses have been made to show how some of these factors can physically affect the results. According to Petersen²⁴, there is evidence that demographic characteristics can influence both pain and therapeutic responses and, therefore, should be treated in future studies. The prior research frequently documents the presence of the substantial demographic differences and its moderations with pain result. Studies could also use control variables to investigate whether saline instillation has differential efficacy for patients of different age, gender so that a clearer picture of its overall utility can be determined.

CONCLUSION AND RECOMMENDATIONS

Conclusion

This research explored the effects of introducing 1 liter of normal saline into the peritoneal cavity after laparoscopic cholecystectomy in managing postoperative pain and opioids use. The findings suggested that saline instillation not only provided better pain relief to patients in the procedure, but also reduced their need for analgesic medications compared to the patients in the control group. In comparing the experimental group to the control group at the 4 hours after surgery, a significantly lower mean pain score of 2.83 was obtained the experimental group as compared to 6.06 among the control group. Analgesic consumption was significantly reduced, with the experimental group using an average of 50.29 mg compared to 91.14 mg in the control group. From these analyses, there is the possibility that saline instillation should be implemented as a complementary method in postoperative pain control, giving patients additional comfort and possibly decreasing the cost to the healthcare systems.

Recommendation

Clinical Protocol Development: Saline instillation during laparoscopic cholecystectomy should follow strict, clinical guidelines that would allow for increased standardization of the practice²⁵. Such protocols should prescribe the ranges of the volume and concentration of

the saline to be infused depending on one's patient. For example, it will be stated that for children, to instill, normal saline at room temperature at a rate of 1 liter should be given, dependent on patient weight. It also reduces variation within the surgical teams to give consistent results and requires fewer other methods of pain management.

Training Programs: Extensive educational sessions for surgical personnel are essential to achieving competence in the practice of saline infusion²⁶. These programs should address the technicality of use of saline and the advantage of saline use. For example, practical exercises could include exposure to the installation process where the staff would be exposed to the process with the help of supervisor²⁷. Adding examples of previous implementations, improvements can be identified in the ability to reduce the usage of opioids and where there is an enhancement in the scores of the pain that patients experienced will also explain the advantages.

Patient Education: Education for patients is needed to develop acceptance of saline instillation as a pain management approach. As per Aroke²⁸, educating patients related to the advantages like declined postoperative pain and lower dependency on analgesics can elevate their involvement in the process of care. For instance, preoperative sessions in which surgical teams explain the procedure and deal with the concerns of patients can develop better understanding and trust.

Research Implication

By developing a significantly efficient and inexpensive intervention for the management of postoperative pain, the research points out the usefulness to evaluate the alternative pain management techniques, especially in resource-limited settings. Therefore, if the use of saline instillation is useful for each process, then the efficiency

of all other procedures that are performed throughout various operations can be improved.

Limitations

The participants seem adequate for early exploration but increasing the sample size would help boost the effect size of the results and overcome limitations of generalizability. Another considerable limitation is performing research in a single hospital that restricts it from generalizability to other areas that might have difference patient characteristics, surgery procedures, and postoperative care mechanisms. The period for follow-up was also limited that fails to assess the prolonged pain results or significant challenges regarding saline instillation. Besides, this research was not blinded that may lead to bias in the pain score and analgesic consumption reporting as both providers and patients may have had preconceived ideas related to the saline installation advantages. The differences in pain assessment that depends on self-reported statistic numeric rating scale may also result subjectivity on the basis of the individual pain threshold and behaviors of reporting.

Direction for Future Research

There is a need for future prospective and execution of studies to determine more impact of saline instillation on chronic pain emergence and recovery rate in various surgical patients. Researchers in the future can conduct research on how saline works to decrease pain and inflammation may also shed light on the parameters that should be employed when using saline to treat pain. More comparative studies are required to demonstrate saline installation against the pain management approaches for developing well-informed clinical decision-making in other surgical aspect beyond laparoscopic cholecystectomy in postoperative settings.

REFERENCES

1. Ali, M., Usman, A., Usman, J., Abid, M., Najeeb, W., Imran, M., & Fakihi, N. (2024). Significance of family history of cholelithiasis in a Pakistani population: A single center, descriptive cross-sectional study. *Medicine*, 103(28), e38925. <https://doi.org/10.1097/md.00000000000038925>
2. Kehlet, H. (2018). Postoperative pain, analgesia, and recovery—bedfellows that cannot be ignored. *Pain*, 159(1), S11-S16. <https://doi.org/10.1097/j.pain.00000000000001243>
3. Adlan, A. S., Azhary, J. M., Tarmidzi, H. Z., Kamarudin, M., Lim, R. C., & Ng, D. S. (2022). Post laparoscopy pain reduction project I (POLYPREP I): Intraperitoneal normal saline instillation—a randomised controlled trial. *BMC Women's Health*, 22(1). <https://doi.org/10.1186/s12905-022-01696-z>
4. Gaziev, K. U. (2022). Current Views on Laparoscopic Cholecystectomy. *Central Asian Journal of Medical and Natural Science*, 3(3), 767-774.
5. Echeverria-Villalobos, M., Stoicea, N., Todeschini, A. B., Fiorda-Diaz, J., Uribe, A. A., Weaver, T., & Bergese, S. D. (2019). Enhanced recovery after surgery (ERAS): a perspective review of postoperative pain management under ERAS pathways and its role on opioid crisis in the United States. *The Clinical Journal of Pain*, 36(3), 219-226. <https://doi.org/10.1097/ajp.0000000000000792>
6. Baig, A. A., Ansari, B., Ahmed, S. I., Ishaque, F., & Farooqui, W. A. (2024).

- Association of demographics, lumbar active range of motion and disability in chronic low back: A baseline data analysis of a randomized controlled trial from Pakistan. *BMC Musculoskeletal Disorders*, 25(1). <https://doi.org/10.1186/s12891-024-07613-9>
7. Rajput, K., & Vadivelu, N. (2021). Acute pain management of chronic pain patients in ambulatory surgery centers. *Current Pain and Headache Reports*, 25(1). <https://doi.org/10.1007/s11916-020-00922-3>
 8. Rosen, D. M., Alcock, M. M., & Palmer, G. M. (2022). Opioids for acute pain management in children. *Anaesthesia and Intensive Care*, 50(1-2), 81-94. <https://doi.org/10.1177/0310057x211065769>
 9. Pillai, V. P. (2020). *A Comparative Study to Assess the Impact of Low Pressure versus Standard Pressure Pneumoperitoneum on Shoulder Tip Pain after Laparoscopic Surgery* (Doctoral dissertation, BLDE (DU)).
 10. Bindu, S., Mazumder, S., & Bandyopadhyay, U. (2020). Non-steroidal anti-inflammatory drugs (NSAIDs) and organ damage: A current perspective. *Biochemical Pharmacology*, 180, 114147. <https://doi.org/10.1016/j.bcp.2020.114147>
 11. Ali, M., Usman, A., Usman, J., Abid, M., Najeeb, W., Imran, M., & Fakihi, N. (2024). Significance of family history of cholelithiasis in a Pakistani population: A single center, descriptive cross-sectional study. *Medicine*, 103(28), e38925. <https://doi.org/10.1097/md.00000000000038925>
 12. Chang, S. J., Kim, E., Kwon, Y. O., Im, H., Park, K., Kim, J., Jeong, D., Kim, D., & Park, J. H. (2023). Benefits and harms of normal saline instillation before endotracheal suctioning in mechanically ventilated adult patients in intensive care units: A systematic literature review and meta-analysis. *Intensive and Critical Care Nursing*, 78, 103477. <https://doi.org/10.1016/j.iccn.2023.103477>
 13. Shafshak, T. S., & Elnemr, R. (2020). The visual analogue scale versus numerical rating scale in measuring pain severity and predicting disability in low back pain. *JCR: Journal of Clinical Rheumatology*, 27(7), 282-285. <https://doi.org/10.1097/rhu.0000000000001320>
 14. Schnabel, A., Yahiaoui-Doktor, M., Meissner, W., Zahn, P. K., & Pogatzki-Zahn, E. M. (2020). Predicting poor postoperative acute pain outcome in adults: An international, multicentre database analysis of risk factors in 50,005 patients. *PAIN Reports*, 5(4), e831. <https://doi.org/10.1097/pr9.00000000000000831>
 15. Lenz, G. S., & Sahn, A. (2020). Achieving statistical significance with control variables and without transparency. *Political Analysis*, 29(3), 356-369. <https://doi.org/10.1017/pan.2020.31>
 16. Eklund, I., Larsson, A., Gustafsson, S., & Forsberg, A. (2020). Patients' experiences of pain and postoperative nausea and vomiting in the early postoperative period after an elective knee arthroplasty. *Journal of PeriAnesthesia Nursing*, 35(4), 382-388. <https://doi.org/10.1016/j.jopan.2019.11.010>
 17. Kepenekian, V., Bhatt, A., Péron, J., Alyami, M., Benzerdjeb, N., Bakrin, N., Falandry, C., Passot, G., Rousset, P., & Glehen, O. (2022). Advances in the management of peritoneal malignancies. *Nature Reviews Clinical Oncology*, 19(11), 698-718. <https://doi.org/10.1038/s41571-022-00675-5>
 18. Amer-Cuenca, J. J., Marín-Buck, A., Vitale, S. G., La Rosa, V. L., Caruso, S., Cianci, A., & Lisón, J. F. (2019). Non-pharmacological pain control in outpatient hysteroscopies. *Minimally Invasive Therapy & Allied Technologies*, 29(1), 10-19. <https://doi.org/10.1080/13645706.2019.1576054>
 19. Adlan, A. S., Azhary, J. M., Tarmidzi, H. Z., Kamarudin, M., Lim, R. C., & Ng, D. S. (2022). Post laparoscopy pain reduction project I (POLYPREP I): Intraperitoneal normal saline instillation—a randomised controlled trial. *BMC Women's Health*, 22(1). <https://doi.org/10.1186/s12905-022-01696-z>
 20. Stamenkovic, D. M., Bezmarevic, M., Bojic, S., Unic-Stojanovic, D., Stojkovic, D., Slavkovic, D. Z., Bancevic, V., Maric, N., & Karanikolas, M. (2021). Updates on wound infiltration use for postoperative pain management: A narrative review. *Journal of Clinical Medicine*, 10(20), 4659. <https://doi.org/10.3390/jcm10204659>
 21. Bai, J. W., An, D., Perlas, A., & Chan, V. (2020). Adjuncts to local anesthetic wound infiltration for postoperative analgesia: A

- systematic review. *Regional Anesthesia & Pain Medicine*, 45(8), 645-655. <https://doi.org/10.1136/rapm-2020-101593>
22. Fakhri, T., Kumar, V., Kumari, N., & Singh, R. (2023). Comparative Study Of Intravenous Paracetamol And Dexmedetomidine On Perioperative Hemodynamics And Postoperative Pain Relief For Laparoscopic Cholecystectomy. *Journal of Pharmaceutical Negative Results*, 14(2). <https://doi.org/10.47750/pnr.2023.14.02.74>
 23. Stamenkovic, D. M., Bezmarevic, M., Bojic, S., Unic-Stojanovic, D., Stojkovic, D., Slavkovic, D. Z., Bancevic, V., Maric, N., & Karanikolas, M. (2021). Updates on wound infiltration use for postoperative pain management: A narrative review. *Journal of Clinical Medicine*, 10(20), 4659. <https://doi.org/10.3390/jcm10204659>
 24. Petersen, K. K., Vaegter, H. B., Stubhaug, A., Wolff, A., Scammell, B. E., Arendt-Nielsen, L., & Larsen, D. B. (2020). The predictive value of quantitative sensory testing: A systematic review on chronic postoperative pain and the analgesic effect of pharmacological therapies in patients with chronic pain. *Pain*, 162(1), 31-44. <https://doi.org/10.1097/j.pain.0000000000002019>
 25. Moldovan, C., Cochior, D., Gorecki, G., Rusu, E., & Ungureanu, F. (2021). Clinical and surgical algorithm for managing iatrogenic bile duct injuries during laparoscopic cholecystectomy: A multicenter study. *Experimental and Therapeutic Medicine*, 22(6). <https://doi.org/10.3892/etm.2021.10821>
 26. Gorski, L. (2022). *Phillips' Man of IV Therapeutics: Evidence-Based Practice for Infusion Therapy*. FA Davis.
 27. Lingard, H., Zhang, R. P., LaBond, C., Clarke, J., & Doan, T. (2022). Situated learning: How interactions with supervisors shape construction apprentices' safety learning and practice. *Journal of Construction Engineering and Management*, 148(10). [https://doi.org/10.1061/\(asce\)co.1943-7862.0002371](https://doi.org/10.1061/(asce)co.1943-7862.0002371)
 28. Aroke, E. N., McMullan, S. P., Woodfin, K. O., Richey, R., Doss, J., & Wilbanks, B. A. (2020). A practical approach to acute postoperative pain management in chronic pain patients. *Journal of PeriAnesthesia Nursing*, 35(6), 564-573. <https://doi.org/10.1016/j.jopan.2020.03.002>