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# Clinical and laboratory evaluation of cholestatic jaundice in a sample of Iraqi infants

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## Abstract

Cholestatic jaundice most probably occurs due to a pathological condition moreover difficult diagnostic problem. The aim of the study: to determine the etiology of cholestatic jaundice in infancy and to evaluate if clinical events and different investigations could assist in the differential diagnosis of intra and extra-hepatic cholestasis. In this hospital-based study analysis of 35 cases diagnosed with cholestatic jaundice aged 3 weeks up to 12 months from two centers carried out from January 2018 to July 2018. Clinical, biochemical, radiological, histopathological results were recorded. Results: Regarding the 35 patients were (54.3% males, 45.7% females), the mean age at presentation was 117.9 ± 86.4 days and mean age at onset of jaundice was 34 ± 59.11 days, All patients were presented with jaundice (100%) and (45.7%) of them were presented with clay color stool, (77.1%) of patients presented with hepatomegaly followed by ( 54.3%) with splenomegaly, regarding the etiology of cholestasis, Extrahepatic biliary atresia was the commonest cause (22.9%) and the most common cause of intrahepatic etiology was Cytomegalovirus (14.3%). While Idiopathic neonatal hepatitis, Alagille syndrome were (8.6%) for each. Progressive familial intrahepatic cholestasis, Galactosemia, Tyrosinemia, and septicemia were (5.7%) for each. Congenital rubella and congenital hypothyroidism and Fatty acid oxidation disorder were (2.9%) for each. Undiagnosed patients represented (14.3%) of all cases. Inconclusion, the etiologies of infantile cholestatic jaundice are numerous. and was no single laboratory investigation that could precisely make a definite diagnosis. Extrahepatic biliary atresia was the most common cause of cholestasis in this study. Jaundice, hepatomegaly, and pale stools were the common clinical features on presentation.

**Keywords**: Clinical Laboratory Evaluation, Cholestatic Jaundice, Iraqi Infants

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## Introduction

Neonatal cholestasis is defined biochemically as prolonged elevation of the serum levels of conjugated bilirubin beyond the 1st 14 days of life. Jaundice that appears after 2 weeks of age, continues to progress, or does not resolve at this time should be evaluated and a conjugated bilirubin level determined. Cholestasis in a newborn can be caused by infectious, genetic, metabolic, or undefined abnormalities giving rise to mechanical obstruction of bile flow or to functional impairment of hepatic excretory function and bile secretion [1]. Neonatal cholestasis results from impaired bile formation by hepatocytes or from the obstruction of bile flow through the intra- or extrahepatic biliary tree leading to the accumulation of biliary substances (bilirubin, bile acids and cholesterol) in the liver, blood and extrahepatic tissues Although the laboratory methods need to be taken into account, neonatal cholestasis can be defined as conjugated hyperbilirubinemia that occurs when conjugated bilirubin is higher than 1 mg/dl, if the total serum bilirubin is ≤5 mg/dl, or >20 % of total serum bilirubin when it is >5 mg/dl [2,3] . The neonatal liver is more susceptible to cholestasis as compared to livers of older children and adults. While the physiologic development of normal hepatic function matures in the later stages of gestation, many other processes are developmentally regulated over the first few months after birth. This physiologic immaturity limits the capacity to synthesize and transport bile acids and affects the metabolism, detoxification, and excretion of drugs, and xenobiotics. Reports on newborn animals have shown that their enterohepatic circulation is characterized by decreased bile salt secretion, flow, and synthesis; a smaller bile acid pool size; a decreased hepatic uptake of portal bile salts; and an inefficient uptake of bile salts in the ileum. This then leads to high levels of circulating bile salt levels [4]. The overall incidence of neonatal liver disease manifesting clinical or biochemical evidence of cholestasis is approximately 1 in 2,500 live births. Idiopathic neonatal hepatitis, an anachronistic term, has been reported to have an incidence of 1 in 4,800 to 9,000 live births. However, reliable figures do not exist regarding the current incidence because newer and more accurate diagnostic methods have decreased markedly the number of infants previously labeled as having idiopathic neonatal hepatitis. The incidence of biliary atresia ranges from 1 in 8,000 to 21,000 live births according to reports from several centers around the world. Extrahepatic biliary atresia is the most common disease and consistently has accounted for one-third of all cases in multiple reports over several decades [5]. The aim of the study: to determine the etiology of cholestatic jaundice in infancy and to evaluate if clinical events and different investigations could assist in the differential diagnosis of intra and extra-hepatic cholestasis.

**Materials and Method**

Hospital-based cross-sectional, descriptive study. This study recruited from the outpatient clinic and inpatient department in Child's Central Teaching Hospital and from the outpatient clinic at the Medical City Digestive Center and Hepatology in Baghdad/Iraq. The analyzed thirty-five cases were term infants ≥ 37 weeks (19 male and 16 female) aged 3 weeks - 12 months old with detected with cholestatic jaundice persisted for at least 2 weeks, from January 2018 till July 2018, cholestasis was identified as conjugated hyperbilirubinemia concentration in an infant at a level above 1.0 mg/dl where the total serum bilirubin is <5.0 mg/dl, or greater than 20 percent of the total serum bilirubin where the total serum bilirubin is >5.0 mg/dl.

All preterm with cholestatic jaundice and infants with indirect hyperbilirubinemia were excluded from the study. Patient gender and age at time of diagnosis was recorded then detailed history was taken from the mothers according to A questionnaire made includes prenatal history (age of the mother any fever, skin rash any illness, drugs, previous abortion), natal history (gestational age at birth, gender, birth weight percentile, mode of delivery, blood group of the mother and the child), postnatal history (incubator care, type of feeding, timing of meconium passage, age of appearance of jaundice, age at 1st presentation, pale stools, dark urine, easy bruising, Hx of pruritis, weight gain since birth, any abdominal distension), family history of similar condition and consanguinity. Physical examination for all patients including weight in (kg) measured by infant weight scale at time of presentation and data are compared to centile charts for age and gender, temperature, the presence of any dysmorphic features, scratching marks, congenital anomalies, heart murmur, purpura rash, abdominal examination (liver and spleen enlargement, the presence of ascites and dilated abdominal wall veins). Appropriate investigations were done depend on preliminary diagnosis and progression of the disease, all cases at admission were investigated for Serum bilirubin TSB, fractionated serum bilirubin, liver function tests as ALT, AST, ALP, GGT, PT, PPT, TSP, S. albumin, renal function (blood urea, S. creatinine, and S. electrolyte), some of the investigations not available were done in private trusted lab.

Ultrasonography of liver and the biliary system was done for all patients which were done after fasting 4 hours looking for the findings to diagnose Biliary atresia (absence of extrahepatic bile ducts, non-visualized or small sized gall bladder < 2.5 cm, triangular cord sign) as well as hepatosplenomegaly, ascites. When EHBA still suspected HIDA and MRCP tests (when available) done for selected cases when U/S was in doubt and Liver biopsy was postponed because of prolonged PT, lack of parental consent or both and time consuming then all suspected cases referred for the surgical department. After

exclusion of BA, investigations were done for other causes of cholestatic jaundice, Infectious screen as TORCH screen works up when clinically indicated (low birth weight, intrauterine growth retardation, hepatosplenomegaly, and rash), complete blood count, CRP, bacterial culture of blood, urine for culture and microscopical examination, thyroid function test (T3, T4, TSH) for hypothyroidism, which were available in hospital. Evaluation for galactosemia (S. Galactose, urine for reducing substances and GALT activity), alpha 1-antitrypsin level, a bone marrow aspiration was examined for two cases with splenomegaly to rule out storage diseases (e.g., Gaucher or Niemann– Pick disease).

Specific investigations were added when needed for suspected cases (Alagille syndrome), as Thoracic X-ray for butterfly vertebrae, Echo study for CHD, Slit lamp eye examination for posterior embryotoxon. Other metabolic diseases were diagnosed by Tandem mass spectrometry (to detect e.g. tyrosinemia), The last step was liver biopsy for those still not reaching a diagnosis, and the final diagnosis was based on the analysis of findings in the Hx, physical examination and investigations [6, 7]. The data analyzed using Statistical Package for Social Sciences (SPSS) version 25. The data presented as mean, standard deviation and ranges. Categorical data presented by frequencies and percentages. Independent t-test (two-tailed) was used to compare the continuous variables among study groups accordingly. Pearson`s Chi-square test was used to assess the statistical association between different variables. A level of P – value less than 0.05 was considered significant.

## Results

The total number of studied patients were 35 cases, all of them have diagnosed with cholestatic jaundice. The distribution of the studied patients by general characteristics is shown in the table (3.1 and 3.2). The age at presentation was ranging from 20 days to 365 days with a mean of 117.9 ± 86.4 days. At the onset of jaundice, age was ranging from one to 300 days with a mean of 34 ± 59.11 days. Birth weight percentile was ranging from 3rd to 90th with a mean of 32.5 ± 26.03. Weight percentile at presentation was ranging from 3rd to 90th with a mean of 12.33 ± 16.85 (Table 1)

**Table 1.**

Means of age at (presentation and onset of jaundice) with their weight percentile at birth and presentation.

| Variable | Mean ± SD |
|---|---|
| **Age at presentation (Days)** | 117.9 ± 86.4 |
| **Age at onset of jaundice (Days)** | 34 ± 59.11 |
| **Birth weight Index (Percentile)** | 32.5 ± 26.03 |
| **Weight Index at presentation (Percentile)** | 12.33 ± 16.85 |

Regarding gender, the proportion of males was higher than that of females (54.3% versus 45.7%) with a male to female ratio of 1.18:1.

About two-thirds of the studied patients showed a positive consanguinity (65.7%) and 37.1% of them showed positive family history. (Table 2)

**Table 2.**

Distribution of study patients by general characteristics

| Variable | No. (n= 35) | Percentage (%) |
|---|---|---|
| **Gender** | | |
| **Male** | 19 | 54.3 |
| **Female** | 16 | 45.7 |
| **Consanguinity** | | |
| **Yes** | 23 | 65.7 |
| **No** | 12 | 34.3 |
| **Family History** | | |
| **Yes** | 13 | 37.1 |
| **No** | 22 | 62.9 |

Table 3 shows the distribution of the studied patients by Ultrasound findings, in the study Twenty-seven patients (77.1%) had hepatomegaly, nineteen patients (54.3%) had splenomegaly, eleven patients (31.4%) had ascites, and five patients (14.3%) had small or non-visualized GB.

**Table 3.**

Distribution of study patients by ultrasound findings

| Variable | No. (n= 35) | Percentage (%) |
|---|---|---|
| **Hepatomegaly** | | |
| **Yes** | 27 | 77.1 |
| **No** | 8 | 22.9 |
| **Splenomegaly** | | |
| **Yes** | 19 | 54.3 |
| **No** | 16 | 45.7 |
| **Ascites** | | |
| **Yes** | 11 | 31.4 |
| **No** | 24 | 68.6 |
| **Other** | | |
| **Small or non-visualized GB** | 5 | 14.3 |
| **No** | 30 | 85.7 |

The distribution of the studied patients by etiology of cholestasis is shown in the table (4), the most common cause was EHBA (22.9%), while CMV cases (14.3%) of all cases, Undiagnosed cases represented (14.3%) of the cases in this study.

**Table 4.**

Distribution of study patients by etiology of cholestasis

| Etiology of Cholestasis | No. (n= 35) | Percentage (%) |
|---|---|---|
| **Extrahepatic** | | |
| **Biliary atresia** | 8 | 22.9 |
| **Intrahepatic** | | |
| **CMV** | 5 | 14.3 |
| **Idiopathic neonatal hepatitis** | 3 | 8.6 |
| **Alagille syndrome** | 3 | 8.6 |
| **PFIC** | 2 | 5.7 |
| **Galactosemia** | 2 | 5.7 |
| **Tyrosinemia** | 2 | 5.7 |
| **Septicemia** | 2 | 5.7 |
| **Cong. Hypothyroidism** | 1 | 2.9 |
| **Cong. Rubella** | 1 | 2.9 |
| **Fatty acid oxidation disorder** | 1 | 2.9 |
| **Undiagnosed** | | |
| **Unknown** | 5 | 14.3 |

The comparison between patients according to intra and extrahepatic causes of cholestasis by general characteristics is shown in the table (5). The means age at presentation and mean age at onset of jaundice were significantly higher in patients with intrahepatic etiology of cholestasis than that in those with extrahepatic etiology (148.5 versus 96.9, P= 0.011 and 46.59 versus 7.25, P= 0.02 respectively). There were no significant differences (P ≥ 0.05)

between means of birth weight and weight at presentation indexes between intra and extrahepatic etiology of cholestasis, as shown in the table (5).

**Table 5.**
Comparison between patients according to intra and extrahepatic causes of cholestasis by general characteristics.

| Variable | Etiology of Cholestasis | | P- Value |
|---|---|---|---|
| | Intrahepatic Mean ± Std. Dev | Extrahepatic Mean ± Std. Dev | |
| **Age at presentation (Days)** | 148.5 ± 37.8 | 96.9 ± 32.1 | **0.002** |
| **Age at onset of jaundice (Days)** | 46.59 ± 40.63 | 7.25 ± 13.26 | **0.001** |
| **Birth wt. Index (Percentile)** | 33.36 ± 26.6 | 30.13 ± 26.0 | **0.769** |
| **Wt. Index at presentation (Percentile)** | 14.09 ± 19.06 | 7.5 ± 7.07 | **0.178** |

Table 6 shows the association between certain demographic characteristics and etiology of cholestasis. It was obvious that there was no significant association (P ≥ 0.05) between etiology of cholestasis and all demographic characteristics.

**Table 6.**
Association between certain demographic characteristics and etiology of cholestasis.

| Variable | Etiology of cholestasis | | Total (%) n= 30 | P- value |
|---|---|---|---|---|
| | Extrahepatic (%) n= 8 | Intrahepatic (%) n= 22 | | |
| **Gender** | | | | |
| **Male** | 2 (12.5) | 14 (87.5) | 16 (53.3) | **0.101** |
| **Female** | 6 (42.9) | 8 (57.1) | 14 (46.7) | |
| **Family history** | | | | |
| **Yes** | 5 (26.3) | 14 (73.7) | 19 (63.3) | **0.954** |
| **No** | 3 (27.3) | 8 (72.7) | 11 (36.7) | |
| **Consanguinity** | | | | |
| **Yes** | 5 (23.8) | 16 (76.2) | 21 (70.0) | **0.589** |
| **No** | 3 (33.3) | 6 (66.7) | 9 (30.0) | |

Table (7) shows the association between clinical presentation and etiology of cholestasis. In this study, eight patients (53.3%) who presented with clay color stool were diagnosed with the extrahepatic cause of cholestasis with a significant association (P= 0.001). Regarding associated anomalies, the highest prevalence of intrahepatic etiology of cholestasis was seen among patients with associated anomalies (89.5%) with a significant association (P=

0.008). There was no significant association (P ≥ 0.05) between etiology of cholestasis and all other clinical presentations.

**Table 7.**

Association between clinical presentation and etiology of cholestasis

| Variable | Etiology of cholestasis | | Total (%) n= 30 | P- value |
|---|---|---|---|---|
| | Extrahepatic (%) n= 8 | Intrahepatic (%) n= 22 | | |
| **Clay color stool** | | | | |
| **Yes** | 8 (53.3) | 7 (46.7) | 15 (50.0) | **0.001** |
| **No** | 0 (0) | 15 (100.0) | 15 (50.0) | |
| **Dark color urine** | | | | |
| **Yes** | 6 (42.9) | 8 (57.1) | 14 (46.7) | **0.06** |
| **No** | 2 (12.5) | 14 (87.5) | 16 (53.3) | |
| **Abd. Distension** | | | | |
| **Yes** | 4 (40.0) | 6 (60.0) | 10 (33.3) | **0.24** |
| **No** | 4 (20.0) | 16 (80.0) | 20 (66.7) | |
| **Scratching** | | | | |
| **Yes** | 0 (0) | 5 (100.0) | 5 (16.7) | **0.287** |
| **No** | 8 (32.0) | 17 (68.0) | 25 (83.3) | |
| **Bruises and Bleeding** | | | | |
| **Yes** | 3 (60.0) | 2 (40.0) | 5 (16.7) | **0.102** |
| **No** | 5 (20.0) | 20 (80.0) | 25 (83.3) | |
| **Associated Anomalies** | | | | |
| **Yes** | 2 (10.5) | 17 (89.5) | 19 (63.3) | **0.008** |
| **No** | 6 (54.5) | 5 (45.5) | 11 (36.7) | |

Table (8) shows the association between U/S finding and etiology of cholestasis. The highest proportion of extrahepatic cause of cholestasis was found in patients with hepatomegaly (36.4%) with a significant association (P= 0.046). All patients with small or non-visualized GB were diagnosed with extrahepatic etiology of cholestasis (100%) with a significant association (P= 0.001). All patients with triangular cord sign were diagnosed with extrahepatic etiology of cholestasis (100%) with a significant association (P= 0.015). There was no significant association (P ≥ 0.05) between etiology of cholestasis ascites or with splenomegaly.

**Table 8.**

Association between U/S finding and etiology of cholestasis

| U/S Finding | Etiology of cholestasis | | Total (%) n= 30 | P- value |
|---|---|---|---|---|
| | Extrahepatic (%) n= 8 | Intrahepatic (%) n= 22 | | |
| **Hepatomegaly** | | | | |
| **Yes** | 8 (36.4) | 14 (63.6) | 22 (73.3) | **0.046** |
| **No** | 0 (0) | 8 (100.0) | 8 (26.7) | |
| **Splenomegaly** | | | | |
| **Yes** | 6 (35.3) | 11 (64.7) | 17 (56.7) | **0.407** |
| **No** | 2 (15.4) | 11 (84.6) | 13 (43.3) | |
| **Ascites** | | | | |
| **Yes** | 2 (22.2) | 7 (77.8) | 9 (30.0) | **0.718** |
| **No** | 6 (28.6) | 15 (71.4) | 21 (70.0) | |
| **Small or non-visualized GB** | | | | |
| **Yes** | 6 (100.0) | 0 (0) | 6 (20.0) | **0.001** |
| **No** | 2 (8.3) | 22 (91.7) | 24 (80.0) | |
| **Triangular cord sign** | | | | |
| **Yes** | 2 (100.0) | 0 (0) | 2 (6.7) | **0.015** |
| **No** | 6 (21.4) | 22 (78.6) | 28 (93.3) | |

The comparison between intra and extrahepatic etiology of cholestasis by the investigation is shown in the table (9). The mean GGT level was significantly higher in patients with extrahepatic etiology of cholestasis than that in those with intrahepatic etiology (489 ± 126.14 versus 254.09± 183.75, (P= 0.001). There were no significant differences (P ≥ 0.05) between intra and extrahepatic etiology of cholestasis regarding all other investigations, as shown in the table (9).

**Table 9.**

Comparison between intra and extrahepatic etiology of cholestasis by the investigation

| Investigation | Etiology of Cholestasis | | P- Value |
|---|---|---|---|
| | Extrahepatic Mean ± Std. Dev | Intrahepatic Mean ± Std. Dev | |
| **TSB** | 16.47 ± 6.57 | 12.83 ± 8.51 | **0.236** |
| **Direct Bilirubin** | 10.76 ± 4.46 | 8.2 ± 3.99 | **0.167** |
| **PT** | 16.35 ± 6.52 | 15.64 ± 4.76 | **0.786** |
| **PTT** | 41.3 ± 15.13 | 38.54 ± 9.35 | **0.64** |
| **AST** | 215.12 ± 197.86 | 236.13 ± 271.41 | **0.82** |
| **ALT** | 249.85 ± 209.89 | 179.9 ± 274.52 | **0.49** |
| **Alkaline P** | 423.37 ± 241.16 | 709.47 ±524.58 | **0.056** |
| **S. Albumin** | 31.17 ± 6.12 | 33.4 ± 7.58 | **0.421** |
| **GGT** | 489.0 ± 126.14 | 254.09 ± 183.75 | **0.001** |

## Discussion

In this study of total 35 cases, the mean age at their presentation was 117.9 ± 86.4 days, this goes with FR Chowdhury et al. study [8] (2014) which found out the mean age was 111.9±21.14 days in line with same inclusion criteria, but disagrees with Malaysian study (9) (2010) done by WS Lee et al. with a mean of (58 days) and with Turkish study [9] (2011) done by Urgancı et al with mean age (60 ± 26 days) and this might due to conduction smaller range of age (16 to 260 days) for Malaysian study and (15 to 240 days) for Turkish study and might due higher awareness in their population and the primary health care. In this study, the age at onset of jaundice is (ranging one to 300) days with a mean of 34 ± 59.11 days, while the Turkish study [10] (2011) done by Urgancı et al showed earlier mean age at onset 17.6 days (range 1 to 90 days).

This depends on Mothers observation and might be explained by the types of IHC cases in the Turkish study that might be presented later in infancy [11, 12]. Regarding the gender proportion of males was higher than that of females (54.3% versus 45.7%) this results similar to Iraqi study [13] (2011) done by LA. Mohammad et al of 50 cases, and Italian study [14] (2009) done by Tufano M. et al of (82 cases) but differs differing from the result of Egyptian study [15] (2010) done by AES Donia et al of 50 cases which showed more female proportion.

Almost all previous studies reported jaundice in all patients so as this study showed (100%) of patients with jaundice, (45.7%) of them were presented with clay color stool, (40%) with dark urine, while Sri Lanka study (16) (2016) done by MIM Luthufdeen et al showed (76.6%) with clay color stool, (61.6%) with dark urine, while the Brazilian study [17] (2010) by Bellomo-Brandao MA et al showed (79%) with clay color stool, (77.9%) with dark urine, these variations might due to difference in samples size. Regarding other findings, this study revealed the same patients by examination and by Abd U/S presented with hepatomegaly (77.1%), which is nearly similar to results of (76.4%) reported by Iranian study [18] (2015) done by Dehghani SM. et al. while the study was done by MIM Luthufdeen et al [16] (2016) and the study was done by Bellomo-Brandao MA et al (17) (2010) both showed (83.3%) and (51.7%) respectively with hepatomegaly. Totally (54.3%) of patients presented with splenomegaly depending on U/S finding, which closes to results by MIM Luthufdeen et al [16] (2016) with (56.6%) while the result of N. Urganci et al [10] (2011) and of Dehghani SM. et al [18] (2015) showed that (65.7%) and (23.8%) respectively presented with splenomegaly. This study showed (31.4%) of total patients had ascites depending on U/S results, while the results by AES Donia et al [15] (2010) showed that (26%) of patients with ascites. These variations in might due to the difference in age at presentation between the

studies which lead to variations in clinical finding along the course of the disease and the difference in percentage between EHC and IHC between studies.

This study classified the patients according to the etiology of cholestasis into two groups, (EHC) extrahepatic cholestasis 22.9%, (IHC) intrahepatic cholestasis 62.8%. and this is nearly similar to the WS Lee et al study [9] (2010) which showed 29% with (EHC) and 69% with (IHC) and nearly similar Dehghani SM. et al [18] (2015) study which showed 24.6% with (EHC) and 52.6% for (IHC), while Bellomo-Brandao MA et al [17] (2010) study revealed 45.2% with (EHC) and 54.8% with (IHC), And German study [19] (2014) by Hoerning et al which showed 41% with (EHC) and 59% with (IHC). These differences may due variations in sample size, and distribution of diseases between populations. All cases of EHC group were biliary atresia which was the most frequent etiology of cholestasis in this study, this was consistent with many studies as by Chowdhury et al [8] (2014), LA. Mohammad et al [13] (2011), AES Donia et al [15] (2010)and Chinese study [20] (2008)by Wongsawasdi L.et al. Regarding infectious causes, a recent study revealed that CMV is the most frequent with four cases (14.3%), two cases with septicemia (5.7%) and one case with congenital Rubella (2.9%), While Turkish study [10] (2011) which conducted 70 cases showed that (44%) of cases had CMV, (5.7%) of cases had septicemia, and (1.4%) had cong. Rubella. Another study by FR Chowdhury et al [37] (2014) which conducted 40 cases showed (5%) had CMV, (2.5%) had Rubella infection and no cases with septicemia. These differences between studies depend on early laboratory detection, sample size, antenatal care, vaccinations given and socioeconomic status of the families.

Regarding other cholestatic etiologies, three cases were detected with idiopathic neonatal hepatitis (INH), three cases with Alagille syndrome (8.6%), and two cases with progressive familial intrahepatic cholestasis (PFIC), while a study with total 82 cases done by Hoerning et al [19] (2014) showed (13%) of cases with INH, (10%) with PFIC, (2%) with Alagille syn. While WS Lee et al [9] (2010) study of 146 cases showed that (38%) had INH, (4%) had PFIC, and (0.7%) had Alagille syn. And the study done by MIM Luthufdeen et al [16] (2016) analyzes 60 cases showed that (26.6%) had INH, (0.06%) had PFIC, and (0.0.3%) had Alagille syn. The metabolic causes of cholestasis in this study are two cases had Galactosemia (5.7%), two cases had tyrosinemia (5.7%), one case had congenital hypothyroidism (2.9%), and one case had fatty acid oxidation disorder (2.9%). Comparing with LA. Mohammad et al [13] (2011) study of 50 cases which showed that (12%) of cases had Galactosemia, (4%) had Tyrosinemia, (2%) of cases had Congenital hypothyroidism, while the Malaysian study [9] (2010) showed (0.7%) had Galactosemia, (2%) had cong. hypothyroidism and no case had Tyrosinemia, this might be explained by the difference in availability of metabolic screening test between centers and consanguinity and frequency of

inherited disorders between populations. Regarding the difference between IHC and EHC by mean age at presentation, the patients had EHC presented earlier than those with IHC and there was a significant association (P= 0.002), this might be explained by the earlier jaundice onset in patients with EHC than patients with IHC in this study make them presented earlier for medical advice, which goes with AES Donia et al [15] (2010) study, but not goes with Bellomo-Brandao MA et al [17] (2010) study 168 cases. Regarding mean age at onset of jaundice, the recent study revealed patients with EHC had earlier jaundice onset than patients with IHC and there was statistically significant (P=0.02), which consistent with N. Urganci et al [10]. Regarding clinical presentation, this study showed higher prevalence of patients who presented with clay color stool in patients with EHC (53.3%) with a significant association (P= 0.001), which goes with studies done by AES Donia et al [15] (2010), Bellomo-Brandao MA et al [17] (2010), N. Urganci [10] (2011) while disagreeing with the Swedish study. Regarding associated anomalies, the highest prevalence of IHC was seen among patients with associated anomalies (89.5%) which was mostly seen in patients with Alagille syn. with a significant association (P= 0.008), but no other study to compare with this result. Regarding the association between U/S finding and etiology of cholestasis, the highest proportion of EHC was found in patients with hepatomegaly (36.4%) with a significant association (P= 0.046), which is in agreement with the Brazilian study [17] (2010), and Swedish study [21] (2001), but disagreed with the Turkish [10] (2011) and the Egyptian [15] (2010) studies who both showed no statistically significant difference. Regarding other U/S finding (splenomegaly, ascites), there was no significant correlation with the etiology of cholestasis. This was consistent with the Turkish [10] (2011), Egyptian [15] (2010) and Swedish [21] (2001) studies. The comparison between EHC and IHC by investigation showed the mean of GGT level was significantly higher in patients with EHC than that in those with IHC (P= 0.001), which is similar to the Brazilian [17] (2010) and Turkish [10] (2011), Chinese [20] (2008) studies that go with facts of γ-glutamyl transpeptidase levels are sensitive indicators of obstruction or inflammation of the biliary tract [22]

## Conclusion

The etiologies of infantile cholestatic jaundice are numerous. and was no single laboratory investigation that could precisely make a definite diagnosis. Extrahepatic biliary atresia was the most common cause of cholestasis in this study. Jaundice, hepatomegaly, and pale stools were the common clinical features on presentation.

## Ethical Approval

The study was approved by the Ethical Committee.

**Conflicts of Interest**

The authors declare that they have no competing interests.

**Authors' Contributions**

All authors shared in conception, design of the study, acquisition of data, and manuscript writing, the critical revising and final approval of the version to be published.

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