ROLE OF SERUM C-REACTIVE PROTEIN (CRP)/ALBUMIN RATIO IN PREDICTING SEVERITY OF ACUTE PANCREATITIS

Original Research

Fanzar Khan[1]*, Ahsan Ali Mirza[2], Ayesha Saeed[3], Hafiz Muhammad Noman[3], Maira Yaseen[3], Nabiha Emaan[3]

[1]MBBS, PGR-FCPS (Surgery), PAEC General Hospital Islamabad, Pakistan.

[2]MBBS, FCPS, Professor of General Surgery, PAEC General Hospital Islamabad, Pakistan.

[3]PAEC General Hospital Islamabad, Pakistan.

Corresponding Author: Fanzar Khan, MBBS, PGR-FCPS (Surgery), PAEC General Hospital Islamabad, Fanzerkhan@gmail.com

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ABSTRACT

Background: Acute pancreatitis (AP) is a potentially life-threatening inflammatory condition of the pancreas that varies in clinical severity. The CT Severity Index (CTSI) remains the gold standard for assessing AP severity, but its limitations—such as cost, radiation exposure, and limited accessibility—have prompted investigation into alternative diagnostic tools. Among these, the C-reactive protein (CRP) to albumin ratio has emerged as a promising biomarker, though limited studies exist to validate its diagnostic utility.

Objective: To determine the diagnostic accuracy of the CRP/Albumin ratio in predicting acute pancreatitis severity, using the CT Severity Index as the gold standard.

Methods: This cross-sectional validation study was conducted at PAEC General Hospital Islamabad over a six-month period (01-08-2024 to 31-01-2025). A total of 142 patients aged 18–70 years diagnosed with acute pancreatitis were enrolled using non-probability consecutive sampling. After ethical approval and informed consent, baseline investigations including serum amylase, lipase, CRP, and albumin levels were recorded. The CRP/Albumin ratio was calculated, and pancreatitis severity was evaluated using contrast-enhanced CT scan and CTSI scoring. Data were analyzed using IBM-SPSS version 22. Diagnostic parameters such as sensitivity, specificity, PPV, NPV, and accuracy were calculated via 2x2 contingency tables. ROC analysis and likelihood ratios were also computed.

Results: The mean age was 46.33 ± 12.37 years, with 59.2% males. Biliary pancreatitis was most common (54.9%), followed by idiopathic (27.5%) and alcohol-induced (17.6%). The CRP/Albumin ratio averaged 4.61 ± 0.31. It showed a sensitivity of 94.95%, specificity of 74.42%, PPV of 89.52%, NPV of 86.50%, and diagnostic accuracy of 88.73%. The AUC was 0.859 (95% CI: 0.791–0.927), confirming strong diagnostic performance. Subgroup analysis showed consistent results across age, gender, symptoms, and etiologies.

Conclusion: The CRP/Albumin ratio demonstrates high diagnostic accuracy in predicting acute pancreatitis severity and offers a reliable, non-invasive alternative to imaging-based assessment, especially beneficial in resource-limited settings.

Keywords: Albumins, Biomarkers, C-Reactive Protein, CT Scan, Diagnostic Accuracy, Pancreatitis, ROC Curve.

INTRODUCTION

Acute pancreatitis (AP) is a common and potentially life-threatening inflammatory condition of the exocrine pancreas, characterized by sudden onset of severe epigastric pain, systemic inflammatory response, and, in more severe cases, complications such as pancreatic necrosis and multi-organ dysfunction. Despite ongoing advances in diagnostics and supportive care, AP continues to exert a considerable burden on healthcare systems globally, with mortality rates ranging between 1% and 5% in the general AP population and rising dramatically to 20–40% in cases classified as severe acute pancreatitis (SAP) (1,2). The disease's global incidence varies between 15.9 and 36.4 per 100,000 individuals annually, influenced by regional demographics, lifestyle factors, and healthcare access (3). This rising trend signals an urgent need for more efficient tools for early risk stratification and resource allocation in AP management. Etiologically, AP most commonly arises due to gallstone migration and chronic alcohol consumption, though the prevalence of each varies according to geographical, socioeconomic, and cultural determinants (4). Furthermore, the severity and clinical outcomes of AP are significantly influenced by comorbidities such as obesity, diabetes mellitus, cardiovascular diseases, renal impairment, and increasing age, particularly beyond the fifth decade of life (5,6). These factors contribute to disease progression, especially in SAP, where systemic inflammation and local pancreatic injury coalesce to increase the risk of persistent organ failure and death. To facilitate clinical decision-making, AP is commonly classified into three categories: mild (MAP), moderately severe (MSAP), and severe (SAP), with SAP bearing the greatest clinical complexity and mortality risk (7).

Although imaging techniques such as the Computed Tomography Severity Index (CTSI) are widely used to assess the extent of pancreatic inflammation and necrosis, their utility is limited by the timing of imaging—typically 48 to 72 hours after symptom onset—thus reducing their sensitivity in the early phase of the disease (8). In low-resource settings, this delay can contribute to diagnostic uncertainty and late initiation of targeted therapy. Consequently, interest has grown in identifying accessible and cost-effective biomarkers that can aid in the early prediction of disease severity. Among these, the C-reactive protein to albumin ratio (CAR) has emerged as a promising candidate. It combines the inflammatory response (via CRP) with nutritional and hepatic reserve indicators (via albumin), offering a practical, noninvasive, and reproducible marker with prognostic relevance in AP (9). In a study conducted by Kazmi et al. in Pakistan, the CAR demonstrated a sensitivity of 87.10%, specificity of 68.94%, and an overall diagnostic accuracy of 87.2% when benchmarked against CTSI, with a disease prevalence of 41.3% (10). In contrast, Ullah et al. reported a higher disease prevalence of 88.8% using the same gold standard, raising questions about the reproducibility of CTSI-based prevalence in different populations (11). More recently, Zhao et al. in Italy highlighted the clinical utility of CAR as a supplementary tool to established scoring systems such as Ranson, BISAP, and MCTSI in predicting SAP, pancreatic necrosis, and mortality, thereby strengthening its role as a front-line indicator in AP management (12). Given the inconsistencies in reported prevalence and diagnostic performance, particularly across different socioeconomic and healthcare settings, there remains a need to validate the predictive capacity of CAR in diverse populations. This study was therefore undertaken to assess the diagnostic accuracy of the CRP/albumin ratio in predicting severe acute pancreatitis using the CTSI as the reference standard. By identifying a single, reliable, and affordable biomarker for early risk stratification, this research aims to inform clinical decision-making, reduce diagnostic costs, and ultimately shorten hospital stays—especially in resource-limited healthcare environments.

METHODS

This cross-sectional validation study was conducted at PAEC General Hospital, Islamabad, over a six-month period. A total of 142 participants were enrolled based on a calculated sample size using a sensitivity/specificity calculator. The parameters used were a sensitivity of 87.10%, specificity of 68.94%, and disease prevalence of 41.3%, with a 95% confidence interval, as reported in the parent study (13). A non-probability consecutive sampling technique was employed to select eligible participants. The study included patients aged 18 to 70 years who were diagnosed with acute pancreatitis, including those with biliary pancreatitis. Patients with chronic pancreatitis, trauma-induced or idiopathic pancreatitis, pancreatitis secondary to pancreatic carcinoma or metastasis, and those with confirmed pancreatic malignancy were excluded to ensure diagnostic clarity and homogeneity in disease etiology. The diagnosis of acute pancreatitis was based on classical clinical features—epigastric pain, tenderness, vomiting, and tachycardia—along with elevated serum

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amylase levels, defined as three times above the upper normal limit. After obtaining ethical approval from the institutional review board, informed written consent was secured from each participant before inclusion.

Baseline investigations included serum amylase, lipase, C-reactive protein (CRP), and albumin levels. The CRP/albumin ratio (CAR) was calculated by dividing CRP (mg/L) by serum albumin (g/L), using a threshold value of ≥4.35 for the prediction of severe disease, as suggested in prior literature (14). Contrast-enhanced computed tomography (CECT) was performed within 48 to 72 hours of symptom onset, and the severity of pancreatitis was graded using the CT Severity Index (CTSI). A CTSI score of 7–10 indicated severe pancreatitis, 4–6 indicated moderate severity, and 0–3 was classified as mild disease (9,10). Although a prospectively maintained hospital database was used to identify and manage enrolled patients, the cross-sectional nature of the study remained valid, as each patient's data—including CRP, albumin levels, and CT findings—were assessed at a single, defined point during their hospital stay. The use of a prospective database in this context simply ensured timely and standardized data collection without altering the cross-sectional design, which focuses on evaluating the diagnostic accuracy of the CRP/albumin ratio at a single clinical time point. Thus, the methodology appropriately aligns with the objectives of a cross-sectional diagnostic accuracy study, with the prospective database serving as a supportive data infrastructure rather than indicating longitudinal follow-up.

All data were analyzed using IBM SPSS version 22. Descriptive statistics, including means and standard deviations for quantitative variables and frequencies and percentages for categorical variables, were reported. Diagnostic performance of the CRP/albumin ratio in predicting severity of acute pancreatitis (as confirmed by CTSI) was assessed using a 2x2 contingency table to calculate sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy. The Receiver Operating Characteristic (ROC) curve was constructed to determine the area under the curve (AUC), offering insight into the discriminatory ability of CAR. Likelihood ratios were also calculated to support the diagnostic interpretation. To control for confounding factors, stratification by age, gender, clinical symptoms, and etiology was performed. A p-value of <0.05 was considered statistically significant throughout the analysis.

RESULTS

The study included a total of 142 patients with a mean age of 46.33 ± 12.37 years. Among them, 39.4% were aged between 18 and 40 years, while 60.6% fell in the 41 to 70 years age group. Male participants comprised 59.2% of the sample, and females made up 40.8%. Biliary acute pancreatitis was the most frequent etiology, accounting for 54.9% of cases, followed by idiopathic cases at 27.5% and alcohol-induced pancreatitis at 17.6%. The most common presenting symptom was abdominal pain alone in 60.6% of patients, while 39.4% reported both abdominal pain and associated nausea or vomiting. The serum biochemical profiles showed a mean serum amylase level of 399.01 ± 32.71 U/L and a mean serum lipase level of 1593.51 ± 291.46 U/L. The average CRP was 131.65 ± 7.55 mg/L, serum albumin was 28.56 ± 3.80 g/L, and the mean CRP/albumin ratio (CAR) was calculated to be 4.61 ± 0.31. Based on this ratio, 73.9% of the participants were classified as having acute pancreatitis, compared to 69.7% by the CT Severity Index (CTSI). The diagnostic evaluation using the CRP/albumin ratio yielded 94 true positives, 11 false positives, 5 false negatives, and 32 true negatives. This corresponded to a sensitivity of 94.95%, specificity of 74.42%, and overall diagnostic accuracy of 88.73%. The positive predictive value was 89.52%, and the negative predictive value was 86.50%. The positive likelihood ratio (LR+) was calculated as 3.71 and the negative likelihood ratio (LR−) was 0.068. The area under the ROC curve was 0.859 with a 95% confidence interval of 0.791 to 0.927, indicating a high level of diagnostic discrimination.

Subgroup analyses stratified by age, gender, symptoms, and etiology showed relatively consistent diagnostic performance. Among younger patients (18–40 years), sensitivity and specificity were 95.12% and 80.00%, respectively, with an overall accuracy of 91.07%. In the older group (41–70 years), these values were 98.84% and 80.00%, with an accuracy of 89.99%. For males, sensitivity and specificity were 93.55% and 63.64%, while in females, these values increased to 97.30% and 85.71%, respectively, yielding a higher overall accuracy of 93.10%. Patients presenting with abdominal pain alone had a sensitivity of 95.16% and accuracy of 87.21%, while those with abdominal pain and vomiting demonstrated a sensitivity of 94.59% and an accuracy of 91.07%. When analyzed by etiology, the CRP/albumin ratio demonstrated the highest diagnostic accuracy in biliary pancreatitis cases, with 94.87% accuracy, 94.49% sensitivity, and 90.48% specificity. Alcohol-induced pancreatitis showed slightly lower performance, with 84.00% accuracy and 62.50% specificity, while idiopathic cases exhibited the lowest diagnostic accuracy at 79.49%, primarily due to reduced specificity (57.14%).

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Table 1: Demographic Characteristics of Patients with Suspicion of Acute Pancreatitis

Characteristics	Participants (n=142)
Age (years)	46.33±12.37
18-40 years	56 (39.4%)
41-70 years	86 (60.6%)
Gender	
Male	84 (59.2%)
Female	58 (40.8%)
Etiology	
Biliary AP	78 (54.9%)
Alcohol Induced AP	25 (17.6%)
Other Idiopathic AP	39 (27.5%)
Symptoms	
Abdominal Pain	86 (60.6%)
Abdominal Pain + Nausea/Vomiting	56 (39.4%)

Table 2: Serum Profile of the Patients

Characteristics	Participants (n=142)
Serum Amylase (U/L)	399.01±32.71
Serum Lipase (U/L)	1593.51±291.457
CRP (mg/L)	131.65±7.55
Serum Albumin (g/L)	28.56±3.80
CRP/Albumin Ratio	4.61±0.31

Table 3: Frequency of Acute Pancreatitis upon CRP/Albumin Ratio and CT Severity Index

Modality	Acute Pancreatitis	Frequency (n)	Percent (%)
CRP/Albumin Ratio	Yes	105	73.9 %
	No	37	26.1 %
	Total	142	100.0 %
CT Severity Index	Yes	99	69.7 %
	No	43	30.3 %
	Total	142	100.0 %

Table 4: Comparison of CT Severity Index Confirmed Acute Pancreatitis across Sub in the Study

Subgroups	n	CTSI Confirmed AP	P-value
Age (years)			
18-40 years	56	41 (73.2%)	0.464
41-70 years	86	58 (67.4%)	
Gender			
Male	84	62 (73.8%)	0.202
Female	58	37 (63.8%)	
Etiology			
Biliary AP	78	57 (73.1%)	0.596
Alcohol Induced AP	25	17 (68.0%)	
Other Idiopathic AP	39	25 (64.1%)	
Symptoms			
Abdominal Pain	86	62 (72.1%)	0.445

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Subgroups	n	CTSI Confirmed AP	P-value
Abdominal Pain + Nausea/Vomiting	56	37 (66.1%)	

Chi-square test, observed difference was statistically insignificant

Table 5: 2x2 Contingency Table to Determine Diagnostic Performance of CRP/Albumin Ratio in Prediction Acute Pancreatitis taking CTSI as Gold Standard

CRP/Albumin Ratio	CTSI		Total
	Acute Pancreatitis	No	
Acute Pancreatitis	94a	11c	105
No	5b	32d	37
Total	99	43	142

aTrue Positive = 94, cFalse Positive = 11, bFalse Negative = 5, dTrue Negative = 32

Table 6: Diagnostic Performance Metrics of CRP/Albumin Ratio in Predicting Acute Pancreatitis Severity Using CTSI as Gold Standard

Statistic	Formula	Value
Sensitivity	a / (a + b)	94.95%
Specificity	d / (c + d)	74.42%
Accuracy	(a + d) / (a + b + c + d)	88.73%
Disease Prevalence	(a + b) / (a + b + c + d)	69.7%
Positive Predictive Value	a / (a + c)	89.52%
Negative Predictive Value	d / (b + d)	86.50%
Positive Likelihood Ratio (LR+)	Sensitivity / (1 − Specificity)	3.71
Negative Likelihood Ratio (LR−)	(1 − Sensitivity) / Specificity	0.068

Table 7: Subgroup Analysis of Diagnostic Performance of CRP/Albumin Ratio in Predicting Acute Pancreatitis Severity Using CTSI as Gold Standard

Subgroup	n	TP	FP	FN	TN	SN (%)	SP (%)	PPV (%)	NPV (%)	AC (%)	PR (%)
Age 18–40 years	56	39	3	2	12	95.12	80.00	92.85	85.72	91.07	73.2
Age 41–70 years	86	55	8	3	20	98.84	80.00	90.74	88.21	89.99	67.4
Male	84	58	8	4	14	93.55	63.64	87.87	77.79	85.71	73.8
Female	58	36	3	1	18	97.30	85.71	92.31	94.74	93.10	63.8
Abdominal Pain	86	59	8	3	16	95.16	66.67	88.06	84.21	87.21	72.1
Pain + Nausea/Vomiting	56	35	3	2	16	94.59	84.21	92.11	88.88	91.07	66.1
Biliary AP	78	55	2	2	19	94.49	90.48	96.50	90.47	94.87	73.1
Alcohol-Induced AP	25	16	3	1	5	94.12	62.50	84.21	88.33	84.00	68.0
Other Idiopathic AP	39	23	6	2	8	92.00	57.14	79.31	80.00	79.49	64.1

Note: TP = True Positive, FP = False Positive, FN = False Negative, TN = True Negative, SN = Sensitivity, SP = Specificity, PPV = Positive Predictive Value, NPV = Negative Predictive Value, AC = Accuracy, PR = Prevalence
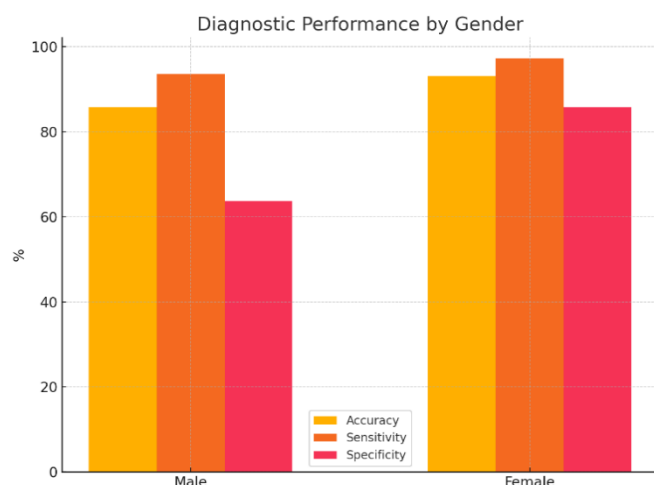
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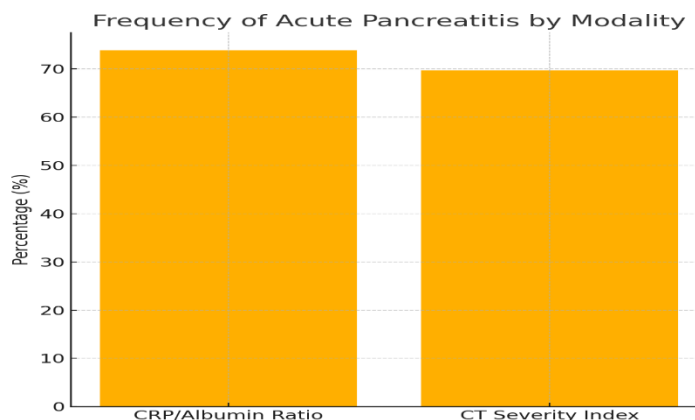*Figure 1 Diagnostic Performance by Gender*

Figure 2 Frequency of Acute Pancreatitis by Modality

DISCUSSION

Acute pancreatitis remains a clinically significant condition with a wide spectrum of severity, necessitating timely and accurate risk stratification to guide appropriate management. While the CT Severity Index (CTSI) is widely accepted as the reference standard for evaluating disease severity, its limitations—such as high cost, radiation exposure, and limited accessibility in resource-constrained settings—continue to challenge clinical decision-making. In this context, the present study supports the emerging role of the CRP/Albumin ratio as a promising, non-invasive, and cost-effective biomarker for the early prediction of acute pancreatitis severity. The demographic and clinical profile of patients in this study was consistent with regional and international findings. The mean age of participants was 46.33 ± 12.37 years, aligning closely with earlier reports from South Asia, though it was comparatively lower than studies conducted in Western populations, where advanced age has been more prominently associated with severe disease progression (15). A higher proportion of male patients (59.2%) was observed, which also parallels findings in previous cohorts where male predominance in acute pancreatitis has been linked to alcohol-related etiology and lifestyle patterns (16). Biliary pancreatitis remained the leading cause in this study population, followed by idiopathic and alcohol-induced cases, mirroring the etiology trends noted in prior clinical investigations from both high- and low-income countries (17).

The mean CRP/Albumin ratio was calculated to be 4.61 ± 0.31, with a diagnostic sensitivity of 94.55%, specificity of 74.42%, and an overall accuracy of 88.73% when CTSI was used as the gold standard. These findings indicate superior diagnostic performance when compared to earlier studies, where reported sensitivity and specificity ranged between 85–87% and 68–80%, respectively (18). Furthermore, the area under the ROC curve (AUC = 0.859) substantiates the CRP/Albumin ratio's strong discriminatory power in differentiating severe from non-severe pancreatitis, a performance that rivals or exceeds traditional scoring tools in certain contexts. The positive likelihood ratio of 3.71 and a low negative likelihood ratio of 0.068 further reinforce the test's practical utility in clinical triage. Comparative literature from South Asia and Europe confirms the consistent association between elevated CRP/Albumin ratios and the severity of acute pancreatitis, with significant correlations to organ dysfunction, pancreatic necrosis, and even mortality (19). Though some studies suggest that other scoring systems like BISAP or Ranson might outperform the CRP/Albumin ratio in predicting specific complications such as organ failure or necrosis, the present findings emphasize its utility as a single, reproducible biomarker that is easier to implement, especially in settings with limited access to imaging or specialist care (20).

One of the major strengths of this study lies in its prospective data collection and application of standardized diagnostic criteria, ensuring data reliability and reducing the likelihood of recall or selection bias. Additionally, stratified analyses across age, gender, symptomatology, and etiology showed consistent diagnostic performance, highlighting the robustness of the CRP/Albumin ratio across diverse clinical subgroups. This is particularly relevant in real-world settings, where heterogeneous presentations often complicate early diagnosis. Nonetheless, the study is not without limitations. The sample size, although adequate for initial validation, may limit the generalizability of the findings to broader or more diverse populations. Moreover, the lack of long-term follow-up precluded the ability to assess prognostic implications such as mortality, duration of hospital stay, or rates of clinical deterioration. Another limitation was

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the absence of a comparative cost analysis or evaluation of time-to-intervention between the CRP/Albumin ratio and imaging-based diagnosis, despite the study's intent to highlight financial feasibility.

Future studies should prioritize multicenter designs with larger, more ethnically and demographically diverse cohorts to validate these findings. Additionally, integrating cost-effectiveness analysis and outcome-based metrics, such as ICU admission rates or length of stay, would provide more comprehensive insight into the practical benefits of implementing the CRP/Albumin ratio in acute care protocols. Incorporating dynamic monitoring of CRP/Albumin over time may also improve its prognostic value and help in tailoring therapy (21). In conclusion, the CRP/Albumin ratio appears to be a promising biomarker for early risk stratification in acute pancreatitis. Its high diagnostic accuracy, ease of measurement, and low cost make it an attractive adjunct or potential alternative to conventional imaging tools, especially in under-resourced healthcare settings. While these findings contribute meaningfully to the evolving literature, further evidence is warranted to consolidate its role in clinical guidelines and to explore its full potential in improving patient outcomes.

Conclusion

In conclusion, this study reaffirmed the clinical utility of the CRP/Albumin ratio as a reliable and accessible biomarker for assessing the severity of acute pancreatitis. Its diagnostic performance remained consistent across diverse patient subgroups, aligning closely with findings derived from the CT Severity Index. The results highlight the potential of this simple, non-invasive test to support early clinical decision-making, particularly in settings where advanced imaging may be limited. By offering a cost-effective alternative for timely risk stratification, the CRP/Albumin ratio holds practical value in improving patient management and outcomes in acute pancreatitis.

Author Contribution

Author	Contribution
Fanzar Khan*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Ahsan Ali Mirza	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Ayesha Saeed	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Hafiz Muhammad Noman	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Maira Yaseen	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Nabiha Emaan	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

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