

## Prevalence and the Underling Factors of Neonatal Jaundice in Neonatal Intensive Care Units in Al-Qalyubia Governorate

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### Abstract:

**Background:** Neonatal jaundice is a common condition in newborns, characterized by the yellowish discoloration of the skin and sclera due to elevated bilirubin levels. Understanding the prevalence and underlying factors of neonatal jaundice in neonatal intensive care units (NICUs) is crucial for effective management and prevention. This study aimed to determine the prevalence and identify the underlying factors of neonatal jaundice among neonates admitted to NICUs in Al-Qalyubia Governorate. **Methods:** This cross-sectional study was conducted on 3214 newborns admitted in five NICUs in Al-Qalyubia Governorate from March 2022 to March 2023. Neonates aged 1 to 28 days with neonatal jaundice requiring admission were included. Data were collected through detailed history taking, physical examination, laboratory investigations, and the Modified Bilirubin-Induced Neurological Dysfunction (BIND) score. **Results:** The prevalence of neonatal jaundice among the studied neonates was 31% (995 out of 3214). The most common cause of jaundice was idiopathic(physiological) (56.3%), followed by ABO incompatibility (30%) and Rh incompatibility (8.5%). The majority of neonates were delivered by cesarean section (84.1%), and 82.4% were breastfed. The mean BIND score was  $1.96 \pm 1.009$ , with mild acute bilirubin encephalopathy observed in 7.1% of cases. All studied neonates underwent phototherapy, with 52% receiving intensive phototherapy. The mean duration of NICU stay was  $4.11 \pm 1.12$  days. Only one case (0.1%) died during blood exchange. **Conclusion:** Neonatal jaundice is a prevalent condition in NICUs, with idiopathic (physiological) cause is the most common. followed by ABO incompatibility, then RH incompatibility.

**Keywords:** Neonatal Intensive Care Units; Neonatal Jaundice, Neurological Dysfunction.

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## Introduction

Jaundice is one of the most common conditions that require medical attention in newborn babies. Jaundice refers to the yellowish discoloration of the skin and sclera caused by raised levels of bilirubin in circulation (a condition known as hyperbilirubinemia) <sup>(1)</sup>. Approximately 60% of term and 80% of preterm babies are still jaundiced at one month of age. Although early jaundice in most babies is harmless, a few will develop very high levels of bilirubin, which can be harmful if not treated <sup>(2)</sup>.

It is essential to identify the risk factors that are involved in increased incidence of neonatal jaundice because its incidence can be decreased by modifying them <sup>(3)</sup>.

It can be neurotoxic and cause kernicterus with diffuse neuronal damage or even death in newborns. Surviving infants may acquire long-term neurodevelopmental sequelae such as cerebral palsy, sensorineural hearing loss, intellectual difficulties, or gross developmental delays <sup>(4)</sup>.

Predictors of neonatal jaundice include neonatal factors (gestational age, male sex, birth weight, APGAR score, birth asphyxia), obstetric factors (prolonged labor, primiparity, oxytocin-assisted delivery, multiple pregnancies, vacuum extraction), maternal factors (drug use during pregnancy, age, hemoglobin level, smoking status, education status, parity, O blood group), and medical factors (thyroid-stimulating hormone, blood group and Rhesus incompatibility, sepsis, total serum bilirubin level, cord blood albumin and bilirubin) <sup>(5)</sup>.

The purpose of this study was to detect the prevalence and the underlying factors of neonatal jaundice among neonates admitted to neonatal intensive care units of Al-Qalyubia Governorate.

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## Patients and methods

This cross-sectional study was conducted on newborns admitted in 5 Neonatal Intensive Care units in Al-Qalyubia

Governorate (Benha University hospital, Benha children Hospital, Benha Insurance hospital, Kafr Shokr specialized Hospital and Toukh Central Hospital). During the period from March 2022 to March 2023, 3214 neonates admitted to the NIC units were included in this study.

Informed written consent was obtained from all the participants' parents. The study was approved by the ethics committee of Benha Faculty of medicine (Ms 16-1-2022).

**Inclusion criteria** were patient age from 1 day to 28 days of both sexes and neonates with neonatal jaundice and required admission according to the American Academy of Pediatrics (AAP) clinical guideline for management of neonatal jaundice <sup>(6)</sup>.

**Exclusion criteria** preterm, age more than 1-month, major congenital malformation, other causes of admission to NICU and neonates whose Parents or caregiver refused to sign the consent.

All studied cases were subjected to the following:

**Detailed history taking** including Personal history of mother (age, residence and socio-economic status), Prenatal history: including maternal risk factor during pregnancy eg chronic medical illness, infection, drug abuse, polyhydramnios, prolonged rupture of membrane, trauma and blood transfusion, fetal risk factor e.g. multiple gestation, fetal distress, and erythroblastosis fetalis, natal history; mood of delivery and if any complications occurred during labor and family history; consanguinity and similar condition, blood group of parents, blood transfusion of the mother and exchange transfusion of sibling.

**Examination:** General examination including consciousness and vital signs as pulse, blood pressure, respiratory rate and temperature and head to foot examination. Local systematic examination including cardiovascular system for detection of any abnormal heart sounds or murmurs.

Respiratory system for detection of any abnormal breath sound, adventitious sounds and respiratory distress. Gastrointestinal Tract (GIT) and abdomen for presence of organomegaly or ascites. Central Nervous System (CNS) and musculoskeletal system for assessment of pupillary reaction, power, tone and reflexes and bilirubin-induced neurological dysfunction (BIND) score <sup>(7)</sup>.

**Laboratory investigations:** The following investigations were done in all enrolled patients, and we obtained it from the patient sheet: Complete blood count, C-reactive protein, blood group of mother and neonate, total serum bilirubin, direct bilirubin and reticulocyte count.

#### **Statistical analysis**

Statistical analysis was performed using SPSS Version 26.0. Normality of variables was assessed with the Kolmogorov Smirnov and Shapiro-Wilk tests. Continuous variables with normal distributions were presented as mean  $\pm$  SD and range, while those with non-normal distributions were summarized as medians and IQR. Categorical variables were expressed as numbers and percentages. Spearman's rho correlation was used for nonparametric variables, and the point-biserial correlation coefficient (rpb) for association between continuous and dichotomous variables. Simple linear and multivariate regression with stepwise selection were used to evaluate predictors and risk factors for elevated TSB level. Statistical significance was set at  $p < 0.05$ , with  $p > 0.05$  considered non-significant.

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## **Results**

This study included 3214 neonates admitted to the NICU. **Table 1** shows the

demographic data of the jaundiced neonates. Most of the studied neonates were delivered by cesarian section (84.1%). As regard type of feeding, about 82.4% were breast fed compared to 17.6% who were formula fed.

The prevalence rate of jaundice among the studied neonates was 31% (995 out of 3214). The prevalence of jaundice was highest at Benha Insurance hospital, and lowest at Benha University hospital (**Table 2**).

The most common cause for neonatal jaundice among the studied group was Idiopathic (physiological) jaundice which accounted for 56.3% of the cases followed by ABO incompatibility (30%), then RH incompatibility (8.5%). Both ABO and RH incompatibility accounted for 2.5% of cases only and the least percentages were for neonatal sepsis and G6PD deficiency (1.8% and 0.9% respectively) (**Table, 3**).

The mean Bind score of the studied neonate was  $1.96 \pm 1.009$  [range 0-5] median bind score (IQR): 2. (1, 3). Bind score 1,2 and 3 reported in 3.5%, 2.4% and 1.2% respectively indicating mild acute bilirubin encephalopathy. Bind score of 4 and 5 was reported in 0.3% and 0.1% respectively indicating severe acute bilirubin encephalopathy (**Table, 4**).

All studied neonates were subjected to phototherapy (100%). Intensive photo was done to 52% of cases. Blood exchange was done in only 3.7% and about 1.3% of studied neonates received IVIG infusion. The mean duration of NICU stay was  $4.11 \pm 1.12$  [range 2-7 days] median duration of NICU stays (IQR): 4 days (3, 5). Only one case (0.1%) died during blood exchange while 99.9% of cases showed improvement.

**Table 1:** Sociodemographic Data of the neonates with jaundice.

Variable	(N = 995)	
Age (days)		
Mean $\pm$ SD (range)	2.72 $\pm$ 0.846 (1-6)	
Median (Q1, Q3)	3 (2, 3)	
Age groups		
	1 day old (n, %)	44 (4.4%)
	2 days old (n, %)	367 (36.9%)
	3 day old (n, %)	437 (43.9%)
	4 days old (n, %)	119 (12%)
	5 days old (n, %)	25 (2.5%)
	$\geq$ 6 days old (n, %)	3 (0.3%)
GA (in weeks)		
Mean $\pm$ SD (range)	38.04 $\pm$ 0.849 (36-40)	
Median (Q1, Q3)	38 (38, 38)	
GA groups		
	36 w (n, %)	1 (0.1%)
	37 w (n, %)	224 (22.5%)
	38 w (n, %)	613 (61.6%)
	39 w (n, %)	46 (4.6%)
	40 w (n, %)	111 (11.2%)
Sex		
	Male (n, %)	610 (61.3%)
	Female (n, %)	385 (38.7%)
Birth weight (kg)		
Mean $\pm$ SD (range)	2.887 $\pm$ 0.274 (2.3-4)	
Median (Q1, Q3)	2.8 (2.7, 3)	
Mode of delivery		
	VD (n, %)	158 (15.9%)
	CS (n, %)	837 (84.1%)
Type of feeding		
	Breast feeding (n, %)	820 (82.4%)
	Formula feeding (n, %)	175 (17.6%)
TSB (mg/dl)		
Mean $\pm$ SD (range)	16.33 $\pm$ 2.7 (8-25)	
Median (Q1, Q3)	16 (14.5, 18)	
Direct bilirubin (mg/dl)		
Mean $\pm$ SD (range)	0.597 $\pm$ 0.227 (0.16-2)	
Median (Q1, Q3)	0.6 (0.5, 0.7)	

**Table 2:** Prevalence of jaundice in each hospital among the studied group.

Hospital	All cases	Jaundice	Prevalence
Benha University hospital,	835	82	9.2%
Benha children Hospital,	1152	377	32.7%
Benha Insurance hospital,	372	217	58.3%
Kafr Shokr Hospital	470	165	35.1%
Tokh Central Hospital	385	154	40.0%
Total	3214	995	31%

**Table 3:** Causes and methods of treatment of neonatal jaundice, (N=995).

Variable	(N = 995)	
Causes of neonatal jaundice	Idiopathic jaundice (n, %)	560 (56.3%)
	ABO incompatibility alone (n, %)	298 (30%)
	RH incompatibility alone (n, %)	85 (8.5%)
	ABO+RH incompatibility (n, %)	25 (2.5%)
	Neonatal sepsis (n, %)	18 (1.8%)
	G6PD deficiency (n, %)	9 (0.9%)
Methods of treatment of neonatal jaundice	Phototherapy	995 (100%)
	Intensive photo	517 (52%)
	Blood exchange	37 (3.7%)
	IVIG	13 (1.3%)
Duration of NICU stay		
Mean $\pm$ SD (range)	4.11 $\pm$ 1.12 (2-7)	
Median (Q1, Q3)	4 (3, 5)	

**Table 4:** Bind score of jaundice among the study neonates (N=995).

Bind score		
Mean $\pm$ SD (range)	1.96 $\pm$ 1.009 (0-5)	
Median (Q1, Q3)	2 (1, 3)	
BIND score grading	Normal (Score 0)	445 (44.8%)
	Mild acute bilirubin encephalopathy (Score 1-3)	71 (7.1%)
	Moderate acute bilirubin encephalopathy (Score 4-6)	4 (0.4%)
	Not done	475 (47.7%)

## Discussion

The prevalence of neonatal jaundice in our study was 31%, this is lower than the prevalence reported in Egypt which ranged between 40% to 69.3%<sup>(7-11)</sup>. Our result was consistent with studies conducted in Ethiopia, Nigeria and Pakistan (12-14), lower prevalence was reported in Ethiopia, Uganda, and North Macedonia<sup>(15-17)</sup>. According to our knowledge, most of the studies in developed countries were on the severe hyperbilirubinemia<sup>(18, 19)</sup> and none about the prevalence of neonatal jaundice in NICU, this because the majority of neonatal jaundice cases usually are managed in the well baby nursery not in NICU. The variation in the results may be due to the study done in single center or

multicenter, the level of the NICU, the duration of the study, also may be due to the difference in the methodology, ethnicity, study design and admission criteria in each unit. This variation of the prevalence of the neonatal jaundice is obvious even in our study, with highest prevalence at Benha Insurance hospital (58.3%), and lowest one at Benha University hospital (9.2%). Benha University hospital is a tertiary care hospital with very busy obstetric department, so most of patients were inborn and admitted for other causes than jaundice like prematurity and respiratory problems. Benha Insurance, Kafr Shokr and Toukh Central Hospitals have level 2+ neonatal care units with limited number of

ventilators so the prevalence of jaundice was higher, however Benha Children hospital has special care neonatal unit for stable neonates including most of jaundice case.

In the present study, the most common cause of jaundice was idiopathic jaundice (56.3%). Similar results were reported in other Egyptian studies in Cairo and Elfayoum university hospitals, with the prevalence reported as 38.5% and 56.3%, respectively <sup>(9, 20)</sup>. Additionally, in cases of severe jaundice in Egypt, Iskander et al. <sup>(10)</sup> reported an undetermined cause in 40% of cases, and Gamaleldin et al. <sup>(21)</sup> reported a higher percentage of 49.8% in 2011. Similar results and even higher rates were observed in low- and middle-income countries like North Macedonia, Thailand, and Iran <sup>(17, 22, 23)</sup>. In the USA, Christensen et al. reported that 66% of neonates with hazardous hyperbilirubinemia and 76% of those with extreme hyperbilirubinemia had no etiological causes <sup>(18)</sup>. Additionally, 55% of cases from the USA kernicterus registry were reported with no etiology <sup>(24)</sup>. In Denmark, Donneborg et al. found that 307 (75%) out of 408 cases with extreme neonatal jaundice had no definite cause <sup>(19)</sup>.

We think that this idiopathic jaundice may be due to multifactorial factors like physiological jaundice plus breast feeding jaundice may be contributing factors in jaundice exaggeration. However, urinary tract infection and other causes should be ruled out in these cases. Genetic causes are mostly the cause in severe jaundice with no identified cause <sup>(25)</sup>.

We found that the second most common cause of jaundice was ABO incompatibility (30%), followed by Rh incompatibility (8.5%). Both ABO and Rh incompatibility accounted for 2.5% of cases only. Similar findings were reported by Abd Elmoktader, who noted that ABO incompatibility and Rh incompatibility accounted for 29.9% and 8.4% of cases, respectively <sup>(9)</sup>. Additionally, Seoud reported comparable results in Cairo

University Hospital, Egypt <sup>(26)</sup>. Immune hemolysis caused by maternal-fetal blood group incompatibilities is a frequent cause of neonatal jaundice (NJ), with ABO incompatibility being the most prevalent in clinical practice <sup>(27)</sup>. Therefore, it is vital to investigate the newborn's blood group before discharge, especially if the mother's blood group is O, to identify ABO incompatibility and provide appropriate advice to the mother regarding the probability of jaundice and the need for neonatal follow-up.

The incidence of Rh isoimmunization has significantly decreased since the application of Rhesus prophylaxis in pregnancy, however it remains an important cause of neonatal morbidity and mortality <sup>(28)</sup>.

Our study revealed that the age of neonates admitted ranged from 1-6 days with mean age of  $2.72 \pm 0.846$  days. Similarly, the mean age of neonates at admission with hyperbilirubinemia was  $2.78 \pm 2.34$  days in study carried out in Cairo University Pediatric Hospital <sup>(20)</sup>, earlier study done in the same hospital reported higher age at admission <sup>(8)</sup>. Most of the infants were admitted in the first three days of life 848/995 (85.2%) this percentage represents the improvement of the health service and also the knowledge of the family for seeking early medical care.

In our study, there was male predominance, this finding is consistent with studies conducted in Egypt <sup>(13,29)</sup>, Ethiopia <sup>(30)</sup>, Sweden <sup>(31)</sup>, Malaysia <sup>(32)</sup>, and this agreed with American Academy of Pediatrics considered male sex as a minor risk factor for development of severe hyperbilirubinemia <sup>(6)</sup>.

In the current study, most of the study neonates were delivered by caesarian section (84.1%) compared with 15.9% delivered through normal vaginal delivery. In contrast, a study found that 72.3% of jaundiced cases were vaginally delivered and concluded that vaginally delivered babies are likely to be discharged early from hospital and this may cause delayed

diagnosis of jaundice and increased risk of kernicterus<sup>(20)</sup>. However, these results should be interpreted cautiously because the very high rate of cesarean section in Egypt<sup>(33)</sup>.

In the current study, as regard mode of feeding, about 82.4% were breast fed compared to 17.6% who were bottle fed. The breast-fed infants may exhibit exaggerated neonatal jaundice during the first days of life<sup>(34,35)</sup>, and breastfed infants had significantly greater need for phototherapy than controls<sup>(36)</sup>. The degree of Neonatal jaundice increases with higher postnatal weight loss<sup>(37)</sup>.

Bilirubin-induced neurologic dysfunction (BIND) is a numeric scoring system created by Johnson et.al.<sup>(7)</sup>, the score was used to evaluate the presence, and the severity of Acute Bilirubin Encephalopathy and has been validated by many studies<sup>(38,39)</sup>. In our study, BIND score was not done in 47.7% of the jaundiced infants, and 44.8% were normal. The application of the score was not done in some hospital and other hospital applied it only with cases of severe hyperbilirubinemia or in cases with exchange transfusion.

Although this study is multi-center study and done in different levels of NICUs with large number of neonates, the study had limitations. The major limitation of this study was the lack of follow up of patients after discharge. Also, this study did not consider some essential causes, like a urinary tract infection. Moreover, this study included only neonates admitted to NICU, didn't include healthy neonates, so the true prevalence and risk factors in the community couldn't be assessed.

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## Conclusion

The neonatal jaundice prevalence in NICU in Qalubia is high and still constitutes a major cause of NICU admission and neonatal health concern, The prevalence is less in tertiary care NICU. The most common cause of the admitted infants with neonatal jaundice is idiopathic which

highlights the need for more careful evaluation. Most of the admitted infants were breastfed and delivered by Cesarean section.

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