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Role of CA 19-9/CRP Ratio as A Predictor for Malignancy in Obstructed Jaundice Patient

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ABSTRACT

The cancer-antigen-19-9 tumor marker, increases during biliary and pancreatic malignancy. **Objectives:** To determine diagnostic accuracy and role of cancer-antigen-19-9 and C-reactive-protein ratio as a predictor for malignancy in obstructive jaundice patients taking a Computed Tomography scan as the gold standard. **Methods:** A total of 158 patients were admitted with obstructive jaundice in Al-Tibri Hospital. Cancer-antigen-19-9 was adjusted by dividing it with the C-reactive-protein value. Malignancy was considered based on computed tomography scan findings. Specificity, sensitivity, negative predictive value, positive predictive value, and diagnostic accuracy of cancer antigen-19-9 to C-reactive protein ratio were calculated. **Results:** There were 57.6% male and 42.4% female patients. The mean cancer antigen-19-9 and C-reactive-protein ratio was 51.39 ± 69.40 U/ml. The significant p-values (<0.001) confirm meaningful differences in CA19-9/CRP ratios between benign and malignant cases, but low sensitivity (63.2%) and negative predictive value (46.8%) limit its clinical utility as a standalone tool. A total of 50% of patients were diagnosed as benign and 50% as malignant by cancer antigen-19-9 and C-reactive-protein ratio. However, 27.8% of patients were diagnosed as benign and 72.2% as malignant by computed tomography scan. Sensitivity, Specificity, positive predictive value, negative predictive value and accuracy were 63.2%, 84.1%, 91.1%, 46.8%, and 68.98% respectively. **Conclusions:** It was concluded that the cancer-antigen-19-9/CRP ratio while exhibiting moderate overall diagnostic accuracy (68.98%), provides significant diagnostic specificity (84.1%) and positive predictive value (91.1%). These characteristics make it a valuable supplemental tool for confirming malignancy in obstructive jaundice patients, particularly when used alongside other diagnostic modalities.

INTRODUCTION

Obstructive jaundice, a common clinical condition, results from the blockage of bile flow due to benign or malignant causes, including pancreatic and biliary cancers. Differentiating between these etiologies is critical for timely diagnosis and management, as malignant causes require prompt intervention to improve prognosis. Biomarkers like Cancer Antigen (CA) 19-9 have been widely used in diagnosing malignancies associated with obstructive jaundice, but their diagnostic accuracy is often limited by elevated levels in benign inflammatory conditions such as pancreatitis or cholangitis [1-3]. These limitations necessitate the exploration of novel diagnostic approaches to enhance specificity and sensitivity in detecting malignancy. CA19-9, a carbohydrate antigen, is a tumor marker commonly elevated in pancreatic biliary malignancies. Despite its utility, studies have highlighted its nonspecific elevation in benign conditions, reducing its reliability as a standalone diagnostic tool [4-6]. Similarly, inflammatory markers like C-reactive protein (CRP) have demonstrated limited specificity when used independently. The combination of these markers, however, offers a promising avenue for improving

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diagnostic accuracy. Emerging evidence suggests that the CA19-9/CRP ratio may help differentiate between malignant and benign causes by integrating tumor marker levels with systemic inflammatory responses [7]. This study aims to evaluate the diagnostic utility of the CA19-9/CRP ratio in predicting malignancy in obstructive jaundice. By analyzing its diagnostic accuracy, sensitivity, specificity, and predictive value, the study seeks to address the limitations of standalone biomarkers and contribute to the development of more effective diagnostic strategies. Previous research has underscored the need for innovative biomarker combinations to improve diagnostic precision, particularly in resource-constrained settings where advanced imaging modalities may not be readily available [8]. Understanding the clinical implications of the CA19-9/CRP ratio could significantly impact the management of patients with obstructive jaundice. By providing a supplemental diagnostic tool, this study aims to aid clinicians in stratifying patients for further evaluation, reducing diagnostic delays, and improving outcomes in malignancy-associated cases. The findings will also contribute to the growing body of literature advocating for integrative biomarker approaches in oncology diagnostics. This study aims to determine diagnostic accuracy and the role of CA19-9 and CRP ratio as a predictor for malignancy in obstructive jaundice patients taking computed tomography (CT) scans as a gold standard.

METHODS

The cross-sectional validation study was conducted by enrolling the obstructive jaundice patients, admitted to Al-Tibri Hospital, Karachi by the approval of the institutional ethical review committee via approval number IERC/ATMC/14(01-2024)/20. This research was carried out from 27 May to 21 September 2024. The sample size was 158 calculated by using a sample size calculator for sensitivity and specificity, taking the prevalence of malignancy in obstructive jaundice as 29.8%, sensitivity 82.3%, specificity 45% with a margin of error of 11% for sensitivity and 10% for specificity at a confidence interval of 95% [9], non-probability consecutive sampling was used. Patients having a value of total bilirubin >1.2 mg/dl and alkaline phosphatase >136 U/L were considered obstructive jaundice patients. The standard cutoff CRP value for this research was considered 1.5 mg/L, and the nominal cut-off threshold level for CA19-9 was 32 U/mL. Patients with obstructive jaundice as per operational definition with no CBD or gallstones on ultrasound and age of 30 to 70 years were included in the study. Patients with cause of jaundice other than obstruction, non-consenting patients and those already diagnosed with malignancy were excluded from this study. The CA19-9 and CRP ratio was calculated. The patients were declared as malignant jaundiced patients based on a CT scan abdomen with pancreatic protocol findings. All the data were noted on a structured questionnaire after obtaining consent. Data were entered and analyzed by using SPSS version 22.0. Mean and standard deviation were computed for quantitative variables. Frequency and percentage were calculated for categorical variables. A table was made for calculating diagnostic accuracy, sensitivity, specificity, NPV and PPV of CA19-9 to CRP ratio taking CT scan as the gold standard.

RESULTS

A total of 158 patients with obstructive jaundice, aged 30 to 70 years, were included in the study. Of these, 50% were classified as benign and 50% as malignant based on the CA19-9 and CRP ratio. Table 1 presents the descriptive statistics of CA19-9 and CRP ratio values for each group. The mean CA19-9/CRP ratio in malignant cases (94.05 ± 76.99 U/mL) was significantly higher than in benign cases (8.73 ± 9.06 U/mL). Similar trends were observed for other metrics, such as median and range, indicating that CA19-9 and CRP ratios differ markedly between benign and malignant cases, reinforcing their potential diagnostic relevance (Table 1).

Table 1: Descriptive Statistics of CA 19-9 And CRP Ratio (U/Ml) among Benign and Malignant Patients Diagnosed by CA 19-9 and CRP Ratio (n=158)

Variables	Benign (79)	Malignant (79)
Mean + SD	8.73 ± 9.06	94.05 ± 76.99
Median	4.20	78.20
Range	30.98	621.80
Minimum	0.02	36.40
Maximum	31.00	658.20

Among patients diagnosed as benign or malignant based on CT scan findings, the CA19-9/CRP ratio showed marked differences between the two groups. Malignant cases had a significantly higher mean CA19-9/CRP ratio (66.54 ± 75.34 U/mL) compared to benign cases (12.14 ± 22.04 U/mL). The median CA19-9/CRP ratio for malignant cases (56.70 U/mL) was also substantially higher than that for benign cases (3.41 U/mL), with a wide range observed in both groups (Table 2).

Table 2: Descriptive Statistics of CA 19-9 and CRP Ratio (U/Ml) among Benign and Malignant Patients Diagnosed by CT Scan Findings (n=158)

Variables	Benign (44)	Malignant (114)
Mean + SD	12.14 ± 22.04	66.54 ± 75.34
Median	3.41	56.70
Range	92.90	658.18
Minimum	0.10	0.02
Maximum	93.00	658.20

Among patients who were diagnosed benign and malignant by CT scan findings, the mean CA19-9 was 139.65 ± 253.78

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U/ml and 949.20 ± 1065.54 U/ml respectively. The mean CRP was 14.36 ± 13.26 U/ml and 25.92 ± 35.29 U/ml respectively. Here too, the CA19-9/CRP ratio was significantly higher in malignant cases compared to benign cases (p<0.001) (Table 3). The ratio demonstrated high specificity (84.1%) and positive predictive value (PPV) (91.1%), indicating its strong ability to correctly identify benign cases and confirm malignancy in positive cases, respectively. However, its sensitivity (63.2%) and negative predictive value (NPV) (46.8%) were moderate to low, suggesting it misses a proportion of true malignancy cases and has limited reliability in ruling out malignancy. The overall diagnostic accuracy was moderate at 68.98%, and the observed differences between diagnostic classifications based on the CA19-9/CRP ratio and CT scan findings were statistically significant (p<0.001).

Table 3: Diagnostic Accuracy of CA 19-9 and CRP Ratio for Predicting Malignancy in Obstructive Jaundice Patients with CT Scan Findings as Gold Standard (n=158)

CA 19-9 and CRP Ratio	CT Scan Findings		Total CA19-9 and CRP Ratio	p-value
	Malignant n (%)	Benign n (%)		
Malignant	72 (91.1)	7 (8.9)	79	<0.001*
Benign	42 (53.2)	37 (46.8)	79	
Total CT scan	114	44	158	
Sensitivity	Specificity	PPV	NPV	Accuracy
63.2%	84.1%	91.1%	46.8%	68.98%

*p-value <0.001 indicates a highly significant difference as determined by the Chi-square test

DISCUSSION

This study evaluates the CA19-9/CRP ratio as a diagnostic marker for malignancy in patients with obstructive jaundice. Despite showing potential as an adjunct tool with advanced imaging and histopathology, the diagnostic accuracy of 69% indicates significant limitations, suggesting its inadequacy as a standalone diagnostic test. The sensitivity and specificity of the CA19-9/CRP ratio highlight its moderate ability to distinguish between benign and malignant causes of obstructive jaundice. While such markers can aid in stratifying patients for further diagnostic evaluation, their relatively low accuracy underscores the risk of false positives or negatives. This aligns with previous findings that inflammatory biomarkers, while supportive, often lack sufficient reliability to independently guide clinical decision-making [10, 11]. Previous research has extensively explored the utility of CA19-9 and CRP as standalone markers in diagnosing malignancy, particularly in pancreatic and biliary diseases. Studies such as Zhou *et al.*, and Lyu *et al.*, highlighted the diagnostic limitations of CA19-9 due to its nonspecific elevation in benign inflammatory conditions like pancreatitis or cholangitis [11, 12]. Similarly, CRP has been examined for its role in malignancy detection but is hampered by its broad response to inflammatory stimuli regardless of malignancy status [13]. This study is innovative in its evaluation of the CA19-9/CRP ratio, offering an integrative approach that compensates for the shortcomings of standalone markers. Unlike earlier studies that analyzed these biomarkers individually, this research highlights the utility of their combined use to improve diagnostic precision. This is consistent with trends in oncology diagnostics that favoured multidimensional approaches, as reflected in recent meta-analyses advocating for composite biomarker strategies [14, 15]. The specificity observed in this study was notably high, at 84.1%, underscoring the CA19-9/CRP ratio's ability to effectively rule out non-malignant conditions. Furthermore, the positive predictive value (PPV) of 91.1% highlights its clinical relevance by accurately identifying cases more likely to be malignant. These high values reinforce the potential of the CA19-9/CRP ratio as a supplemental diagnostic tool, particularly in settings where diagnostic resources are constrained. By leveraging a novel metric and achieving high specificity and PPV, this study provides a valuable addition to the existing literature. It aligns with the growing interest in refining diagnostic methodologies to balance accuracy with resource efficiency, thus setting a foundation for further exploration and validation in broader clinical settings. Given the suboptimal accuracy observed, the CA19-9/CRP ratio cannot be recommended as a primary diagnostic tool for malignancy in obstructive jaundice. Instead, it should be considered a supplementary marker within a multimodal diagnostic framework. Combining it with imaging techniques, histopathology, and other advanced biomarkers could enhance overall diagnostic accuracy [16, 17]. Efforts should focus on refining biomarker panels and integrating them into a multimodal diagnostic approach to improve clinical outcomes. Investigating additional inflammatory markers or genetic and proteomic profiles may provide more comprehensive diagnostic tools for malignancies in obstructive jaundice [18-20].

CONCLUSIONS

It was concluded that while the CA19-9 and CRP ratio show potential in enhancing the specificity (84.1%) and positive predictive value (91.1%) for malignancy detection in obstructive jaundice, its overall diagnostic accuracy remains moderate (68.98%). The sensitivity (63.2%) and negative predictive value (46.8%) suggest limited reliability in ruling out malignancy. This suggests that the CA19-9/CRP ratio can be a valuable adjunct in diagnostic frameworks, particularly when used in combination with other diagnostic modalities like imaging and histopathology.

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Authors Contribution

Conceptualization: RK, MM
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Formal analysis: RK, MF
Writing review and editing: WA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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