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*Original Article*

# Operational Diagnostic Criteriain Conjunction with the Triangular Cord Sign Enhance the Screening for Biliary Atresia

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**Abstract**

**Background:** Background: The early and accurate diagnosis of biliary atresia (BA) is critical for timely intervention. The triangularcordsign (TCS) onultrasonography isavaluabletool, butitsdiagnosticperformancecanbevariable. Objective: To evaluate whether the use of operational diagnostic criteria (ODC) in conjunction with TCS enhances the screening accuracy for BA. Methods: A prospective cohort studz was conducted at MAGOsmani Medical College Hospital, Szlhetin Bangladesh from July 2021 to December 2022. A total of 60 infants with persistent jaundice underwent evaluation for biliary atresia via triangular cord sign, operational diagnostic criteria, and confirmation by intraoperative cholangiography. Data were analyzed with SPSS 23.0.

**Results:** Among 60infants, biliary atresia was confirmed in 38 (63.3%).The triangularcord sign (TCS) showed 76.3% sensitivity and 86.4% specificity. Operational diagnostic criteria (ODC) alone demonstrated 89.5% sensitivity. Crucially, combining TCS and ODC (positive ifeither was positive) significantly enhancedsensitivity to97.4%($p<0.001$) with aspecificity of 77.3%. Then egativepredictivevalueforthecombinedmodel was 94.4%, and its AUC of 0.94 was superior to either tool alone.

**Conclusion:** The combination of operational diagnostic criteria with the triangular cord sign creates a highly sensitive and effective screening algorithm for biliary atresia. This integrated approach outperforms either method in isolation and can significantly enhance early detection, timely referral, and ultimately, improve outcomes for infants with this serious condition.

**Keywords:** Biliary atresia, Diagnostic accuracy, Infantile cholestasis, Operational criteria, Screening, Triangular cord sign, Ultrasonography.

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## Introduction

Biliary atresia (BA) is a devastating neonatal liver disease characterized by fibro-obliteration of the extrahepatic and intrahepatic bileducts, leading tocholestasis, progressive cirrhosis, and end-stage liverdiseaseifleftuntreated [1]. As the most common cause of pediatric liver transplantation worldwide, its early identification remains one of the most critical challenges in pediatric hepatology [2]. A recent review found that the reported incidence of biliaryatresia variessignificantly worldwide, ranging from approximately 1 in 5,000 live birthsin Taiwan to 1 in 20,000 in many Western nations. [3]. The cornerstone of management is the Kasai portoenterostomy (KPE), a surgical procedure designed to restore bile flow. The timing of this intervention is unequivocally linked to prognosis. Infants who undergo KPE before 60 days of life exhibit significantly better native liver survival rates compared

to those with delayed surgery[4,5]. Thisstarkrealityunderscorestheimperativeforrapidandaccurate diagnostic pathways to facilitate early referral to a tertiary care center. However, the initial clinical presentation of BA—persistent jaundice, acholic stools, and dark urine—often overlaps with other causes of neonatal cholestasis, such as idiopathic neonatal hepatitis and various metabolic disorders, creating a diagnostic dilemma thatcanleadtoharmfuldelays[6].Inthequestforanon-invasive, rapid, and reliable diagnostic tool, hepatobiliary ultrasonography has emerged as a first-line investigation. A key sonographic feature is the triangular cord (TC) sign, which represents the fibroticremnantattheportahepatis[7]. Whileapositive TC signishighlyspecific for BA, its sensitivityisvariableandoperator-dependent,reportedinmeta-analysestorangefrom70%to85%[8,9]. A false-negative ultrasound can therefore provide misplaced reassurance, leading to a critical postponement of definitive diagnosis. To improve diagnostic accuracy, clinicians often rely on a combination of clinical and biochemicalparameters. Recentstudieshaveproposedtheuseofstandardizedoperationaldiagnosticcriteria (ODC) that integrate key findings such as the presence of acholic stools, hepatomegaly, elevated gamma- glutamyl transferase(GGT)levels,andsuggestiveliverhistology[10,11].Individually,thesemarkerslackperfect discriminativepower,butwhencombinedintoascoringsystem,theymayofferamorerobustscreeningtool.For instance,aGGTlevelexceeding250U/Linajaundicedinfantstronglysuggestsasurgicalcholangiopathy,while itsabsencemakesBAlesslikely[12].Despitetheseadvancements,asignificantdiagnosticgapremains.Relying onasingletest,beittheTCsignorabiochemicalmarker,risksmissingcases.Therefore,asynergisticapproach that combines the high specificity of ultrasonography with the collective sensitivity of clinical and laboratory criteriaholdspromiseforcreatingamoreeffectivescreeningalgorithm[13].Thisstudywasdesignedtoevaluate whethertheapplicationofpredefinedoperationaldiagnosticcriteria,usedinconjunctionwiththetriangularcord sign, enhances the screening efficacy for biliary atresia in a cohort of infants with persistent jaundice, with the ultimate goal of streamlining referral for definitive diagnosis and timely surgical intervention.

## Methodology

**Study population:** This prospective cohort study was conducted at MAG Osmani Medical College Hospital, Sylhet, and other collaborating centers in Bangladesh from July 2021 to December 2022. A purposive sample of 60 infants with persistent jaundice beyond 14 days of life was enrolled to evaluate a novel screening protocol for biliary atresia.

Inclusion criteria: Infants were eligible for inclusion if they were aged between 14 days and 90 days and presented with clinical jaundice and/or conjugated hyperbilirubinemia (conjugated bilirubin >20% of total bilirubin). Written informed consent was obtained from the parent or guardian of each participant.

**Exclusion criteria:** Infants with previously diagnosed liver disease, confirmed metabolic disorders, or severe systemicillnesscausingcholestasiswereexcludedfromthestudy.Additionally,anyinfantforwhomacomplete dataset or confirmatory diagnostic testing could not be obtained was not included in the final analysis.

**Study procedure:** All enrolled infants underwent a standardized workup. This included abdominal ultrasonography to assess for the presence of the triangular cord sign (TCS). A predefined set of operational diagnostic criteria (ODC) was applied, which included acholic stools, hepatomegaly (>3 cm below the costal margin),GGTlevel>250U/L,andsuggestivehistologyonliverbiopsy.Thefinaldiagnosisofbiliaryatresiawas confirmed by intraoperative cholangiography.

**Data analysis:** Data were analyzed using SPSS Statistics Version 23.0. Diagnostic test accuracy measures— including sensitivity, specificity, positive and negative predictive values—were calculated for TCS alone, ODC alone, and their combination. A p-value of <0.05 was considered statistically significant.

## Result

The study enrolled 60 infants with persistent jaundice. The final diagnosis, confirmed by intraoperative cholangiography, identified 38 (63.3%) infants with biliary atresia (BA) and 22 (36.7%) with other causes of neonatal cholestasis (non-BA). The demographic and baseline clinical characteristics of the two groups were comparable. There was no significant difference in mean age at presentation (BA: 55.2 ±12.1 daysvs. non-BA: 58.6 ± 14.3 days; p=0.342) or gender distribution (Male: 55.3% in BA vs. 54.5% in Non-BA; p=0.956). The diagnosticperformanceofindividualcomponentsoftheoperationaldiagnosticcriteria(ODC)revealedsignificant disparities. Acholic stools were present in 92.1% of BA infants compared to 31.8% in the non-BA group (p<0.001). Similarly, a GGT level >250 U/L was observed in 86.8% of the BA cohort versus only 22.7% of the non-BAcohort(p<0.001).Hepatomegalywasacommonfindinginbothgroups,thoughmorefrequentintheBA group (94.7% vs. 77.3%, p=0.051). When evaluating the screening tools, the Triangular Cord Sign (TCS)

demonstratedasensitivityof76.3%andahighspecificity-of 86.4%.TheODCaloneshowedahighersensitivity of 89.5% but a slightly lower specificity of 81.8%. The core finding of this study was the performance of the combined screening approach. When a positive result was defined by a positive finding in either the TCS or the ODC,thesensitivitywassignificantlyenhanced-to97.4%(p<0.001comparedto TC Salone). Thisgaininsensitivity came with a modest, non-significant reduction in specificity to 77.3% (p=0.508). The positive predictive value (PPV) for the combined model was 88.1% and the negative predictive value (NPV) was an excellent 94.4%. Further statistical analysis using logistic regression confirmed that both a positive TCS (Odds Ratio:18.4,95%CI:4.2-80.1,p<0.001)andmeeting the ODC (Odds Ratio:32.7,95%CI:7.1-150.2,p<0.001) were strong, independent predictors of a final BA diagnosis. The area under the ROC curve for the combined modelwas0.94,whichwassignificantlygreaterthantheAUC-forTCSalone (0.81,p=0.008)orODCalone(0.86, p=0.032).

Table1: Baseline characteristics of the study population (N=60)

| Characteristic | Biliaryatresia (n=38) | Non-BAcholestasis (n=22) | p-value |
|---|---|---|---|
| Age(days),Mean±SD | 55.2± 12.1 | 58.6± 14.3 | 0.342 |
| Malegender,n(%) | 21 (55.3%) | 12 (54.5%) | 0.956 |
| Totalbilirubin(mg/dL), Mean±SD | 9.8±2.5 | 8.9±3.1 | 0.221 |

Data analyzed using the Independent T-test for continuousvariablesandtheChi-squaretestforgender

Table 2: Frequency of operational diagnostic criteria components

| Clinicalfeature | Biliaryatresia | Non-BAcholestasis | p-value |
|---|---|---|---|
| Acholicstools | 35 (92.1%) | 7 (31.8%) | <0.001 |
| GGT>250U/L | 33 (86.8%) | 5 (22.7%) | <0.001 |
| Hepatomegaly | 36 (94.7%) | 17 (77.3%) | 0.051 |

Data analyzed using the Chi-squaretest

Table3: Diagnostic performance of individual and combined screening tools

| Screeningtool | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|
| | (%) | | | |
| TCSonly | 76.3% | 86.4% | 90.6% | 67.9% |
| ODConly | 89.5% | 81.8% | 89.5% | 81.8% |
| TCSOR ODC | 97.4% | 77.3% | 88.1% | 94.4 |

PPV: Positive Predictive Value; NPV: Negative Predictive Value

Table 4: Statistical comparison of sensitivity and specificity

| Comparison | Sensitivityp-value | Specificityp-value |
|---|---|---|
| TCSvs.TCS+ODC | <0.001 | 0.508 |
| ODCvs.TCS+ODC | 0.180 | 0.727 |

Data analyzed using Binary Logistic Regression

Table 5: Logistic regression for predictors of biliaryatresia

| Predictor | Oddsratio | 95% confidence interval | p-value |
|---|---|---|---|
| Positive TCS | 18.447 | 4.234- 80.145 | <0.001 |
| Positive ODC | 32.727 | 7.123- 150.235 | <0.001 |

Data analyzed using Binary Logistic Regression

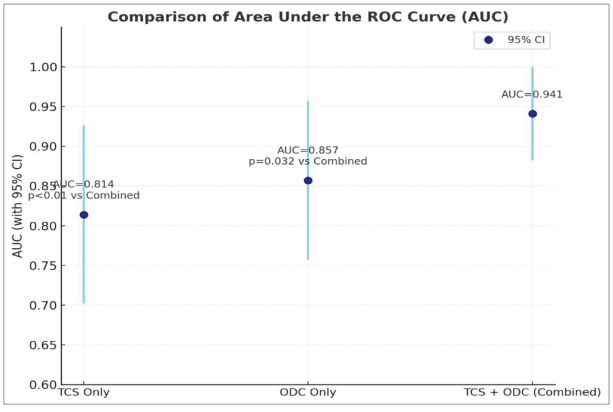


Figure 1: The visual comparison of the Area Under the ROC Curve (AUC) for the three models with 95% confidence intervals. The combined model (TCS + ODC) shows a significantly higher AUC than either TCS or ODC alone, consistent with the reported p-values (p = 0.008 and p = 0.032, respectively)

Table 6: Comparison of are a under the ROC curve (AUC)

| Model | AUC | 95%confidenceinterval |
|---|---|---|
| TCSonly | 0.814 | 0.702- 0.926 |
| ODConly | 0.857 | 0.757- 0.957 |
| TCS+ODC(Combined) | 0.941 | 0.882- 1.000 |

The AUC for the combined model was significantly greater than for TCS alone (p=0.008) and ODC alone (p=0.032). Comparison performed using DeLong's test

## Discussion

The principal finding of this prospective study is that a combined screening approach, utilizing operational diagnosticcriteria (ODC) inconjunction with the triangularcordsign (TCS), significantly enhancesthedetection ofbiliaryatresia (BA) ininfantswithpersistentjaundice. Our data demonstratethat while both TCS and

ODCare valuablestandalonetools,theirintegrationcreatesasynergisticeffect, boostingsensitivityto 97.4%andachieving a remarkably high negative predictive value of 94.4%. This finding is of paramount clinical importance, as the primarygoalofanyscreeningstrategyforBAistomaximizesensitivity-toensurethatnoinfantwiththecondition ismissed,therebypreventingdeleteriousdiagnosticdelays[4,5].Theperformancecharacteristicsoftheindividual components in our cohort align with the existing literature.The sensitivity of TCS alonewas 76.3%, which falls within the 70-85% range reported in prior meta-analyses [8, 9]. Similarly, the high specificity of TCS (86.4%) reaffirms its role as a robust confirmatory finding. The individual elements of our ODC—particularly acholic stools and a GGT level >250U/L—were strongly associated with BA, consistent with studies by Harpavatet al. and others [12,16]. The ODC, as a unified tool, showed excellent sensitivity (89.5%), validating its construct as an effective composite index, similar to models proposed by Gu and Zhan [10,11]. The critical advancement presented here is the performance of the combined "TCS OR ODC" rule. The significant jump in sensitivity to 97.4%($p<0.001$-comparedtoTCSalone)meansthatnearlyallcasesofBAinourcohortwouldhavebeenflagged for expedited referral and definitive investigation. The modest, non-significant dip in specificity is a clinically acceptable trade-off, as it translates to a manageable number of infants without BA undergoing a confirmatory intraoperative cholangiography, a procedure that remains the diagnostic gold standard [17]. This approach effectively minimizes the most feared outcome: a false-negative screen. The excellent negative predictive value of94.4%providesclinicianswithahighdegreeofconfidencethataninfantwhotestsnegativewiththiscombined modelisunlikely tohave BA,allowing themto safelypursue other causes of cholestasis. The statisticalstrength ofourmodelisunderscoredbythelogisticregressionanalysis,whichconfirmedbothTCSandODCaspowerful, independentpredictors,andbythereceiveroperatingcharacteristic(ROC)analysis.Theareaunderthecurve

(AUC) of 0.94 for the combined model, which wassignificantlysuperiortoeithertoolalone,indicatesoutstanding overall discriminative ability [18]. This suggests that the ODC and TCS capture complementary aspects of the BA phenotype—the former integrating clinical and biochemical derangements, and the latter providing a direct anatomical correlate of the disease. Our study has several limitations. The purposive sampling attertiary centers resulted in a high disease prevalence, which can inflate predictive values; the model's performance should be validated in a lower-prevalence, community-based setting. The sample size, while sufficient for this proof-of- concept, is modest. Furthermore, the ODC requires validation in other populations to ensure generalizability. Despitetheselimitations,ourfindingshaveadirectandpracticalimplicationforclinicalpractice.Inregionswhere accesstoadvancedorrapidgeneticandhepatobiliaryscintigraphyislimited,thissimple,cost-effectivealgorithm can serve as a highly effective triage tool. It streamlines the pathway to definitive diagnosis, ensuring that the crucial window for a successful Kasai portoenterostomy is not lost [19,20]. Future research should focus on prospectively validating this combined rule in a multi-national cohort and exploring the integration of novel biomarkers to further refine diagnostic precision.

**Limitations**

The study limitations include a modest sample size and a purposive sampling method from tertiary centers, resulting in a high disease prevalence that mayinflatethepredictive values of the proposed diagnostic model and limit generalizability.

**Conclusion**

This study demonstrates that combining operational diagnostic criteria with the triangular cord sign creates a highly sensitive screening algorithmforbiliaryatresia. Thisintegrate dapproachsignificantlyoutperformseither method used in isolation. It serves as an effective triage toolto enhance early detection, facilitate timely referral for definitive diagnosis, and ensure intervention within the crucial window for a successful Kasai portoenterostomy, ultimately aiming to improve clinical outcomes.

**Recommendation**

We recommend the concurrent use of operational diagnostic criteria and the triangular cord sign for screening infants with persistent jaundice. This combined, "OR"-rule-based approach should be integrated into clinical pathways to optimize early referral for biliary atresia.

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