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## Association of Severity of Cholecystitis and Gallstone Size

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### ABSTRACT

**Background:** Cholecystitis, an inflammation of the gallbladder, most commonly arises in association with gallstone disease. Understanding the relationship between these two entities has important clinical implications. The objective of this study was to determine the association between the severity of cholecystitis and gallstone size.

**Place and Duration of Study:** Department of Surgery, Combined Military Hospital, Rawalpindi, from 22<sup>nd</sup> August 2024 to 21<sup>st</sup> September 2024.

**Methodology:** This study utilized a cross-sectional design to explore the relation between severity of cholecystitis as assessed by the Parkland grading system and gallstone size, following Ethics Review Board approval. The sample included 67 respondents diagnosed with cholecystitis who underwent laparoscopic cholecystectomy during the study period after obtaining written consent. Data on Parkland grading scores and gallstone size were collected. Gallstone diameter was measured using vernier callipers, while patients' severity of cholecystitis during surgical intervention was labelled as per Parkland grading. Gallstone size served as the dependent variable, and Parkland grading was the independent variable.

**Results:** Study show that there is a statistically significant association between the severity of cholecystitis and gallstone size ( $p < 0.001$ ). This suggests that more severe grades of cholecystitis were associated with larger gallstone sizes.

**Conclusion:** A significant relationship was observed between the Parkland Grading Score and Gallstone size.

**Keywords:** Cholecystitis, Gallstone Size, Parkland Grading, Clinical Assessment, Gallstones, Statistical Analysis, Gallstone Disease

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## INTRODUCTION

Cholecystitis, an inflammation of the gallbladder, along with gallstones are a common pathophysiological condition and a global health issue affecting millions worldwide.<sup>1,2</sup>

Gallstones are rigid formations develop within the gallbladder, and their size often dictates the severity of clinical symptoms and the treatment approach required.<sup>3,4</sup>

The Parkland grading system is a clinical tool used to assess the severity of conditions associated with gallstones<sup>3-6</sup>. The Parkland Grading Scale system comprises of five grades. Grade 1 indicates a normal gallbladder (GB) with no adhesions. Grade 2 involves minor adhesions at the neck of the gallbladder. Grade 3 is characterized by the presence of any of the following: hyperaemia, peri-cholecystic fluid, adhesions to the body of the gallbladder, or a distended gallbladder. Grade 4 includes cases with adhesions obscuring much of the gallbladder or Grades 1–3 accompanied by abnormal liver anatomy, intrahepatic gallbladder, or an impacted stone (Mirizzi syndrome). Finally, Grade 5 encompasses conditions such as perforation, necrosis, or the inability to visualize the gallbladder due to extensive adhesions.

Gallstones are often associated with more severe clinical manifestations such as biliary pancreatitis, particularly when they cause obstructions.<sup>3</sup>

However, the precise relationship between the severity of cholecystitis and gallstone size is not fully understood. The need for a better understanding of this association is particularly urgent, as gallstone disease is one of the leading causes of emergency surgical admissions globally, placing a substantial burden on healthcare systems.<sup>1-3</sup>

This research aims to elucidate the link between the severity of cholecystitis and gallstone size. Understanding the factors that influence gallstone size is critical for anticipating the progression and severity of the disease, as well as for guiding treatment decisions.<sup>7</sup>

By establishing this connection, doctors may enhance risk stratification, optimize treatment strategies, and improve prognostic capabilities. This study is poised to contribute valuable insights into the relationship between cholecystitis and cholelithiasis followed by its management.

## METHODOLOGY

### Study Design

This was a cross-sectional study conducted to investigate the relationship between the severity of cholecystitis, as assessed by the Parkland grading system, and gallstone size. The study was approved by the Ethics Review Board of Combined Military Hospital Rawalpindi.

### Inclusion and Exclusion Criteria

#### Inclusion Criteria

Patients aged 18 years and older, diagnosed with cholecystitis based on clinical, laboratory, imaging findings and having at least one gallstone confirmed via imaging were included. All participants provided informed consent.

#### Exclusion Criteria

Patients with a history of chronic cholecystitis without acute exacerbation, prior cholecystectomy, or other gallbladder conditions (e.g., gallbladder cancer, biliary colic without cholecystitis) were excluded. Individuals with severe comorbidities, such as advanced liver disease or renal failure, as well as pregnant individuals and those unable or unwilling to comply with the study protocols, were also excluded.

## Data Collection

Occurrence of cholecystitis and cholelithiasis was determined through a review of medical records and direct interviews after obtaining consent. The sample size of 67 patients who met the inclusion criteria underwent laparoscopic cholecystectomy at the Department of Surgery between August 22, 2024, and September 21, 2024. The size of the gallstones was measured postoperatively using Vernier Calipers, recorded in millimetres. The severity of cholecystitis was evaluated using the Parkland grading system.<sup>10,11</sup>

The Parkland Grading Scale classifies gallbladder conditions into five grades:

- **Grade 1:** Normal gallbladder with no adhesions.
- **Grade 2:** Minor adhesions at the gallbladder neck.
- **Grade 3:** Includes hyperaemia, pericholecystic fluid, adhesions to the body, or a distended gallbladder.
- **Grade 4:** Severe adhesions obscuring much of the gallbladder or abnormalities like impacted stones or abnormal liver anatomy.
- **Grade 5:** Conditions such as perforation, necrosis, or inability to visualize the gallbladder due to extensive adhesions.

## Data Analysis

Quantitative analysis was done by using the software called Statistical Package for Social Sciences (SPSS), version 25. Hence, quantitative variables are presented as mean and standard deviation while percentages and frequencies are calculated for qualitative variables. Association between severity of cholecystitis and gallstone size was compared by the analysis of variance

(ANOVA) to test the significance of association between various grades of severity of cholecystitis and stone size ( $p$ -value  $\leq 0.05$ ). Study confounders such as age, gender, and BMI were controlled by stratification. Post stratification ANOVA test was applied and a  $p$ -value  $\leq 0.05$  was considered statistically significant.

## RESULTS

### Clinical and Demographic Profile

The study was female-dominant with cumulative mean age as  $41.60 \pm 10.04$  years (ranging from 18 to 66 years). Other descriptive variables such as BMI and cholesterol level in the total study population calculated as  $27.36 \pm 3.99$  kg/m<sup>2</sup> and  $198.06 \pm 18.20$  mg/dL. The mean gallstone size was  $22.20 \pm 3.99$  mm, ranging from 15.12 mm to 31.35 mm. Patients were further categorized in different age and BMI groups and it was observed that majority of patients fell into the 40-49 years age group (41.8%), followed by <40 years (38.8%), on the other hand, most of the patients were overweight (25-29 kg/m<sup>2</sup>), representing 43.3% of the study population. The most common severity grade observed was Grade 3 (31.3%), followed by Grade 4 (23.9%). However, the highest severity grade (Grade 5) was the least common (7.5%) (table 1).

### Association between severity of cholecystitis (Parkland Grading) & gallstone size

A statistically significant association was found between severity of cholecystitis and gallstone size ( $p < 0.001$ ). Patients with Grade 1 cholecystitis had a mean gallstone size of  $18.36 \pm 3.23$  mm, while those with Grade 5 had a significantly larger mean size of  $28.67 \pm 2.41$  mm. This suggests that severe grades of cholecystitis were associated with larger gallstone sizes (table 2).

### Stratification of association between severity of cholecystitis (Parkland Grading) & gallstone size among different genders, age groups and BMI groups

Among males, the association between gallstone size and cholecystitis severity was statistically significant ( $p = 0.001$ ). Mean gallstone size ranged from  $18.00 \pm 2.33$  mm for Grade 1 to  $31.35$  mm for Grade 5. Among females, the association was even stronger ( $p < 0.001$ ). Gallstone size increased from  $18.66 \pm 4.04$  mm in Grade 1 to  $28.00 \pm 2.18$  mm in Grade 5. Similarly, patients aged  $<40$  years, the association was significant ( $p = 0.001$ ) with gallstone size increasing from  $17.45 \pm 2.29$  mm in Grade 1 to  $26.72 \pm 0.54$  mm in Grade 5. For those aged 40-49 years, the association was also significant ( $p = 0.002$ ) with gallstone sizes ranging from  $18.56 \pm 3.48$  mm in Grade 1 to  $27.35$  mm in Grade 5. In the  $\geq 50$  years age group, the association remained statistically significant ( $p = 0.034$ ), and gallstone size increased from  $20.36 \pm 6.63$  mm in Grade 2 to  $31.28 \pm 0.10$  mm in Grade 5. For patients with normal BMI ( $<25$  kg/m<sup>2</sup>), gallstone size significantly increased with cholecystitis severity ( $p < 0.001$ ), ranging from  $16.65 \pm 2.39$  mm in Grade 1 to  $29.28 \pm 2.73$  mm in Grade 5. Among the overweight group (25-29 kg/m<sup>2</sup>), the association was significant ( $p = 0.021$ ) with gallstone size increasing from  $19.62 \pm 4.10$  mm in Grade 1 to  $26.72 \pm 0.54$  mm in Grade 5. In the obese group ( $\geq 30$  kg/m<sup>2</sup>), the association was highly significant ( $p < 0.001$ ), with gallstone size ranging from  $18.65 \pm 0.57$  mm in Grade 1 to  $31.35$  mm in Grade 5. Stratification analysis is presented in table 3-5.

**TABLE-1:** Demographic & Clinical Profile of the study Population

Variable	Frequency	Percentage
<b>Gender</b>		
<b>Males</b>	32	47.8
<b>Females</b>	35	52.2
<b>Total</b>	67	100.0

Variable	Frequency	Percentage
<b>Age Groups</b>		
<b>&lt; 40 Years</b>	26	38.8
<b>40 – 49 Years</b>	28	41.8
<b><math>\geq 50</math> Years</b>	13	19.4
<b>Total</b>	67	100.0
<b>BMI Groups</b>		
<b>&lt; 25 kg/m<sup>2</sup> (Normal)</b>	21	31.3
<b>25-29 kg/m<sup>2</sup> (Over-Weight)</b>	29	43.3
<b><math>\geq 30</math> kg/m<sup>2</sup> (Obese)</b>	17	25.4
<b>Total</b>	67	100.0
<b>Cholecystitis Severity (Parkland Grading Scale)</b>		
<b>1</b>	11	16.4
<b>2</b>	14	20.9
<b>3</b>	21	31.3
<b>4</b>	16	23.9
<b>5</b>	5	7.5
<b>Total</b>	67	100.0

**TABLE-II:** Association between severity of cholecystitis (based on The Parkland Grading Scale) and gallstone size in overall study population

Cholecystitis Severity (Parkland Grading Scale)	N	Minimum	Maximum	Mean $\pm$ Std. Deviation	$p$ -value (ANOVA Test)
<b>1</b>	11	15.12	25.77	$18.36 \pm 3.23$	0.000
<b>2</b>	14	15.93	27.98	$20.40 \pm 3.36$	
<b>3</b>	21	18.13	25.73	$21.62 \pm 2.10$	
<b>4</b>	16	20.29	29.34	$25.14 \pm 2.92$	
<b>5</b>	5	26.34	31.35	$28.67 \pm 2.41$	
<b>Total</b>	67	15.12	31.35	$22.20 \pm 3.99$	

**TABLE-III:** Association between severity of cholecystitis (The Parkland Grading Scale) and gallstone in overall study population (Gender-based stratification)

Gender	Cholecystitis Severity (Parkland Grading Scale)	N	Minimum	Maximum	Mean $\pm$ Std. Deviation	$p$ -value (ANOVA Test)
Male	<b>1</b>	5	15.67	21.23	$18.00 \pm 2.33$	0.001
	<b>2</b>	9	15.93	27.98	$21.47 \pm 3.70$	
	<b>3</b>	10	18.13	24.33	$20.95 \pm 1.85$	
	<b>4</b>	7	20.78	29.34	$24.68 \pm 3.22$	

Gender	Cholecystitis Severity (Parkland Grading Scale)	N	Minimum	Maximum	Mean ± Std. Deviation	p-value (ANOVA Test)
	5	1	31.35	31.35	31.35 ± ****	
	Total	32	15.67	31.35	21.78 ± 3.83	
Female	1	6	15.12	25.77	18.66 ± 4.04	0.000
	2	5	17.16	20.38	18.48 ± 1.41	
	3	11	19.25	25.73	22.22 ± 2.22	
	4	9	20.29	28.83	25.50 ± 2.81	
	5	4	26.34	31.21	28.00 ± 2.18	
	Total	35	15.12	31.21	22.58 ± 4.16	

**TABLE-IV:** Association between severity of cholecystitis (The Parkland Grading Scale) and gallstone in overall study population (Age-based stratification)

Age Groups	Cholecystitis Severity (Parkland Grading Scale)	N	Minimum	Maximum	Mean ± Std. Deviation	p-value (ANOVA Test)
< 40 Years	1	2	15.83	19.07	17.45 ± 2.29	0.001
	2	6	17.73	22.81	20.10 ± 2.15	
	3	10	18.13	25.73	21.55 ± 2.44	
	4	6	20.29	29.34	25.07 ± 3.22	
	5	2	26.34	27.10	26.72 ± 0.54	
	Total	26	15.83	29.34	22.11 ± 3.46	
40 – 49 Years	1	9	15.12	25.77	18.56 ± 3.48	0.002
	2	5	17.57	25.27	20.80 ± 2.91	
	3	5	19.25	22.90	20.44 ± 1.45	
	4	8	20.78	28.83	25.16 ± 3.19	
	5	1	27.35	27.35	27.35 ± ***	
	Total	28	15.12	28.83	21.50 ± 4.03	
≥ 50 Years	2	3	15.93	27.98	20.36 ± 6.63	0.034
	3	6	20.43	24.61	22.71 ± 1.58	
	4	2	23.67	26.89	25.28 ± 2.28	
	5	2	31.21	31.35	31.28 ± 0.10	
	Total	13	15.93	31.35	23.88 ± 4.69	

**TABLE-V:** Association between severity of cholecystitis (The Parkland Grading Scale) and gallstone size in overall study population (BMI-based stratification)

BMI Groups	Cholecystitis Severity (Parkland Grading Scale)	N	Minimum	Maximum	Mean ± Std. Deviation	p-value (ANOVA Test)
< 25 kg/m <sup>2</sup> (Normal)	1	4	15.12	20.21	16.65 ± 2.39	0.000
	2	4	17.73	22.81	21.20 ± 2.35	
	3	5	19.60	22.90	21.00 ± 1.41	
	4	6	20.29	28.65	23.79 ± 3.07	
	5	2	27.35	31.21	29.28 ± 2.73	
	Total	21	15.12	31.21	21.79 ± 4.14	
25 - 29 kg/m <sup>2</sup> (Over-weight)	1	5	15.67	25.77	19.62 ± 4.10	0.021
	2	8	15.93	27.98	20.46 ± 4.11	
	3	10	18.13	25.73	22.41 ± 2.55	
	4	4	22.99	29.34	26.00 ± 2.74	
	5	2	26.34	27.10	26.72 ± 0.54	
	Total	29	15.67	29.34	22.18 ± 3.89	
≥ 30 kg/m <sup>2</sup> (Obese)	1	2	18.24	19.05	18.65 ± 0.57	0.000
	2	2	17.57	19.57	18.57 ± 1.41	
	3	6	19.33	22.85	20.81 ± 1.42	
	4	6	22.13	28.83	25.93 ± 2.86	
	5	1	31.35	31.35	31.35 ± ***	
	Total	17	17.57	31.35	22.72 ± 4.18	

**DISCUSSION**

The findings of this study indicate a significant positive relationship between the severity of cholecystitis, as assessed by the Parkland grading system, and gallstone size. This is consistent with previous research and literature that has demonstrated similar relation between the severity of cholecystitis and gallstone size. For instance, Arguello, et al. explored the relationship between the Parkland grading scale and surgical difficulty in laparoscopic cholecystectomy,

noting that higher grades were associated with larger gallstones, which contributed to greater surgical challenges<sup>1</sup>. Additionally, Buhavac, et al. emphasized that larger gallstones often exacerbate clinical manifestations, including obstructive symptoms, thereby increasing the complexity of the treatment process.<sup>2</sup>

The study shows that the variability of gallstone size could be attributed to cholecystitis severity, underscoring the importance of using the Parkland grading system as a predictor of gallstone size and disease severity. This is in line with findings by Shrestha et al., who validated the Parkland grading system's role in predicting intraoperative challenges during laparoscopic cholecystectomy.<sup>3</sup> Similarly, Elkbuli, et al. supported the idea that grading systems, such as Parkland, provide vital information for tailoring treatment pathways in cases of cholecystitis.<sup>4</sup>

From a clinical perspective, this study reaffirms the utility of the Parkland grading system for guiding treatment decisions. Uçaner, et al. demonstrated the relationship between preoperative ultrasonography findings and the Parkland grading scale in determining the difficulty of laparoscopic cholecystectomy, further supporting the use of this grading system for preoperative planning.<sup>5</sup> Madni, et al. established that the proposal of the Parkland system helps clinicians anticipate potential complications and plan surgical interventions accordingly, which could improve patient outcomes.<sup>6</sup>

Furthermore, Baral, et al. and Schuster, et al. recommend conducting future research with larger cohorts to confirm these findings and to explore the underlying mechanisms that link gallstone size with clinical outcomes.<sup>7,8</sup> These studies could help identify additional risk factors, refine grading systems, and enhance the management of gallstone disease.

In terms of surgical practice, this study underscores the critical role of predictive models like the Parkland grading scale in optimizing patient care. Rangel-Olvera, et al. found that intraoperative complexity, which often correlates with gallstone size, is a key risk factor for conversion to open surgery during laparoscopic cholecystectomy.<sup>9</sup> This further reinforces the relevance of preoperative grading systems in anticipating potential complications and guiding surgical approaches.

In addition, Badawy, et al. highlighted the importance of using sonographic predictors for identifying difficult laparoscopic cholecystectomy cases, noting that larger gallstones often indicate a higher likelihood of complications.<sup>10</sup> Similarly, Tongyoo, et al. proposed a new classification system for assessing surgical difficulty in laparoscopic cholecystectomy, which could complement the Parkland grading scale and provide more nuanced risk assessments.<sup>11</sup>

The relationship between surgical complexity and gallstone size has also been explored by Sah, et al., who developed an operative difficulty grading scale specifically for laparoscopic cholecystectomy, showing that larger stones are associated with more challenging surgeries.<sup>12</sup> Similarly, Gupta, et al. have discussed the importance of various grading methods for predicting difficult laparoscopic cholecystectomy and emphasized the value of incorporating multiple clinical factors into preoperative evaluations<sup>13</sup>

Chhoda, et al. noted that managing gallstone disease in the elderly can be particularly challenging due to the higher prevalence of large stones and severe cholecystitis in this population.<sup>14</sup> As such, grading systems like Parkland are especially useful in older patients for predicting disease severity and guiding treatment decisions.

Murry, et al., Lee, et al. and Pinto, et al. research on managing difficult gallbladders suggest that clinical classification schemes such as Parkland are essential for identifying high-risk cases and improving surgical outcomes.<sup>15-17</sup> Similarly, Cripps, et al. and Serrano-González, et al. have highlighted the importance of standardized classification systems for acute cholecystitis to ensure consistent and effective patient care.<sup>18,19</sup>

As noted in our study, more severe grades of cholecystitis were consistently linked to larger gallstones, regardless of factors like age, gender, and BMI.

Therefore, current literature supports our study findings that extent of inflammation in the gallbladder has a role in determining the size of the gallstone.

### LIMITATIONS

Nevertheless, the study has several limitations that should be acknowledged. The study sample consisted primarily of young patients, which may restrict the generalizability of the findings to older populations. This emphasizes the need for larger and more diverse samples to better understand the relationship between cholecystitis severity and gallstone size.

Moreover, this study did not examine potential postoperative complications that manifest and relate to severity of cholecystitis and gallstone size, such as prolonged hospital stay which have been identified as outcomes of high-grade cholecystitis. Investigating the role of such factors in future research could provide a more comprehensive understanding of the variables contributing to disease severity and therefore gallstone size.

Despite these limitations, the study adds to the growing body of literature that supports the Parkland grading system as a reliable predictor of increased severity in patients with larger gallstone size, followed by the importance of predictive grading systems in improving surgical outcomes by facilitating better preoperative planning.

Finally, the small sample size could affect the robustness of the conclusions drawn. Future studies should aim to include a larger and a more diverse population.

### CONCLUSION

According to the study findings, more severe grades of cholecystitis were consistently associated with larger gallstones across a variety of clinical and demographic groups, such as age, gender, and BMI categories. With increasing severity grades, the mean gallstone size gradually increased, suggesting that gallstone size may serve as a predictive measure in determining the severity of cholecystitis, giving doctors a useful tool for controlling and forecasting the course of the condition.

### Ethical Approval

Approved by the Ethical Committee/ Institutional Review Board of Combined Military Hospital, Rawalpindi.

### Conflict of Interest

The authors declared no conflict of interest.

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