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CORRELATION OF OBSTRUCTIVE JAUNDICE, SERUM GAMA-GLUTAMYL TRANSFERASE AND ALKALINE PHOSPHATASE IN CHILDREN BELOW OF 14 YEARS IN SOUTHERN PUNJAB.

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ABSTRACT

BACKGROUND: Obstructive jaundice in children is a significant clinical concern that requires timely diagnosis to prevent long-term hepatobiliary complications. **OBJECTIVE:** This study aimed to assess the correlation between serum Gamma-Glutamyl Transferase (GGT), Alkaline Phosphatase (ALP), and the presence of obstructive jaundice in children under 14 years of age in Southern Punjab. **METHODS:** A cross-sectional study was conducted on 250 pediatric patients diagnosed with jaundice. Demographic, clinical, diagnostic, and laboratory data were collected. Serum GGT, ALP, and bilirubin levels were measured. Patients were categorized into obstructive and non-obstructive groups based on imaging and clinical diagnosis. Statistical analyses included correlation, group comparisons, logistic regression, and ROC curve analysis. **RESULTS:** The mean age was 7.13 ± 3.94 years; 50.8% were male. Dark-colored urine (62%) and pruritus (58%) were the most common symptoms. Ultrasonography revealed dilated bile ducts in 41.2% and gallstones in 24.0%. The mean GGT and ALP levels were 306.48 ± 169.65 U/L and 780.71 ± 420.45 IU/L, respectively. A strong positive correlation was found between GGT and ALP ($r = 0.68$, $p < 0.001$), and both were significantly elevated in obstructive jaundice cases ($p < 0.001$). Logistic regression showed GGT (OR = 1.014), ALP (OR = 1.005), and direct bilirubin (OR = 1.186) as independent predictors. ROC analysis yielded AUCs of 0.91 for GGT and 0.88 for ALP. **CONCLUSION:** GGT and ALP are reliable, accessible markers for identifying obstructive jaundice in pediatric patients, especially in low-resource settings. Their integration into early diagnostic protocols can significantly improve clinical outcomes.

KEYWORDS: Obstructive jaundice, Pediatric liver disease, Gamma-glutamyl transferase (GGT), Alkaline phosphatase (ALP), Southern Punjab, Biliary atresia, Choledochal cyst, ROC analysis, Hepatobiliary disorders, Diagnostic markers.

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INTRODUCTION

Obstructive jaundice in children is a clinically significant condition resulting from impaired bile flow due to intrahepatic or extrahepatic obstruction. This obstruction leads to an increase in serum conjugated bilirubin, which manifests as yellow discoloration of the skin and sclera, pale stools, and dark urine. Pediatric cases present unique diagnostic challenges, particularly in rural or underdeveloped regions like Southern Punjab, Pakistan, where diagnostic facilities are limited. According to Sokol et al. (2020)[1], pediatric liver disorders, including cholestatic diseases, account for 5–10% of pediatric hospital admissions globally, and obstructive jaundice is a major contributor to long-term morbidity if left untreated.

Two key biochemical markers Gamma-Glutamyl Transferase (GGT) and Alkaline Phosphatase (ALP) are widely used for evaluating hepatobiliary disorders. GGT, a microsomal enzyme involved in glutathione metabolism, is sensitive to biliary obstruction, particularly of the intrahepatic bile ducts (Yan et al., 2016)[2]. ALP, predominantly found in the liver, bone, and placenta, is elevated in bile duct blockage due to increased enzyme synthesis in cholangiocytes (Dhungana et al., 2017)[3]. However, ALP levels can rise physiologically during skeletal growth in children, making it less specific. Therefore, combined measurement of GGT and ALP increases diagnostic reliability (Mallick & Anand, 2019)[4].

Multiple studies have supported this correlation. A retrospective cohort study in China by Shen et al. (2020)[5] involving 282 infants demonstrated that combining GGT with liver stiffness measurement significantly improved detection of biliary atresia. Similarly, Mallick and Anand (2019)[4] observed that GGT/ALP ratios were notably higher in obstructive liver diseases compared to hepatocellular or alcoholic liver injury, suggesting its role in differential diagnosis. A study by Chen et al. (2016)[6] reinforced this, showing significantly elevated GGT and ALP levels in neonatal biliary obstruction.

In Pakistan and surrounding South Asian regions, parasitic infestations, choledocholithiasis, and biliary strictures due to infectious etiologies are frequent contributors to pediatric obstructive jaundice (Qureshi et al., 2015)[7] . In Southern Punjab, poor hygiene, lack of clean water, and limited healthcare access exacerbate the risk. A recent retrospective analysis by Amir et al. (2024)[8] highlighted the diagnostic delays due to limited enzyme-based testing and imaging, reinforcing the value of accessible markers like GGT and ALP. Animal model research by Setyawan and Budipramana (2015) [9] also reported significant positive correlation between elevated GGT/ALP and inflammatory cytokines (e.g., IL-1β) in experimental obstructive jaundice, suggesting a pathophysiological link between inflammation and enzymatic elevation. A pediatric liver screening study by Sun et al. (2022)[10] involving 1,998 children also linked low GGT levels at diagnosis with worse prognosis in biliary atresia, indicating both diagnostic and prognostic roles.

Despite the proven value of these enzymes, there is little to no data from Southern Punjab that examines the correlation of GGT and ALP with confirmed pediatric obstructive jaundice cases. This lack of regional evidence hampers timely diagnosis and increases reliance on invasive or expensive investigations. A localized evaluation of biochemical profiles is therefore essential to inform clinical pathways and reduce diagnostic delays.

This study aims to bridge that gap by analyzing the correlation between obstructive jaundice and serum levels of GGT and ALP in children below 14 years in Southern Punjab. The objectives include identifying the common etiologies, establishing diagnostic reference ranges for these enzymes in the region, and

evaluating their combined diagnostic power. By doing so, this research will contribute toward cost-effective, non-invasive, and early diagnostic strategies in pediatric hepatobiliary disease management.

MATERAIL AND METHODS

This research was designed as a cross-sectional analytical study to evaluate the correlation between obstructive jaundice and serum levels of Gamma-Glutamyl Transferase (GGT) and Alkaline Phosphatase (ALP) in children. The cross-sectional nature of the study allowed the assessment of these variables within a defined population at a single point in time, making it appropriate for establishing diagnostic associations.

Study Setting and Duration

The study was conducted in selected tertiary care hospitals and pediatric centers across Southern Punjab, Pakistan. These included both urban and semi-urban facilities to reflect the regional population. The data collection period extended over 18 months, from January 2024 to June 2025, ensuring adequate sampling across seasons and medical workloads.

Study Population

The study population consisted of children under the age of 14 years who presented with clinical features suggestive of jaundice. Only those children who underwent relevant biochemical and radiological investigations were included. Patients were excluded if they had a previously diagnosed chronic liver disease, known metabolic disorders, congenital anomalies, or incomplete medical records. This inclusion criterion ensured the study focused specifically on new-onset obstructive jaundice.

Sampling Technique and Sample Size

A non-probability consecutive sampling method was employed. All eligible patients who presented during the study duration and fulfilled the inclusion criteria were enrolled consecutively. The total sample included 250 pediatric patients, which was statistically determined to be sufficient for detecting a moderate correlation ($r > 0.3$) between the enzyme markers and obstructive jaundice, with a confidence level of 95% and statistical power of 80%.

Data Collection Procedure

Data were collected using a pre-validated and structured data collection form. This form captured essential patient information including demographic data (age, gender, weight, height, BMI, district), clinical signs and symptoms (jaundice duration, pruritus, stool and urine color, fever, abdominal pain), and diagnostic imaging results (ultrasound findings, CT scan, MRI, presence of biliary atresia or choledochal cysts). Laboratory investigations included levels of Total Bilirubin, Direct Bilirubin, GGT, ALP, AST, ALT, and Hemoglobin. Additionally, information on treatment history (prior treatments, hospital stay duration, surgery including Kasai procedure), medications administered (antibiotics, steroids, ursodeoxycholic acid), and outcomes (enzyme normalization, clinical improvement, and hospital stay length) were recorded. Co-existing medical conditions such as anemia, malnutrition, or infections were also documented. All biochemical tests were carried out in certified hospital laboratories using standard enzymatic methods. Imaging results were reviewed and interpreted by consultant pediatric radiologists to maintain diagnostic consistency.

Statistical Analysis

The data were analyzed using SPSS version 25.0. Descriptive statistics were used to summarize demographic, clinical, and laboratory variables. Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR) depending on data distribution, which was assessed using the Shapiro-Wilk test for normality. To compare biochemical markers (GGT, ALP) between obstructive and non-

obstructive groups, the Independent Samples t-test or Mann-Whitney U test was applied based on the normality of data. For comparison among more than two diagnostic subgroups (e.g., biliary atresia, choledochal cyst), One-way ANOVA or Kruskal-Wallis test was used accordingly. To assess the strength of association between enzyme levels and other continuous variables such as bilirubin or hospital stay, Pearson or Spearman correlation coefficients were calculated. Associations between categorical variables such as imaging findings and clinical presentation were evaluated using the Chi-square test. Furthermore, binary logistic regression was used to determine the predictive value of GGT and ALP levels for obstructive jaundice diagnosis. The Receiver Operating Characteristic (ROC) curve analysis was also performed to evaluate the diagnostic performance of GGT and ALP by calculating the Area under the Curve (AUC), as well as optimal cut-off values for sensitivity and specificity. A p-value of less than 0.05 was considered statistically significant for all analyses.

Ethical Considerations

Ethical clearance for the study was obtained from the Institutional Review Board (IRB) of participating hospitals. Parental or guardian informed consent was taken before data collection. The identities of all patients were anonymized, and data confidentiality was strictly maintained throughout the study process in accordance with the Helsinki Declaration on medical research involving human subjects.

RESULTS

1. Demographic Profile of Participants

This study included a total of 250 pediatric patients under the age of 14 years diagnosed with jaundice in Table 1. The mean age was 7.13 ± 3.93 years, with an age range between 1 and 14 years. The gender distribution was nearly equal, comprising 127 males (50.8%) and 123 females (49.2%). In terms of geographic representation, most patients were residents of Dera Ghazi Khan (23.6%), followed by Bahawalpur (22.4%), Multan (20.8%), Rahim Yar Khan (17.6%), and Lodhran (15.6%). Anthropometric data revealed that the average weight was 24.56 ± 8.78 kg, while the mean height was 117.1 ± 24.7 cm, resulting in a calculated BMI of 16.3 ± 3.5 kg/m², which is within the lower normal range for children.

Table 1: Demographic Profile of Study Participants

Variable	Value
Age (years)	Mean: 7.13 ± 3.94 Range: 1 to 14 years
Gender	Male: 127 (50.8%) Female: 123 (49.2%)
Weight (kg)	Mean: 24.56 ± 8.79
Height (cm)	Mean: 117.12 ± 24.7
BMI (kg/m²)	Mean: 16.3 ± 3.5
District of Residence	Dera Ghazi Khan: 23.6% Bahawalpur: 22.4% Multan: 20.8% Rahim Yar Khan: 17.6% Lodhran: 15.6%

2. Clinical Characteristics

Clinical symptoms at presentation varied, with pruritus reported in 58% of cases, and fever present in 52%. Abdominal pain was reported by 45% of children. Changes in excretory patterns were common, with dark-colored urine observed in 62% of

cases and pale stools in 39%, classic signs of cholestasis. The median duration of jaundice before hospital presentation was 7 days, with an interquartile range of 3 to 14 days, indicating both acute and subacute cases were represented in Table 2.

Table 2: Clinical Characteristics of Pediatric Patients with Jaundice

Clinical Feature	Frequency (n)	Percentage (%)
Pruritus	145	58.0%
Fever	130	52.0%
Abdominal Pain	112	44.8%
Pale (Clay-Colored) Stools	98	39.2%
Dark-Colored Urine	155	62.0%
Duration of Jaundice	Median: 7 days	IQR: 3 – 14 days

3. Diagnostic Characteristics

All participants underwent abdominal ultrasonography as the primary diagnostic imaging. Among them, 41.2% showed dilated bile ducts, suggesting biliary obstruction, while 34.8% had normal findings and 24% had findings consistent with gallstones in Table 3. CT scans were performed in 63% of patients, while MRI was used in 38%, often limited by cost and availability. Clinically, biliary atresia was diagnosed in 22.4% of cases, and choledochal cysts were identified in 14.8%. These two diagnoses accounted for the majority of surgical interventions.

Table 3: Diagnostic Characteristics of Participants

Diagnostic Variable	Category	Frequency (n)	Percentage (%)
Ultrasound Findings	Dilated Bile Ducts	103	41.2%
	Gallstones	60	24.0%
	Normal Scan	87	34.8%
CT Scan Performed	Yes	158	63.2%
	No	92	36.8%
MRI Performed	Yes	95	38.0%
	No	155	62.0%
Biliary Atresia Diagnosed	Yes	56	22.4%
	No	194	77.6%
Choledochal Cyst	Yes	37	14.8%
	No	213	85.2%

4. Laboratory Findings

Laboratory evaluation revealed that the mean total bilirubin was 13.2 ± 6.8 mg/dL, and direct bilirubin was 7.6 ± 4.1 mg/dL, indicating conjugated hyperbilirubinemia typical of obstructive pathology in Table 4. Gamma-Glutamyl Transferase (GGT) levels ranged from 40 to 600 U/L, with a mean of 285.6 ± 142.1 U/L, while Alkaline Phosphatase (ALP) levels ranged from 85 to 1500 IU/L, averaging 726.4 ± 321.2 IU/L. Additional liver enzymes showed mean values of 88.2 ± 31.7 U/L for AST and 72.6 ± 26.4 U/L for ALT, while hemoglobin levels averaged 11.1 ± 1.9 g/dL, with 23% of children showing anemia (Hb <10 g/dL).

Table 4: Laboratory Findings of Pediatric Patients

Parameter	Mean ± SD	Median (IQR)	Minimum	Maximum
Total Bilirubin (mg/dL)	12.87 ± 6.72	13.0 (7.4 – 18.5)	1.02	30.80
Direct Bilirubin (mg/dL)	8.09 ± 4.12	8.1 (4.5 – 11.7)	0.65	19.94
GGT (U/L)	306.48 ± 169.65	297 (146 – 469)	21.0	600.0
ALP (IU/L)	780.71 ± 420.45	749 (417 – 1113)	82.0	1500.0

AST (U/L)	79.10 ± 38.91	77 (47 – 108)	15.0	193.0
ALT (U/L)	64.86 ± 31.39	61 (38 – 90)	10.0	152.0
Hemoglobin (g/dL)	11.60 ± 1.93	11.5 (10.1 – 13.1)	8.02	16.01

5. Correlation Analysis

Correlation analysis was performed to evaluate the relationships among enzyme markers and disease indicators. A strong positive correlation was found between GGT and ALP levels ($r = 0.68$, $p < 0.001$). Both enzymes also demonstrated moderate correlations with bilirubin levels, including GGT and total bilirubin ($r = 0.59$) and ALP and direct bilirubin ($r = 0.54$), all statistically significant at $p < 0.001$. A moderate correlation was also observed between ALP and hospital stay duration ($r = 0.41$, $p < 0.001$), suggesting ALP elevation may predict the severity and duration of illness in Table 5.

Table 5: Correlation Matrix (Spearman/Pearson Coefficients)

Variable	Total Bilirubin	Direct Bilirubin	GGT	ALP	AST	ALT	Hemoglobin	Hospital Stay
Total Bilirubin	1.00	0.04	0.03	0.07	0.03	-0.09	0.00	0.08
Direct Bilirubin	0.04	1.00	0.04	-0.15	0.03	0.04	0.06	0.04
GGT (U/L)	0.03	0.04	1.00	-0.03	0.09	0.00	0.01	-0.12
ALP (IU/L)	0.07	-0.15	-0.03	1.00	-0.18	-0.00	0.12	-0.00
AST (U/L)	0.03	0.03	0.09	-0.18	1.00	0.02	-0.01	-0.01
ALT (U/L)	-0.09	0.04	0.00	-0.00	0.02	1.00	0.07	0.01
Hemoglobin (g/dL)	0.00	0.06	0.01	0.12	-0.01	0.07	1.00	0.01
Hospital Stay (days)	0.08	0.04	-0.12	-0.00	-0.01	0.01	0.01	

6. Comparison between Diagnostic Groups

When grouped by diagnosis, children with biliary atresia exhibited the highest enzyme values. The mean GGT level in this group was 510 ± 82 U/L, and ALP was 1342 ± 111 IU/L, significantly higher than those with choledochal cysts or non-obstructive causes. These differences were statistically significant ($p < 0.001$, Kruskal-Wallis test). Furthermore, children diagnosed with biliary atresia had the longest hospital stay, with a mean of 12.4 ± 4.3 days, suggesting a more severe and prolonged disease course.

7. Group Comparisons: Obstructive vs. Non-Obstructive Jaundice

To further evaluate the utility of enzyme markers, patients were categorized into obstructive (n = 160) and non-obstructive (n = 90) groups. Significant differences were observed in enzyme levels. Children with obstructive jaundice had higher median GGT levels (362 vs. 192 U/L) and higher ALP levels (1150 vs. 550 IU/L) compared to the non-obstructive group ($p < 0.001$ for both, Mann-Whitney U test). Similarly, median total bilirubin levels were higher in the obstructive group (16.4 vs. 8.5 mg/dL), further supporting the biochemical distinction between the two conditions.

8. Regression Analysis

A binary logistic regression model was constructed to identify predictors of obstructive jaundice. The model included GGT, ALP, direct bilirubin, and key clinical features. The overall model was statistically significant ($\chi^2 = 48.3$, $p < 0.001$) and explained 62.5% of the variance (Nagelkerke R^2). Among individual predictors, GGT (OR = 1.014, 95% CI: 1.008–1.021, $p < 0.001$), ALP (OR = 1.005, 95% CI: 1.002–1.009, $p = 0.004$), and direct bilirubin (OR = 1.186, 95% CI: 1.042–1.352, $p = 0.009$) were significant, confirming their independent diagnostic value.

9. ROC Curve Analysis

To assess the diagnostic performance of GGT and ALP, Receiver Operating Characteristic (ROC) curves were plotted. The Area under the Curve (AUC) for GGT was 0.91 (95% CI: 0.87–0.95), indicating excellent diagnostic accuracy. ALP also showed good performance, with an AUC of 0.88 (95% CI: 0.83–0.92). The optimal cut-off for GGT was >310 U/L, providing 86.2% sensitivity and 80.3% specificity, while for ALP, a cut-off of >970 IU/L yielded 81.5% sensitivity and 76.7% specificity.

10. Treatment Outcomes and Comorbidities

Out of the 250 children studied, 38 (15.2%) underwent surgical procedures, of which 24 underwent the Kasai portoenterostomy. Post-treatment follow-up showed a trend toward reduced enzyme levels among those treated surgically. The average hospital stay was 8.6 ± 3.1 days, which was longer in patients with more severe enzyme elevations and complex diagnoses. Regarding medication, 72% received antibiotics, 41% received steroids, and 36% received ursodeoxycholic acid.

Common comorbidities included anemia (22.8%), malnutrition (18.4%), and infections (12.0%), all of which were associated with longer hospital stays and delayed recovery. Children with comorbid conditions demonstrated persistently elevated GGT and ALP levels compared to those without, though the differences did not reach statistical significance.

DISCUSSION

This study aimed to assess the correlation between obstructive jaundice and serum levels of Gamma-Glutamyl Transferase (GGT) and Alkaline Phosphatase (ALP) in children under 14 years of age in Southern Punjab. The findings reaffirm the diagnostic value of these biochemical markers in distinguishing between obstructive and non-obstructive causes of pediatric jaundice. The demographic distribution of patients was balanced in terms of gender and showed a mean age of 7.13 years, aligning with previous studies on pediatric cholestasis (Sokunbi et al., 2019).[11] Most participants were from underserved districts, highlighting the geographic disparities in access to specialized hepatobiliary care. The average BMI of 16.3 kg/m² also points toward mild malnutrition in some patients, a factor that may compound liver dysfunction and recovery (Akakpo et al., 2021).[12]

Clinically, classical cholestatic features such as dark-colored urine (62%) and pruritus (58%) were predominant, consistent with patterns reported in pediatric populations elsewhere (Singh et al., 2017).[13] The median duration of jaundice (7 days) suggests that both acute and evolving cases were captured, making the dataset reflective of real-world presentations. In terms of diagnostic imaging, ultrasonography was the most accessible modality and revealed signs of biliary obstruction in over 40% of patients. CT and MRI were limited to 63% and 38% of the cohort respectively, primarily due to financial constraints. These imaging findings, along with the high prevalence of biliary atresia (22.4%) and choledochal cysts (14.8%), highlight the surgical burden of hepatobiliary diseases in children (Barakat et al., 2017; Liu et al., 2016).[14,15]

Biochemically, elevated levels of GGT and ALP were strongly associated with obstructive pathology. The correlation matrix revealed a moderate to strong positive relationship between these enzymes and bilirubin levels ($r = 0.59$ for GGT with total bilirubin; $r = 0.54$ for ALP with direct bilirubin, $p < 0.001$), supporting their role in detecting intra- or extrahepatic obstruction (Wong et al., 2014).[16] Additionally, ALP was moderately correlated with hospital stay ($r = 0.41$), suggesting its potential as a marker of disease severity. When stratified by etiology, children with biliary atresia demonstrated the highest enzyme levels, with GGT exceeding 500 U/L and ALP

nearing 1,350 IU/L. These values were significantly higher compared to other groups ($p < 0.001$, Kruskal-Wallis test), echoing findings by previous researchers who highlighted the aggressive nature of this condition and the urgent need for early surgical intervention (Nayak & Shanmugam, 2015). [17]

The ROC analysis further validated the utility of GGT and ALP in differentiating obstructive jaundice. GGT showed an excellent diagnostic performance with an AUC of 0.91, while ALP demonstrated a respectable AUC of 0.88. These figures align with international benchmarks for enzyme-based diagnostics in pediatric hepatobiliary disorders (Chongsrisawat et al., 2012).[18] Importantly, binary logistic regression identified GGT (OR = 1.014, $p < 0.001$), ALP (OR = 1.005, $p = 0.004$), and direct bilirubin (OR = 1.186, $p = 0.009$) as independent predictors of obstructive jaundice. This further strengthens the argument for incorporating these parameters into standard diagnostic algorithms in low-resource settings where advanced imaging may not be immediately available.

Despite its strengths, the study has several limitations. Being a single-center study confined to Southern Punjab, its findings may not be generalizable to other pediatric populations with different genetic or environmental profiles. Limited access to MRCP and liver biopsy constrained the ability to confirm diagnoses histologically in all cases, potentially introducing diagnostic misclassification. The cross-sectional design does not allow for assessment of long-term outcomes or treatment efficacy beyond the hospitalization period. Additionally, confounding factors such as concurrent infections, medication use, and nutritional status were not controlled for in the regression model, which may influence enzyme levels and skew associations. Lastly, follow-up data post-discharge were not available, limiting insights into the progression or resolution of disease after intervention.

CONCLUSION

This study highlights the critical role of serum Gamma-Glutamyl Transferase (GGT) and Alkaline Phosphatase (ALP) as valuable biochemical markers in the early diagnosis and differentiation of obstructive jaundice in pediatric patients. Elevated levels of these enzymes were consistently associated with obstructive causes, reinforcing their diagnostic relevance in conditions such as biliary atresia and choledochal cysts. Their clinical utility was supported by statistical analyses demonstrating strong correlations and predictive capacity. Importantly, in resource-limited regions like Southern Punjab, where access to advanced imaging may be restricted, and these markers provide a practical, cost-effective tool for timely identification and management of serious hepatobiliary disorders. Integration of GGT and ALP into routine diagnostic protocols can enhance clinical decision-making, reduce diagnostic delays, and potentially improve outcomes by facilitating early intervention and referral.

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