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Evaluation of the hematological profile of neonatal jaundice among neonates in Erbil city

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Abstract

Background and objectives: Neonatal jaundice is the most commonly encountered medical problem in the first two weeks of life, and a common cause of readmission to the hospitals, this study is designed to investigate different hematological parameters in neonatal jaundice and compare them to normal infants, to determine the association of hematological profile of different etiologies of jaundice in neonates.

Methods: This prospective cross-sectional study, investigates blood samples of 600 neonates (300 healthy and 300 jaundice confirmed neonates, regardless of genders), that were admitted to Raparin Pediatric Teaching, and Erbil Maternity Teaching Hospitals, from July 2022 to July 2023. Samples were subjected to the hematological investigations, including complete blood count (CBC), ABO, and Rh for both the fetus and the mother. Additionally, direct antiglobulin test (Coomb´s), reticulocytes count, and G6PD enzyme assay were also assessed.

Results: Clinical presentation of neonatal jaundice showed that more than half (57.8%) of the cases were males, and 42.2% were females, oxytocin used for 31.2% of mothers during delivery; 6.5% of patients faced Rh-incompatibility and just 11.3% faced ABO- incompatibility. The most common etiologies for neonatal jaundice were physiological (64%), while others were pathological (36%). Among the pathological, the ABO incompatibility was (20.7%), followed by Rh incompatibility (9%), and G6PD deficiency (6.3%). There was a significance correlation between the jaundice type and evaluated hematological profiles for each group.

Conclusion: Most of the neonatal jaundice cases were physiological in nature, with ABO incompatibility as the most common type, while G6PD was the least common pathological type.

Keywords: Cross-sectional study, G6PD, Hyperbilirubinemia, Jaundice, Neonate

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Introduction

The term jaundice derives from the French word "jaune," which means yellow, and a common cause of readmission to the hospital after birth in almost half of full-term, and most of preterm neonates[1-4]. It's clinically defined as yellowish discoloration of the skin, sclera, and mucous membranes, resulting from over production of bilirubin.[3,4] It has been observed that the disproportion between the production of bilirubin, and the rate of its conjugation, plays a key role, and this predisposition to the production of bilirubin in infants, together with their limited ability to excrete the already over-produced bilirubin, resulting in neonatal jaundice. Infants, especially preterm infants, have higher rates of bilirubin production than adults, because they have red cells with a higher turnover rate, and a shorter life span.[5-7] Neonatal jaundice could be physiological, or due to a variety of etiological factors like; Glucose-6-phosphate dehydrogenase (GRPD) deficiency, blood and/or Rh incompatibility, septicemia, intracranial hemorrhage, biliary atresia, and congenital syphilis, or it could be even idiopathic in its origin.[7- 9] In contrast to physiological unconjugated hyperbilirubinemia, which requires careful monitoring but is common and usually benign, the presence of significant conjugated bilirubin always indicates pathology. As with many other homeostatic mechanisms, the bilirubin conjugation pathway has been untested until birth, and is immediately subjected to maximum load. It is vital to identify the presence of conjugated bilirubin as early as possible.[9,10] This study is designed to investigate different hematological parameters , associated with neonatal jaundice, and compare them to the same parameters in normal infants of the control group, to determine the association of hematological profile of different etiological factors of jaundice in neonates, to determine the prevalence of ABO incompatibility, Rh incompatibility, and G6PD deficiency, to find the association of types, and severity of the diseases, to assess the relevance, and the impact of other clinical characteristics (like age, gender, weight, bilirubin concentration, maternal health history to the severity or the state of the neonatal jaundice as a clinical condition. Therefore, this study aims to investigate and compare various hematological parameters between neonatal jaundice and normal infants to determine the association of hematological profile of different etiologies of neonatal jaundice.

Patients and methods:

This prospective cross-sectional study was conducted by collecting blood samples from 600 neonates (aged between 0 day - 1 month and weighed between 2.5 – 3.5 kg) that were admitted to Raparin Pediatric Teaching, and Erbil Maternity Teaching Hospitals at Erbil City, Iraq. Study subjects were gathered and enrolled to the study by selection from routine cases attending newborn unit, or recently got admitted to the Department of Pediatric Medicine at Raparin Teaching Hospital at Erbil City. With clinical evidence of jaundice in neonates, history including age, gender, birth weight, level of education of their mother, mother's age, detailed medical history, mother's knowledge about the impact of hyperbilirubinemia on neonate, the onset time of hyperbilirubinemia, the onset of breast feeding, history of formula feeding, history of intravenous oxytocin infusion during labor, technique of delivery, time of meconium passage, times of first medical visit of neonate, the family history of jaundice & their cause in other siblings will be re-taken from mothers. Infants less than 37 weeks of age, preterm or premature infants, and infants with other medical conditions (those who suspect to have metabolic disorders), or any congenital conditions/underweight, or over weight infants with total serum bilirubin (TSB) being

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<12 mg/dl for the jaundice diagnosed neonate were instantly excluded from study. The process was explained to the parents, and their written consents were also taken. Blood samples were collected within a period of one year (between July 2022 to July2023), and a total of 600 randomly selected males and female neonates were enrolled, in which 300 of the subjects were normal neonates, that were medically fit and free of any systemic diseases, and they were used as a reference and represented the control group of the study, and the other 300 cases were selected based on confirmed and diagnosed hyperbilirubinemia, following guidelines described by American Academy of Pediatrics committee, 2004.[4] Each blood sample then was divided into two tubes, 3 mL was placed into a sterilized tube containing EDTA, was mixed well and subjected to the hematological investigations, including CBC, morphology of blood, ABO, and Rh blood group typing, for both the fetus and the mother. Additionally, direct antiglobulin test (Coomb´s), reticulocytes count, and G6PD enzyme assay were also assessed. Statistical analysis was performed, using the Statistical Package for the Social Sciences (SPSS.), Chicago, IL, USA, version 23. The result was considered significant, if probability value (p) was <0.05 for highest significance. The study was approved by ethical committee of Kurdistan Higher Council of Medical Specialties.

Results

The clinical presentation of neonatal jaundice (NJ) showed that more than half (57.8%) of them were males, and 42.2% of cases were females, oxytocin used for 31.2% of mothers during delivery; 6.5% of patients faced Rh-incompatibility, 11.3% of them faced ABO-incompatibility. Regarding direct Coomb's test, the vast majority (98.7%) of cases were negative, while only 1.3% were positive. Most patients (98%) did not transfer blood, while 2% underwent blood exchange. Also, 3.2% of newborns had G6PD enzyme deficiency, while majority (96.8%) had normal level, as shown in Table (1), and Figure (1) showing the Frequency of distribution of various etiologies of NJ in our study.

Table (1): Gender, blood exchange and incompatibility tests of participants (Neonatal jaundice and healthy appearance)

Variables	Categories	Frequency	Percentage
Sex	Male	347	57.8
	Female	253	42.2
Oxytocin use in delivery	Yes	187	31.2
	No	413	68.8
Rh-incompatibility	Yes	39	6.5
	No	561	93.5
ABO- incompatibility	Yes	68	11.3
	No	532	88.7
Direct Coomb's test	Positive	8	1.3
	Negative	592	98.7
Blood exchange	Yes	12	2
	No	588	98
G6PD	Yes	19	3.2
	No	581	96.8
Total		600	100

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During admission to the hospital or neonate unit, most of jaundice cases were in 2nd day (51%), while least in 1st day in which its regarded pathological type.Regarding duration of treatment of jaundice patient, most of them were received treatment only for one day (78.7%), and others for two (13.7%) or three days (7.7%), as shown in Table (2).

Table (2): Phototherapy and age of neonatal jaundice cases.

Variables	Categories	Frequency	Percentage
Age of newborn in days when jaundice appeared	1 day	16	5.3
	2 days	153	51
	3 days	87	29
	4 days	24	8
	5 days and more	20	6.7
Duration of phototherapy (days)	1 day	236	78.7
	2 days	41	13.7
	3 days	23	7.7
Total		300	100

Regarding different variables between jaundice and healthy persons; delivery use of oxytocin, ABO incompatibility, blood exchange and G6PD results were significant ($p<0.001$). Regarding Rh incompatibility and Direct Coomb's test, there is no significant difference between both study groups (jaundice confirmed and healthy groups) ($p>0.001$), as shown in Table (3).

Table (3): Association between study type and different variables.

Variable	Study type		p-value
	Neonatal jaundice	Apparently healthy	
	Number (%)		
Oxytocin use in delivery	73 (24.3)	114 (38)	<0.001
Rh-incompatibility	27 (9)	12 (4)	0.013
ABO- incompatibility	62 (20.7)	6 (2)	<0.001
Direct Coomb's test	8 (2.7)	0 (0)	0.004
Blood exchange	12 (4)	0 (0)	<0.001
G6PD	19 (6.3)	0 (0)	<0.001
Total	300	300	
	100	100	

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According to hematological parameters, there is significant difference between study types in Hb, PCV and reticulocyte count ($p<0.001$), and not significant ($p>0.001$) regarding WBC and platelets. Regarding bilirubin level; there is significant difference ($p<0.001$) in total bilirubin and direct bilirubin level, while not significant in indirect bilirubin level, as shown in Table (4).

Table (4): The difference of mean hematological parameters and bilirubin between study groups**.**

Parameter	Study type	N	Mean	Std. Deviation	p-value
Hemoglobin (g/dl)	Neonatal jaundice	300	14.79	3.47	<0.001
	Apparently healthy	300	15.73	2.86	
WBC	Neonatal jaundice	300	13.22	4.88	0.013
	Apparently healthy	300	12.23	4.87	
Platelet	Neonatal jaundice	300	255.20	105.66	0.060
	Apparently healthy	300	272.14	114.76	
Total bilirubin	Neonatal jaundice	300	18.04	5.39	<0.001
	Apparently healthy	300	2.32	0.72	
Direct bilirubin	Neonatal jaundice	300	1.34	0.76	<0.001
	Apparently healthy	300	0.53	0.37	
Indirect bilirubin	Neonatal jaundice	300	16.70	5.09	<0.001
	Apparently healthy	300	1.78	0.77	
Reticulocyte count	Neonatal jaundice	300	6.36	3.57	<0.001
	Apparently healthy	300	3.24	1.19	
PCV	Neonatal jaundice	300	44.38	11.82	<0.001
	Apparently healthy	300	48.30	10.79	

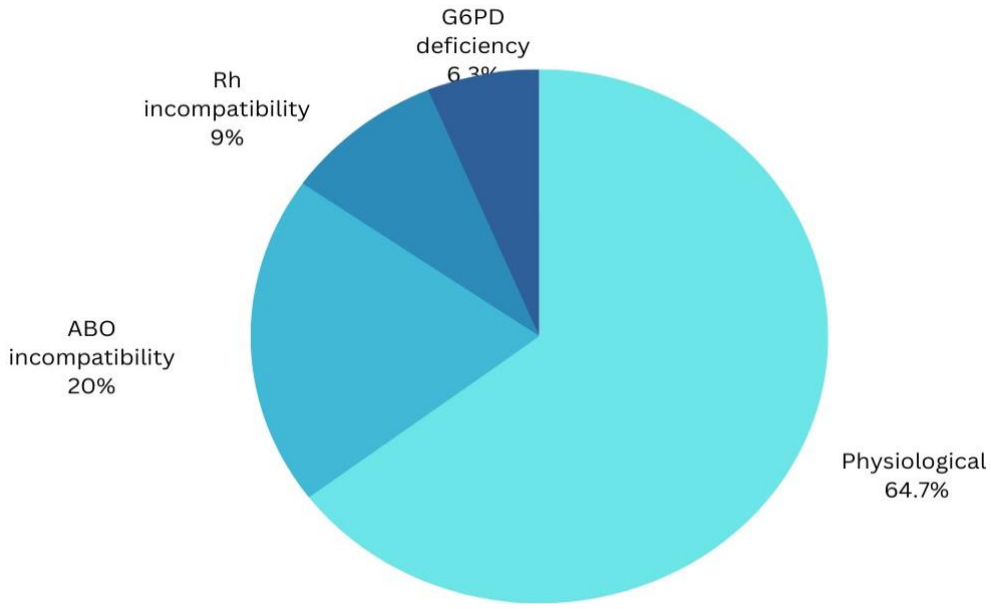

Figure (1): Frequency of distribution of various etiologies of NJ

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Discussion:

Neonatal jaundice is considered to be a benign neonatal condition born at term or near-term gestation in the first two weeks of life, and a common cause of readmission to the hospital after birth in almost half of full-term, and most of preterm neonates.[4,5] Neonates have higher rates of bilirubin production than adults, because they have red cells with a higher turnover, and a shorter life span.[11] Almost all the studies that investigated the frequencies of etiologies of NJ identified, the physiological jaundice as the most common etiology which is the same what we observed too.[1,2,5,7-9] We also, detected that among the pathological cases of NJ; the ABO incompatibility represented the majority, making it the most common etiology for NJ in our study, and that was also the observations of several local and international researchers.[3.4,6-9.13] We also, observed that the second majority of cases were of Rh incompatibility type, while the number of cases presented with G6PD deficiency were only (6.3%). In a recent study, that was conducted locally which investigated the prevalence of G6PD as an etiology of NJ in Duhok, Iraq 16% were G6PD deficient, and they also noticed a significant difference in the level of serum indirect bilirubin among. G6PD-deficient neonate in comparison to G6PD none-deficient neonates.[1] In our study the frequency of occurrence of G6PD was observed to be the lowest among the other etiologies for pathological NJ, and this could be due to smaller sample size compared to ours (600 cases vs just 100 cases). Reviewing data from neighboring geographical regions, and international data showed the followings; according to a study from Iran among 436 cases, the prevalence of NJ among neonates was as follows: ABO blood groups incompatibility 16.9%, Rh incompatibility was 4%, and G6PD was calculated to be 2.1%, while physiological NJ was the major etiology (77%) [3], which is the near to our clarifications in ranking the etiologies of pathological NJ taking in consideration, that the sample size in this particular study is close to our study, and it comes from a neighboring country. The national Turkish registry for NJ data, demonstrated that ABO incompatibility was the most common cause of NJ (21%), which is close to our observations, followed by Rh incompatibility (18.7%).[12,13] In a study that investigated NJ in the Makkah region (Saudi Arabia), and included 239 neonates with NJ; ABO incompatibility was observed in 36.6% of neonates, and G6PD deficiency was observed in 7.5% of neonates, while Rh incompatibility was found in only 2.6% of neonates.[2] This study offers that the second major etiology for pathological NJ is G6PD, though the frequency of its occurrence is so close to what we observed (just 6.3% were G6PD deficient in this study). In another study in Egypt; out of 2782 neonates, 2646 (95.1%) newborns were normal, 17 (0.6%) exhibited mild-level deficiency; 119 newborns showed G6PD deficiency for an overall prevalence of G6PD deficiency of 4.3% [11-13], which is more or less, and of greater sample size is close to what we observed regarding the G6PD occurrence rate. In Macedonia a study that enrolled 167 cases of NJ (24.6%) of which presented with ABO/Rhesus type hemolytic jaundice, and the rest with unspecific type of jaundice [5], and this finding is relatively close to our study finding, regarding the occurrence rate of ABO incompatibility (20.79%), though the sample size is much smaller than ours. In a study that has been conducted in India showed that out of 100 neonates the frequency of physiological jaundice was 57%, followed by G6PD deficiency (23%), and Rh incompatibility (13.4%), while only (6.6%) of the neonates were observed to have ABO incompatibility and according to this study the major etiology for pathological NJ

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is G6PD [16], and this contradict our findings in both ranking of etiologies for pathological NJ and frequency of occurrence (as only 6.3% were G6PD deficit in our study as a 3rd and least common etiological factor for NJ), this could be justified by smaller sample size or even geographical influence on NJ occurrence itself. In a study in Nepal, it was observed that 32.9% neonates were ABO incompatible and only 4.1% were Rh incompatible, while just 3.2% suffered from G6PD deficiency.[7] In another study in Pakistan, that enrolled only 63 cases of NJ, shown to be relatively more common in males as compared to female neonates, 40 (62%) cases were diagnosed as having physiological jaundice, while ABO incompatibility (15%), Rh incompatibility (8%) and G6PD deficiency just accounted for (3%) of the cases [16], the observations and outcomes of that study is relatively close to our findings, aside of much smaller sample size (63 cases versus 600 cases of our study), taking the differences in climate, weather and geographical locations in consideration.

Conclusion:

This study demonstrated that majority of the neonatal jaundice cases were physiological in their nature and ABO incompatibility is the most common etiology for neonatal jaundice in Erbil, Iraq, while G6PD was the least common pathological etiology. Other relevant investigations like hormonal assay, especially thyroid stimulating hormone (TSH) should also be done. We recommend a larger prospective and community-based studies are required, to clarify the true burden of NJ and its subsequent management.

Conflict of interest

All authors declare that they have no conflicts of interest to disclose.

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