Correlation of CA 19-9 and total bilirubin levels with pancreatic cancer staging: a retrospective study at RSUP Haji Adam Malik Medan

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Abstract

Introduction: Pancreatic cancer is one of the deadliest cancers, often diagnosed at an advanced stage. Biomarkers such as Carbohydrate Antigen 19-9 (CA 19-9) and total bilirubin are commonly elevated in these patients, but their combined role in assessing cancer staging remains underexplored. This study aims to evaluate the correlation between CA 19-9 levels, total bilirubin, and cancer staging in pancreatic cancer patients.

Methods: A cross-sectional study was conducted on 203 pancreatic cancer patients treated at RSUP Haji Adam Malik Medan from January 2016 to December 2020. Data on patient demographics, CA 19-9 levels, total bilirubin levels, and cancer staging were collected from medical records. Statistical analysis was performed to assess the relationships between these variables.

Results: The average age of the patients was 62.59 ± 4.28 years, with a male predominance (78.3%). The mean CA 19-9 level was 145.28 ± 44.28 U/mL, and the mean total bilirubin level was 10.55 ± 2.75 mg/dL. Most patients (38.4%) were diagnosed at stage III. Both CA 19-9 and total bilirubin levels were significantly correlated with advanced cancer stages ($p < 0.05$).

Discussion: This study demonstrates a significant correlation between elevated CA 19-9 and total bilirubin levels with more advanced stages of pancreatic cancer. These findings suggest that combining CA 19-9 and bilirubin measurements could improve the accuracy of staging and prognostication in pancreatic cancer, ultimately guiding treatment decisions.

Keywords: Pancreatic cancer, CA 19-9, Total bilirubin, Cancer staging, Biomarkers

1. Introduction

Pancreatic cancer is one of the most aggressive malignancies, representing the twelfth most common cancer globally but accounting for the sixth leading cause of cancer-related mortality. The GLOBOCAN 2022 report estimates that approximately 510,992 new cases of pancreatic cancer occur annually, resulting in 467,409 deaths worldwide, with a five-year survival rate of only 4-6% due to late-stage diagnosis and limited treatment options (1). In Indonesia, pancreatic cancer ranks as the tenth leading cause of cancer-related deaths, with an increasing incidence attributed to factors such as aging populations, smoking, and genetic predispositions (2). Despite advances in medical imaging and therapeutic interventions, pancreatic cancer continues to be diagnosed at advanced stage, contributing to its poor prognosis.

Carbohydrate Antigen 19-9 (CA 19-9) is a commonly used tumour marker in pancreatic cancer, known for its sensitivity in detecting advanced stages of the disease. CA 19-9 is produced by pancreatic ductal adenocarcinoma cells and is found in the serum of approximately 80% of pancreatic cancer patients (3). However, its specificity is limited, especially in cases where jaundice is present due to bile duct obstruction, a common occurrence in tumours located at the head of the pancreas. Elevated levels of CA 19-9 can also be seen in benign conditions such as cholangitis, cirrhosis, and other hepatobiliary diseases, complicating its diagnostic use (4).

Total bilirubin (TB) is another biochemical marker often elevated in pancreatic cancer patients, particularly those with tumours obstructing the bile ducts. Hyperbilirubinemia in these patients often signals advanced disease, as biliary obstruction indicates significant tumour growth or local invasion (5). The combination of CA 19-9 and TB measurements may offer a more accurate assessment of disease stage and prognosis in pancreatic cancer, particularly in patients with jaundice.

The aim of this study was to investigate the relationship between CA 19-9, total bilirubin levels, and the stage of pancreatic cancer in patients treated at RSUP Haji Adam Malik Medan. By examining the correlation between these biomarkers and disease stage, we seek to provide insights into their combined use for improving diagnostic and prognostic accuracy in pancreatic cancer.

2. Methods

2.1 Study Design and Population

This cross-sectional study was conducted between January 2016 and December 2020 at RSUP Haji Adam Malik Medan. A total of 203 patients diagnosed with pancreatic cancer were included. Inclusion criteria consisted of confirmed histopathological diagnosis of pancreatic cancer, availability of serum CA 19-9 and total bilirubin levels, and complete medical records with detailed cancer staging. Patients with incomplete

records, previous cholecystectomy, or primary hepatobiliary diseases unrelated to pancreatic cancer were excluded to avoid confounding factors.

2.2 Data Collection

Data were collected retrospectively from electronic medical records. Information regarding patient demographics (age, sex), CA 19-9 levels, total bilirubin levels, and cancer stage was gathered. CA 19-9 levels were measured using the enzyme-linked immunosorbent assay (ELISA), while total bilirubin was measured by standard biochemical methods. Cancer staging was determined according to the American Joint Committee on Cancer (AJCC) TNM staging system based on imaging studies such as CT scans.

2.3 Statistical Analysis

Descriptive statistics were used to summarize the patient demographics and biomarker levels. Continuous variables, including CA 19-9 and TB levels, were expressed as means and standard deviations. One-way ANOVA was employed to compare CA 19-9 and TB levels across different cancer stages. Post-hoc Bonferroni tests were used for pairwise comparisons. Eta statistical analysis was performed to evaluate the strength of the relationship between CA 19-9, TB levels, and pancreatic cancer stage. A p-value of <0.05 was considered statistically significant. All statistical analyses were performed using SPSS software version 24 (IBM Corp., Armonk, NY, USA).

3. Results

3.1 Demographic Characteristics

Table 1. Characteristics of subjects

Characteristics (n = 203)	n (%)	Mean ± SD
Age (years)		62,59 ± 4,28
Gender		
Male	159 (78,3%)	
Female	44 (21,7%)	
Total bilirubin (mg/dL)		10,55 ± 2,75
CA 19-9 (U/mL)		145,28 ± 44,28
Pancreatic cancer stage		
I	32 (15,7%)	
II	50 (24,6%)	
III	78 (38,4%)	
IV	43 (21,3%)	

The study cohort included 203 patients, with a mean age of 62.59 ± 4.28 years. The majority of patients were male (78.3%, n=159), while the remaining 21.7% (n=44) were female. The distribution of cancer stages revealed that 15.7% of patients (n=32) were diagnosed at stage I, 24.6% (n=50) at stage II,

38.4% (n=78) at stage III, and 21.3% (n=43) at stage IV.

3.2 CA 19-9 and Total Bilirubin Levels by Pancreatic Cancer Stage

The mean serum CA 19-9 level across all patients was 145.28 ± 44.28 U/mL, while the mean total bilirubin level was 10.55 ± 2.75 mg/dL. A significant positive correlation was found between increasing cancer stage and CA 19-9 levels (r = 0.62, p < 0.001), as well as total bilirubin levels (r = 0.58, p < 0.001).

Table 2. Distribution of total bilirubin levels by pancreatic cancer stage

Stage	Total bilirubin (mg/dL)	*p value*	Post-hoc test
I	6,7 ± 0,62		
II	8,99 ± 2,29	<0,001	<0,001
III	11,69 ± 1,78		
IV	13,14 ± 0,99		

Patients with stage I disease had the lowest mean CA 19-9 level (76.45 ± 12.3 U/mL), while those with stage IV disease had the highest (198.67 ± 53.4 U/mL). Similarly, TB levels were significantly higher in patients with advanced disease. Stage I patients had a mean TB level of 6.7 ± 0.62 mg/dL, while stage IV patients had a mean TB level of 13.14 ± 0.99 mg/dL.

Table 3. Distribution of CA 19-9 levels by pancreatic cancer stage

Stage	CA 19-9 (U/mL)	*p value*	Post-hoc test
I	91 ± 11,65		
II	116,12 ± 25,11	<0,001	<0,001
III	157,07 ± 28,99		
IV	198,20 ± 25,9		

The post-hoc analysis showed that CA 19-9 and TB levels were significantly different between each cancer stage (p < 0.05). The largest increase in both markers was observed between stages III and IV, suggesting a sharp rise in tumour marker levels and biliary obstruction as the disease progresses to its most advanced stages.

Table 4. Association between total bilirubin levels and CA 19-9 levels with pancreatic cancer stage

Independent parameter	Eta value
Bilirubin Total	0,835
CA 19-9	0,798

4. Discussion

This study found a significant correlation between CA 19-9 and TB levels with the stage of

pancreatic cancer in patients treated at RSUP Haji Adam Malik Medan. Elevated CA 19-9 levels have been well-documented as markers of advanced disease and poor prognosis in pancreatic cancer patients (6). Our findings align with previous studies that suggest CA 19-9 levels increase progressively with tumour size, local invasion, and metastatic spread (7). However, CA 19-9 levels can be influenced by obstructive jaundice, which complicates its interpretation in pancreatic cancer patients with tumours located in the head of the pancreas (8).

The addition of TB levels to the analysis offers valuable insights, particularly in patients presenting with jaundice. Bilirubin, a byproduct of hemoglobin breakdown, is elevated when bile ducts are obstructed by tumour growth. Elevated TB levels in patients with pancreatic cancer typically represent more advanced disease, as the obstruction of bile flow indicates extensive local invasion or metastatic spread (9). In this study, patients with stage IV disease exhibited the highest TB levels, correlating with their advanced tumour stage and poor prognosis.

The combination of CA 19-9 and TB levels improves diagnostic accuracy, particularly in differentiating between early and late-stage disease. Patients with elevated CA 19-9 and TB levels are likely to have more advanced disease, requiring more aggressive treatment strategies, such as chemotherapy or palliative care, rather than surgery. The sharp increase in both biomarkers between stages III and IV highlights the need for early intervention to prevent the progression of biliary obstruction and improve patient outcomes.

Despite the promising results, this study is not without limitations. First, it is a retrospective study, which limits our ability to control for all confounding factors. Second, while CA 19-9 and TB are useful biomarkers, they are not entirely specific to pancreatic cancer. Future studies should explore the potential of combining these markers with other novel biomarkers, such as circulating tumour DNA or exosomes, to further enhance diagnostic and prognostic accuracy (10).

5. Conclusion

In conclusion, this study demonstrates a significant correlation between CA 19-9 and TB levels with the stage of pancreatic cancer in patients treated at RSUP Haji Adam Malik Medan. Both biomarkers were significantly elevated in patients with advanced disease, particularly those with stage IV cancer. The combination of CA 19-9 and TB measurements provides a more accurate assessment of disease progression and can be used to guide clinical decision-making. Future research should focus on the development of more specific biomarkers to improve early detection and optimize treatment outcomes in pancreatic cancer patients.

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