MECHANICAL JAUNDICE AND CLINICAL-LABORATORY CORRELATIONS

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Abstract

Introduction: Post-hepatic or mechanical jaundice is a pathology of the biliary tract usually caused by biliary calculi and tumors. The aim of the study is to evaluate the clinical-laboratory correlations in patients with mechanical jaundice.

Material and Methods: This is a prospective study conducted during the period 2012–2015 at the "Mother Teresa" University Hospital Center in Tirana, specifically in the Department of Gastroenterology. The study included patients admitted to the Gastroenterology ward with the clinical diagnosis of "Obstructive Jaundice."

Results: The study included 163 patients, with a mean age of 63.5 (±13.1) years, ranging from 20–85 years; 35.2% were male and 65.6% were female. According to the admission diagnosis, mechanical jaundice cases predominated (62.6%), followed by acute pancreatitis (12.8%). Malignant diagnoses were observed in 45.4% of patients. Men were 1.3 times more likely to develop malignancies. In the multivariate logistic regression model, it was found that direct bilirubin (mg/dl), CA 19-9 (U/mL), and GGT (U/L) are independent predictors of malignancy. Furthermore, the combination of predictors for malignancy—weight loss >10%, bilirubin >3 mg/dl, and CA 19-9 >35 U/ml—significantly increased the sensitivity, specificity, and positive predictive value (100%) compared to each factor individually.

Conclusion: The importance of early diagnosis and timely treatment of obstructive jaundice or cholestasis is crucial, as early etiological treatment of mechanical jaundice can prevent complications from disease progression. The investigation and management of obstructive jaundice require a multidisciplinary team composed of surgeons, radiologists, pathologists, gastroenterologists, and oncologists.

Keywords: Mechanical jaundice, jaundice, calculosis, tumor

IKTERI MEKANIK DHE KORRELACIONET KLINIKO LABORATORIKE

Abstrakt

Hyrje: Ikteri post hepatik ose mekanik eshte nje patologji e traktit biliar qe zakonisht shkaktohet nga kalkuloza biliare dhe tumore. Qellimi i studimit eshte vlerësimi i korrelacioneve kliniko-laboratorike tek pacientet me ikter mekanik.

Materiali dhe Metodat: Ky është një studim prospektiv i kryer në periudhën 2012-2015 në Qendrën Spitalore Universitare "Nënë Tereza" Tiranë si dhe në repartin e Gastroenterologjisë. Në studim janë përfshirë pacientët e shtruar në repartin e Gastroenterologjisë me diagnozë klinike "Verdhëz obstruktive".

Rezultate: Në studim morën pjesë 163 pacientë, mosha mesatare e të cilëve është 63.5 (±13.1) rangu 20-85 vjeç; (35.2%) meshkuj dhe (65.6%) femra. Sipas diagnozës së shtrimit, mbizotërojnë rastet me Ikter mekanik (62.6%) ndjekur nga pankreatiti akut (12.8%). Me diagnozë malinje rezultuan 45.4% e pacientëve. Meshkujt kanë 1.3 here më tepër gjasa të preken nga malinjiteti. Në modelin e regresionit logjistik multivariat u gjet që: B.direkte (mg/dl),CA19_9 (U/mL), GGT (U/L) janë faktorë të pavarur prediktorë të malinjitetit. Gjithashtu, u gjet që kombinimi i faktorëve parashikues të malinjitetit: rënia në peshë më > 10%, bilirubina >3 mg / dl dhe CA 19-9 > 35 U / ml rrit ne menyre te ndjeshme vlerat e sensitivitetit, specificitetit dhe vleres parashikuese positive (100%) krahasuar me secilin nga faktoret veçmas.

Përfundim: Rëndësia e diagnozës së hershme dhe trajtimi në kohë i verdhëzës ose kolestazës obstruktive është vendimtare, meqenëse trajtimi etiologjik ne kohe I ikterit mekanik do parandalonte komplikacionet nga ecuria e semundjes.Investigimi dhe menaxhimi i verdhëzës obstruktive kerkon nje ekip multidisiplinar të përbërë nga kirurgë, radiologë, patologë, gastroenterologë dhe onkologë.

Fjalët kyçe: ikter mekanik, verdhëz, kalkulozë, tumor

Introduction

Mechanical jaundice refers to a specific condition in medicine that deals with a particular type of jaundice, a state caused by the accumulation of bilirubin in the blood, and how this increase influences laboratory tests and the patient's clinical signs (1). Mechanical jaundice typically occurs due to an obstruction in the biliary pathways, which can be blocked by stones, tumors, or inflammation. This blockage prevents the normal flow of bile from the liver to the intestines, resulting in elevated bilirubin levels in the blood and the characteristic yellow discoloration of the skin and eyes (2). The clinical-laboratory correlations in cases of mechanical jaundice include findings from blood analyses, such as elevated direct bilirubin levels, and other specific changes like increases in liver enzyme levels, indicating damage or inflammation of the liver and biliary pathways. These laboratory findings, together with clinical symptoms and imaging techniques such as ultrasound or MRCP (magnetic resonance cholangiopancreatography), help in diagnosing and managing this condition (3). In diagnosing mechanical jaundice and detecting possible malignancy in the liver, biomarkers play a critical role. Their values help doctors differentiate between various causes of jaundice and identify the presence of cancer in the liver or bile ducts (4). The use of these biomarkers, in combination with imaging techniques, offers a comprehensive approach that assists in accurate diagnosis and appropriate medical intervention (5). This is essential for effective patient management and improving health outcomes. The aim of the study is to evaluate the clinical-laboratory correlations in patients with mechanical jaundice.

Material and Methods

This is a prospective study conducted during the period 2012–2015 at the "Mother Teresa" University Hospital Center in Tirana, specifically in the Gastroenterology Department.

Inclusion Criteria

Our study included patients admitted to the Gastroenterology ward with a clinical diagnosis of "Obstructive Jaundice."

ExclusionCriteria

Patients were excluded from the study based on the following criteria: primary or metastatic malignancy of the liver (hepatocellular carcinoma), chronic or parallel liver diseases, primary sclerosing cholangitis, choledochocele, congenital hepatobiliary anomalies, endoscopic sphincterotomy or stent placement, and sphincter of Oddi dysfunction.

Data Collection

Data for each patient were collected using a structured questionnaire. All patients underwent a detailed medical history, clinical examination, and laboratory investigations, including liver function tests. Laboratory parameters of blood and urine were studied as potential predictive factors for differentiating choledocholithiasis from biliopancreatic malignancy. All patients underwent liver function tests to assess bilirubin levels, alkaline phosphatase (ALP), ALT, and AST. Bilirubin levels were measured upon patient admission and again 48 hours after admission.

Statistical analysis

Data analysis was performed using the SPSS 20.0 statistical package. The Kolmogorov-Smirnov test was used to assess the distribution of continuous variables. Descriptive statistics of continuous variables were presented as means and standard deviations, while categorical variables were presented as absolute frequencies and percentages. The chi-square test and Fisher’s exact test were used to compare proportions between categorical variables. The Student's t-test was used for comparing means of continuous variables. A multivariate logistic regression model was employed to control for all possible confounders and to assess biomarkers as independent predictors of malignancy. Statistical significance was determined at $p \leq 0.05$. All statistical tests were two-tailed.

Results

The study included 163 patients with a mean age of 63.5 (±13.1) years, ranging from 20–85 years. Of these, 35.2% were male (n=56) and 65.6% were female (n=107), with a statistically significant difference between the groups ($p<0.05$). The mean age of male patients was 65.7 (±11.5) years (range 31–85), while the mean age of female patients was 59.6 (±15.1) years (range 20–82), showing no statistically significant difference ($t=1.9$, $p=0.06$).

Table 1. Characteristics of patients in the study (N=163)

Variables	N	%
Gender		
Female	107	65.6
Male	56	35.2
Age, Mean (SD)	63.5	(13.1)
Age group, years		
20–29	4	2.5
30–39	4	2.5
40–49	14	8.6
50–59	30	18.4
60–69	51	31.3
≥70	60	36.8
Employment Status		
Economic assistance	49	30.1
Pension	78	47.9
Employed	36	22.1

Admission Diagnosis

Of the total 163 cases, the most frequent diagnosis was mechanical jaundice (62.6%) followed by acute pancreatitis (12.3%). Other diagnoses included ampullary tumors (1.8%), pancreatic cancer (4.9%), and acute cholangitis (6.7%). Mechanical jaundice cases showed a statistically significant difference compared to other diagnoses (χ^2=121, p<0.01).

Table 2. Distribution of cases according to admission diagnosis

Admission Diagnosis	N	%
Ampullary tumor	3	1.8
Pancreatic cancer	8	4.9
Acute cholangitis	11	6.7
Head of pancreas mass	3	1.8
Jaundice	5	3.1
Mechanical jaundice	102	62.6
Ventricular neoplasm	8	4.9
Acute pancreatitis	20	12.3
Biliary acute pancreatitis	3	1.8
Total	**163**	**100.0**

Malignancy Distribution

In total, 45.4% of patients (n=74) were diagnosed with malignant conditions (95% CI: 37.95–53.06), while 54.6% (n=89) had benign diagnoses (95% CI: 46.93–62.05).

Table 3. Frequency of malignancy

Malignancy	N	%	95% CI
No	89	54.6	46.93 – 62.05
Yes	74	45.4	37.95 – 53.06
Total	**163**	**100.0**	

Comparison of Biomarkers

Statistically significant differences were observed between patients with benign and malignant pathologies in the values of certain biomarkers:

- Higher WBC, RBC, and PLT levels were seen in benign cases.
- Higher total bilirubin, direct bilirubin, CA 19-9, ALT, AST, ALP, and GGT levels were found in malignant cases.

Table 4. Comparison of hematobiochemical biomarkers by pathology

Biomarkers	**Benign Pathology M (SD)**	**Malignant Pathology M (SD)**	**P**
WBC (10^3µL)	7.6 (2.8)	6.8 (2.1)	0.04*
RBC (10^6µL)	4.3 (2.5)	3.8 (1.9)	0.04*
PLT (10^5µL)	316.0 (99.1)	181.1 (97.4)	0.02*
Hb (g/dl)	12.1 (1.8)	11.0 (1.8)	0.7
HCT (%)	38.0 (3.4)	32.7 (4.1)	0.4
Glucose (mg/dl)	102 (2.1.1)	108 (20.3)	0.8
BUN (mg/dl)	28 (4.2)	31 (4.8)	0.2
Creatinine (mg/dl)	0.8 (0.2)	0.9 (0.2)	0.9
Total bilirubin (mg/dl)	3.8 (3.2)	13.1 (5.3)	<0.01*
Direct bilirubin (mg/dl)	1.5 (2.1)	8.5 (4.3)	<0.01*
CA 19-9 (U/mL)	90 (41.1)	324 (63.8)	0.01*
ALT (U/L)	91 (28.9)	137 (66.3)	0.02*
AST (U/L)	88 (30.2)	129 (53.6)	0.03*
ALP (U/L)	168 (54.2)	301 (65.9)	0.02*
GGT (U/L)	196 (77.3)	424 (91.4)	<0.01*

*Statistically significant difference

Changes after 48 hours of treatment

For patients with benign conditions, ALT (U/L), AST (U/L), direct bilirubin (mg/dl), and WBC (10^3/µL) values significantly decreased 48 hours after treatment compared to admission values. In contrast, for patients with malignant conditions, these values showed no significant change, and direct bilirubin levels even increased.

Multivariate Logistic Regression

In the multivariate logistic regression model, the following were identified as independent predictors of malignancy:

- **Direct bilirubin** (mg/dl) (OR=3.5, 95% CI: 1.73–10.30, p<0.01),
- **CA 19-9** (U/mL) (OR=4.4, 95% CI: 2.86–11.57, p<0.01),

- **GGT** (U/L) (OR=3.8, 95% CI: 2.25–7.19, p<0.01).

The combination of malignancy predictors—weight loss >10%, bilirubin >3 mg/dl, and CA 19-9 >35 U/ml—significantly increased sensitivity, specificity, and positive predictive value to 100% compared to each factor alone.

Table 5. Risk factors for malignant pathology: Multivariate logistic regression

Variables	N (%)	OR	95% CI	P
Age, Mean (SD)	65.5 (±14.4)	1.4	0.24 – 8.42	0.7
Gender				
Male	21 (37.5)	Ref		
Female	30 (28.0)	1.5	0.53 – 3.17	0.5
Biomarkers*				
AFP (ng/ml)	64 (39.3)	1.7	0.64 – 9.12	0.2
Total bilirubin (mg/dl)	98 (60.2)	2.4	0.73 – 2.77	0.3
Direct bilirubin (mg/dl)	59 (36.2)	3.5	1.73 – 10.30	<0.01
CA 19-9 (U/mL)	64 (39.3)	4.4	2.86 – 11.57	<0.01
CEA (ng/ml)	91 (55.8)	2.2	0.32 – 8.41	0.09
GGT (U/L)	62 (38.0)	3.8	2.25 – 7.19	<0.01
ALP (U/L)	73 (44.8)	1.9	0.38 – 11.54	0.2
ALT (U/L)	91 (55.8)	2.1	0.78 – 5.13	0.1
AST (U/L)	96 (58.9)	1.8	0.57 – 10.11	0.2

*Values above cut off.

Discussion

Obstructive jaundice is a common surgical problem that occurs when there is an obstruction preventing the conjugated bilirubin from passing from the liver cells to the intestines (6). It remains one of the most challenging surgical conditions, significantly contributing to high morbidity and mortality (7–10). Given that patients with obstructive jaundice have high morbidity and mortality rates, early diagnosis of the cause of obstruction is critical, especially in malignant cases, as surgical resection is only possible in the early stages (11). Obstructive jaundice can be caused by a heterogeneous group of diseases, including both benign and malignant conditions (12). The common etiologies of obstructive jaundice differ from individual to individual (13). Obstructive jaundice is not a final diagnosis, and early investigation to clarify its exact cause is of great importance because systemic pathological changes can occur if the obstruction is not relieved. Several invasive and non-invasive diagnostic tests exist to determine the cause of obstructive jaundice, including laboratory and imaging tests (14). An interesting observation in this study was the importance of elevated CA 19-9 levels in patients with a mass in the head of the pancreas. CA 19-9 antigen is synthesized by both normal biliary epithelial cells and tumor cells and is excreted through bile (15). It has been suggested that elevated CA 19-9 levels in patients with both benign and malignant obstructive jaundice reflect the reflux of bile into the bloodstream due to biliary stasis and increased permeability between bile and blood (16). In the absence of obstructive jaundice, CA 19-9 present in the blood originates exclusively from tumor cells, excluding the possibility of false positivity caused by the biliary epithelium. Therefore, patients with a mass

in the head of the pancreas without jaundice but with elevated CA 19-9 levels are more likely to have malignancy compared to jaundiced patients. Other authors (17) have compared CA 19-9 levels in patients with benign and malignant pancreatic pathologies with and without jaundice and observed similar importance of elevated CA 19-9 levels in patients without jaundice. However, this observation requires further studies with larger cohorts. At a CA 19-9 value of 300 U/ml, both specificity and positive predictive value were high for predicting malignancy. Although isolated cases of elevated CA 19-9 have been reported in benign conditions (18), it is still considered an independent predictor of malignancy in pancreatic masses. This finding has also been confirmed by other researchers studying massive lesions in chronic pancreatitis (19). Nonetheless, dedicated studies on extremely high CA 19-9 levels would provide further clarity.

Combination of Predictors. It was observed that the combination of predictive factors for malignancy—weight loss >10%, bilirubin >3 mg/dl, and CA 19-9 >35 U/ml—significantly increased sensitivity, specificity, and positive predictive value compared to each factor alone.

In this study, the demographics were comparable between the benign and malignant groups. For most patients, weight documented at hospital admission was used, while for others, weight from six months prior to diagnosis was referenced. Weight loss, jaundice, and CA 19-9 levels were significantly higher in the malignant group and were further analyzed to determine the optimal cut-off values for predicting malignancy with maximum accuracy. A weight loss of more than 10% of body weight was used as the clinical cut-off for significant weight loss (20). In the multivariate analysis, the combination of weight loss >10%, bilirubin >3 mg/dl, and CA 19-9 >35 U/ml showed a specificity and positive predictive value of 100% for identifying malignancy in the pancreatic head mass. To our knowledge, Tessler et al. (21) were the first to correlate the combination of clinical and biochemical parameters to enhance the efficiency of differentiating malignant from benign lesions without requiring histological diagnosis and its associated complications. In their study of 150 patients, they found that weight loss and bilirubin levels were significantly higher in the malignant group. In the multivariate analysis, a combination of weight loss >10%, bilirubin >3 mg/dl, and CA 19-9 >37 U/ml achieved a specificity and positive predictive value of 100% for predicting malignancy. Our study findings align with other studies reported in the literature (22). Early diagnosis and timely treatment of obstructive jaundice or cholestasis are crucial because pathological changes can develop in the liver if mechanical jaundice is not treated according to its etiology. Investigating and managing obstructive jaundice requires a multidisciplinary team consisting of surgeons, radiologists, pathologists, gastroenterologists, and oncologists.

Conclusion: The importance of early diagnosis and timely treatment of obstructive jaundice or cholestasis is crucial, as early etiological treatment of mechanical jaundice can prevent complications from disease progression. The investigation and management of obstructive jaundice require a multidisciplinary team composed of surgeons, radiologists, pathologists, gastroenterologists, and oncologists.

Conflict of interests. None

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