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A study of the relationship between the incidence of congenital hyperbilirubinemia and specific physiological criteria in a sample of births from sanatoriums and Bani Waleed General Hospital

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دراسة العلاقة بين حدوث فرط بيليروبين الدم الولادي وبعض المعايير الفسيولوجية في عينة من المواليد من المصحات ومستشفى بني وليد العام

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Abstract:
Jaundice is a prevalent condition encountered by newborns during the first week of life. It is particularly common among those born preterm and is regarded as a natural phenomenon that occurs in over 55% of newborns, typically resolving gradually. This study aims to identify the incidence of elevated bile substances and examine their association with factors such as the sex of the fetus and the type of lactation in newborns in the city of Bani Waleed. The investigation involved 150 newborns from specialized medical facilities, including Bani Waleed Hospital, Avicenna Sanatorium, and Al-Yaqeen Laboratory. Conducted between July and September 2023, data were collected from mothers using a disease-related questionnaire, followed by laboratory tests to assess bilirubin levels in the newborns' blood. Results indicated that 67% of children with hyperbilirubinemia exhibited bilirubin levels averaging 6.747 ± 4.1433 mg/dL. Furthermore, there was a statistically significant increase ($p < 0.05$) in serum bilirubin levels in newborns with neonatal jaundice who were reliant on artificial feeding and those with a blood group incompatible with that of their mothers. Notably, the Rh factor distribution revealed that 59% of mothers were Rh-negative and 41% Rh-positive, while 68% of newborns were Rh-negative and 32% Rh-positive. This discrepancy poses a significant risk for fetal hemolysis.

Keywords: Jaundice, Hyperbilirubinemia, Breastfeeding, Bani waleed.

الملخص
اليرقان هو حالة شائعة تصيب الأطفال حديثي الولادة خلال الأسبوع الأول من الحياة. وهو شائع بشكل خاص بين الأطفال الخدج ويعتبر ظاهرة طبيعية تحدث في أكثر من 55٪ من الأطفال حديثي الولادة، وعادة ما تختفي تدريجيًا. تهدف هذه الدراسة إلى تحديد حدوث ارتفاع المواد الصفراوية وفحص ارتباطها بعوامل مثل جنس الجنين ونوع الرضاعة لدى الأطفال حديثي الولادة في مدينة بني وليد. شملت الدراسة 150 مولودًا جديدًا من المرافق الطبية المتخصصة، بما في ذلك مستشفى بني وليد، ومصحة ابن سينا، ومختبر اليقين. أجريت بين يوليو وسبتمبر 2023، وتم جمع البيانات من الأمهات باستخدام استبيان متعلق بالمرض، يلي ذلك اختبارات معملية لتقييم مستويات البيليروبين في دم الأطفال حديثي الولادة. أشارت النتائج إلى أن 67٪ من الأطفال المصابين بفرط بيليروبين الدم أظهروا مستويات بيليروبين بمعدل 6.747 ± 4.1433 مجم / ديسيلتر. علاوة على ذلك، كان هناك زيادة ذات دلالة إحصائية (ص < 0.05) في مستويات البيليروبين في المصل لدى الأطفال حديثي الولادة المصابين باليرقان الوليدي والذين اعتمدوا على الرضاعة الصناعية والذين لديهم فصيلة دم غير متوافقة مع فصيلة دم أمهاتهم. والجدير بالذكر أن توزيع عامل الريسيسي Rh كشف أن 59٪ من الأمهات سلبيات Rh و

41٪ إيجابيات Rh، بينما كان 68٪ من الأطفال حديثي الولادة سلبيات Rh و 32٪ إيجابيات Rh. يشكل هذا التناقض خطرًا كبيرًا على انحلال الدم الجنيني.

الكلمات المفتاحية: اليرقان، فرط بيليروبين الدم، الرضاعة الطبيعية، بني وليد.

Introduction

Neonatal jaundice is a prevalent condition among newborns, particularly in infants born preterm, specifically those delivered before 38 weeks of gestation. Typically, these infants present with elevated bilirubin levels, with clinical symptoms emerging 2 to 4 days postpartum. Jaundice is characterized by a yellowing of body tissues attributable to the accumulation of excess bilirubin. Bilirubin deposition occurs exclusively when there is an excess of this substance, signifying either increased production or impaired hepatic secretion. Normal bilirubin levels in the bloodstream are generally considered to be below 1 mg/dL; however, the clinical manifestation of jaundice, specifically peripheral yellowing of the sclera, becomes apparent only when serum bilirubin levels exceed 3 mg/dL. The sclera is particularly susceptible to bilirubin accumulation due to its high elastin content **(Leung *et al.,* 2019).** As serum bilirubin levels rise, the skin undergoes a progressive color change from lemon yellow to apple green, especially in cases of prolonged elevation; this green hue is attributed to the presence of biliverdin **(Roche *et al.,* 2004)**. It is essential to recognize that a modest increase in bilirubin levels is common among most newborns in utero, with the placenta playing a crucial role in the excretion of this pigment. This phenomenon, referred to as physiological hyperbilirubinemia, is typically benign and does not pose risks to the infant's health or development **(Hussein, 2015).** Conversely, jaundice can become clinically significant when bilirubin accumulates within the central nervous system, leading to kernicterus, a severe condition associated with potential neurodevelopmental impairments such as mental retardation and motor paralysis. The threshold bilirubin levels at which jaundice poses a risk vary based on the infant's weight and age, as well as the presence of clinical signs associated with hepatic and biliary dysfunction **(Dawood & Hameed, 2010).** Hyperbilirubinemia in newborns is one of the most prevalent clinical conditions, particularly during the first week of life **(Bhutani *et al.*, 2013; Olusanya *et al.*, 2015)**. This condition is diagnosed when the total bilirubin level in the blood exceeds the established high-risk threshold during this critical period **(Burke *et al.*, 2009)**. Epidemiological studies indicate that approximately 8% to 11% of newborns develop hyperbilirubinemia, with 60% exhibiting signs of neonatal jaundice **(Chou *et al.*, 2003).** Neonatal jaundice is clinically characterized by a yellow discoloration of the skin resulting from bilirubin accumulation (**Ogunfowora & Daniel, 2006)**, which can elicit significant anxiety among healthcare providers and parents alike. Cutaneous jaundice is typically first observed on the face; as bilirubin levels continue to rise, the discoloration progresses to the trunk and extremities. Bilirubin comprises two distinct forms: unconjugated (indirect) and conjugated (direct). An elevation in either form can precipitate jaundice. Jaundice serves as a primary clinical indicator of liver dysfunction, among other pathological conditions **(Vítek & Ostrow, 2009).** Furthermore, yellowing of the skin that spares the sclera may suggest the presence of carotenoderma, a benign condition often seen in individuals with excessive dietary intake of carotene. It is imperative to recognize that jaundice is not solely an excess of bilirubin; it can have significant physiological consequences. Nevertheless, bilirubin, similar to uric acid, functions as a crucial antioxidant within the biological systems of newborns **(Nag *et al.*, 2009; Barikbin *et al.*, 2011).** Elevated bilirubin levels can be neurotoxic, posing risks to the developing central nervous system and potentially resulting in behavioral and neurological impairments, a condition referred to as kernicterus (**Nass & Frank, 2010; Gartner & Lee, 1999).** The etiology of neonatal jaundice is multifactorial, encompassing variables such as birth weight, gestational age, premature rupture of membranes, maternal infectious diseases, and other complications that may arise during pregnancy **(Mesic *et al.*, 2014)**.

Materials and Methods

Data were extracted from the archives of Bani Waleed Hospital and systematically recorded in tabular format. Integrated analyses were obtained from Avicenna Sanatorium and Al-Yaqeen Laboratory. In addition, several questionnaires were administered to gather supplementary information. The compiled data were subsequently uploaded to statistical processing software, including Microsoft Excel and SPSS, to facilitate a comprehensive analysis of the sample results.

Steps for the Analysis of Total Bilirubin (Indirect): A solution of R1 (250 microliters) was carefully drawn using a pipette and transferred to the sample tube. Subsequently, 2 milliliters of normal saline solution were added to both the sample tube and the control tube using a pipette. Following this, 200 microliters of serum were introduced into each tube. The contents of both tubes were thoroughly mixed using a pipette and then incubated at room temperature for a duration of 7 to 10 minutes. Upon completion of the incubation period, the tubes were positioned in the reading compartment of the analytical device. The results will be displayed on the device screen, represented by the following calculation: Indirect Bilirubin = (sample sample concentration) / absorption amount of the control. It is essential to ensure that the filter is installed in the device prior to inserting the sample tube.

Results

The study included a total of 150 mothers and their newborns, with data collected from three facilities: Dhahra Shelter Sanatorium (15 cases), Avicenna Sanatorium (75 cases), and Bani Waleed General Hospital (60 cases). The integrated sample data revealed that more than half of the participants exhibited hyperbilirubinemia. The subjects were categorized into two groups based on bilirubin levels in the blood: the hyperbilirubinemia group consisted of 98 cases (65.3%), while the non-hyperbilirubinemia group included 52 cases (34.7%).

Table (1) Distribution of sample members by jaundice.

Jaundice	Issue	The ratio%
Not injured	52	34.6%
Injured	98	65.3%
Total	150	100%

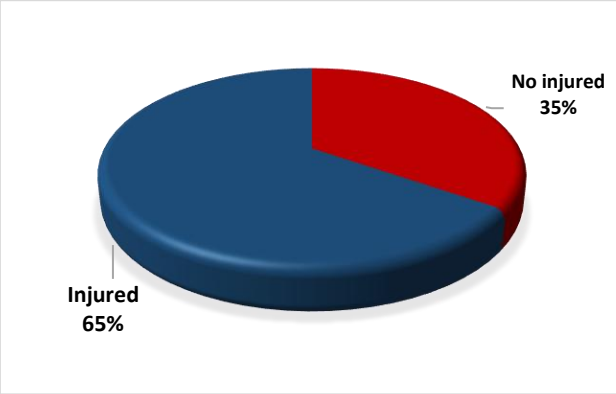


Diagram (1) Distribution of the Sample by Jaundice Incidence.

The distribution of births with hyperbilirubinemia by age revealed that the age group with the highest percentage was 0-3 days, accounting for 55.1%. This was followed by the age group of 4-7 days, while the age group of 8 days and older showed the lowest percentage of hyperbilirubinemia at 6.21%.

Table (2) Distribution of respondents by jaundice incidence.

Age (in day)	3_1	4_7	8and above	Total
Iterations	55	33	10	98
The ratio%	55.10%	32.60%	6.21%	100%

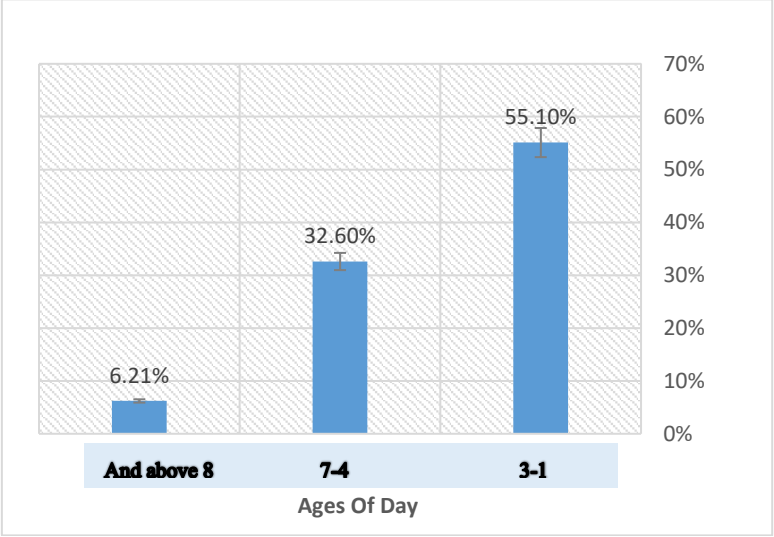


Diagram (2) Distribution of respondents by jaundice incidence.

The table presents the mean ± standard deviation (SD) of the distribution of the study sample according to the age of the child in days, reflecting both higher and lower values. The analysis revealed statistically significant differences in total bilirubin and direct bilirubin levels across all age groups of newborns. Specifically, the p-values associated with the variables (age and severity of anaphylaxis) were recorded as 4.14 for total bilirubin, indicating significant differences in bilirubin levels in relation to the child's age. Furthermore, the results suggest that $p > 0.05$ supports the acceptance of this hypothesis.

Table (3) summarizes the findings derived from the statistical analysis conducted using SPSS (version 22, IBM).

Descriptive Statistics	N	Minimum	Maximum	Mean ± Std. Deviation
Age (Day)	98	1	10	3.85±2.509
T Bilirubin	98	0.2	14.6	6.747±4.1433
D Bilirubin	98	0.3	2.3	0.88±0.4842

The Relationship Between the Incidence of Hyperbilirubinemia and the Sex of the Newborn. The table presents the distribution of hyperbilirubinemia cases stratified by the sex of the newborn. The analysis reveals that the highest incidence of hyperbilirubinemia was observed in males (68%), compared to females (32%). This disparity underscores the need for further investigation into potential sex-related factors influencing the prevalence of hyperbilirubinemia in neonates.

Table (4) Relationship Between the Incidence of Hyperbilirubinemia and the Sex of the Newborn.

Gender	Males	Females	Total
Iterations	67	31	98
Percentage ratio	68.30%	31.60%	100%

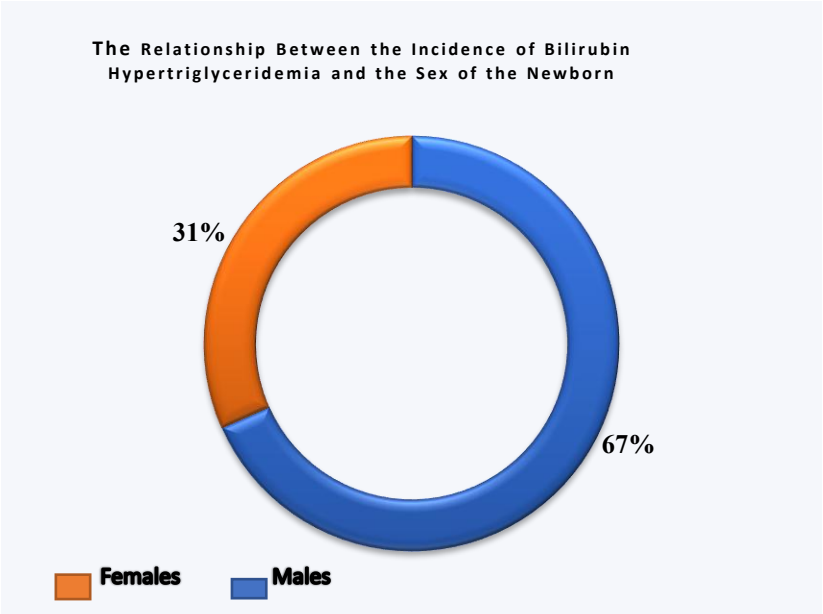
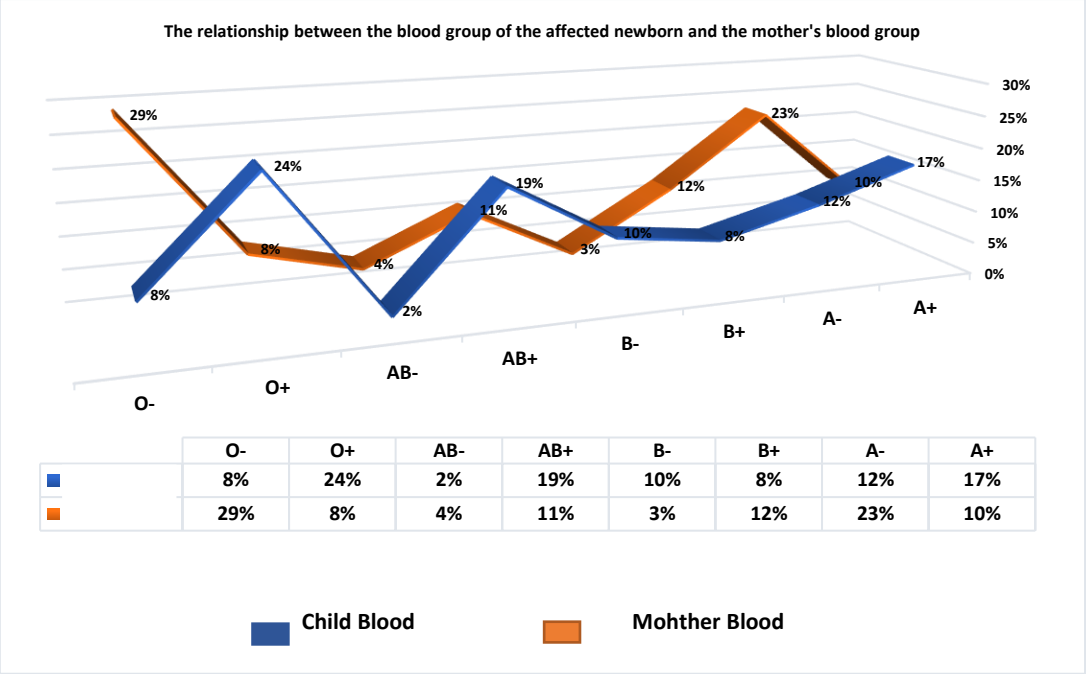


Diagram (4) The Relationship Between the Incidence of Hyperbilirubinemia and the Sex of the Newborn.

Sample Members by Blood Group and Rh Factor of the Newborn and Mother, the results indicated an inverse relationship between the blood groups of the mother and the newborn concerning jaundice incidence. The highest percentage of infection was observed in pregnant women with blood group O+, while the proportions in the other blood groups were lower, as illustrated in Table (5).

Table (5) Distribution of Sample Members by Blood Group and Rh Factor of the Newborn and Mother

Blood groups	A-	A+	B-	B+	O-	O+	AB-	AB+
The child's blood group	%12	%17	%10	%8	%8	%24	%2	%19
Mother's blood type	%23	%10	%3	%12	%29	%8	%4	%11



	O-	O+	AB-	AB+	B-	B+	A-	A+
	8%	24%	2%	19%	10%	8%	12%	17%
	29%	8%	4%	11%	3%	12%	23%	10%

Diagram (5) The relationship between the blood group of the affected newborn and the mother's blood group.

Table (6): shows the distribution of sample members by Rh factor.

The Rh factor	Rh-	Rh+
The Rh factor of the newborn	%32	%68
The Rh factor of L	%59	%41

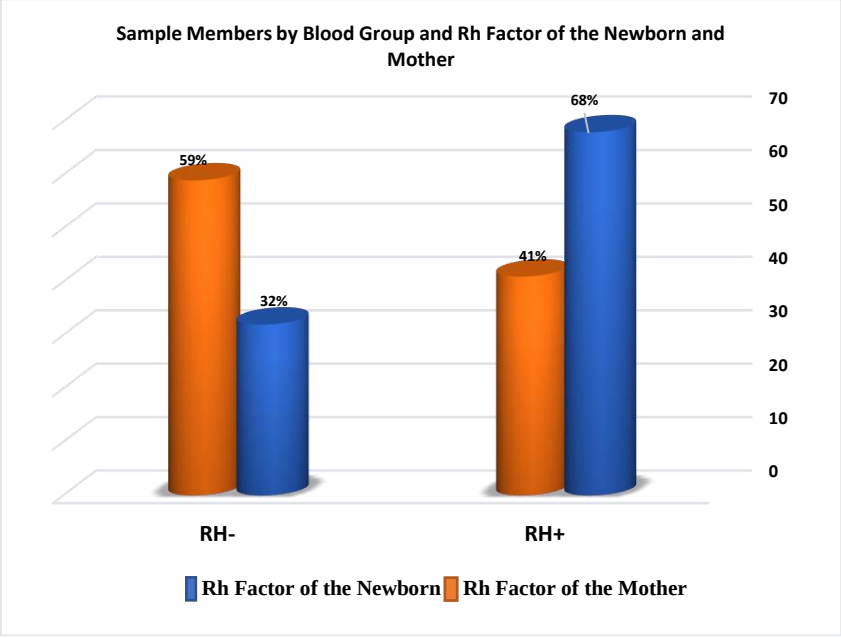


Diagram (6) Distribution of sample members by RH factor.

This section examines the relationship between the timing and type of lactation, as represented by the distribution of the study sample. The findings indicate that the highest percentage, 61.2%, was observed in the first category corresponding to the first day, predominantly involving artificial feeding. The percentages related to the timing of the initiation of breastfeeding are detailed in Table (7).

Table (7) provides a comprehensive overview of the distribution of the sample based on the timing of lactation initiation and the type of lactation.

Time to start lactation	Artificial feeding		Breastfeeding	Mixed lactation
The first day	%61.2		%23.4	%15.3
The second day	%45.9		34.6%	%19.3
Total	%107.1		%58	%34.6

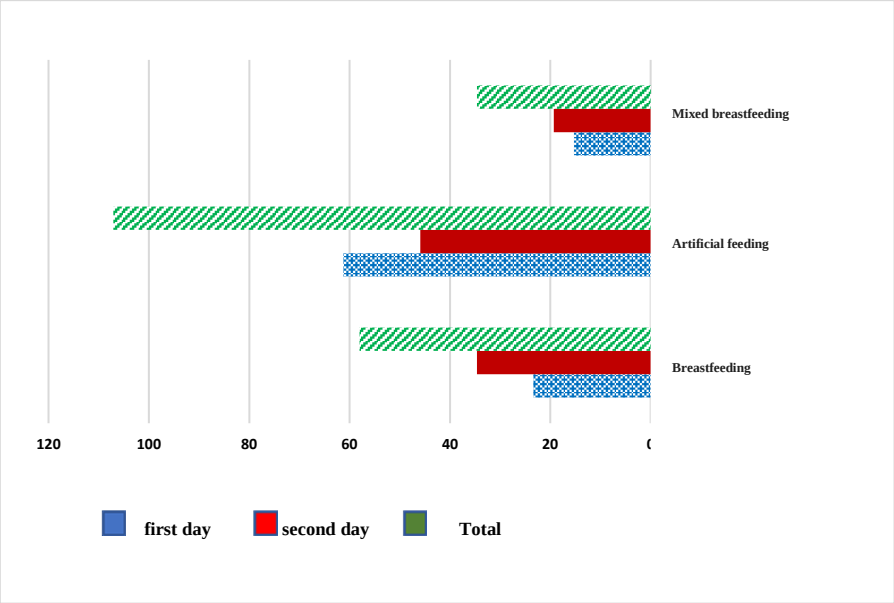


Diagram (7) Shows the Provides a comprehensive overview of the distribution of the sample based on the timing of lactation initiation and the type of lactation.

Discussion

The results showed the distribution of cases of hyperbilirubinemia by the sex of the fetus, with the highest incidence rate observed in males (68%), followed by females (32%). This finding is consistent with the results reported by **Bashir (2021)**, which indicated that the incidence among males was higher than that among females, with 52% of the infected being males and 48% females. The influence of sex on the concentration of total bilirubin in the blood, as well as weight and gestational period in patients with neonatal jaundice, is further illustrated in Table (1). Figure (1) shows an increase in the incidence of neonatal jaundice in males (67.5%) compared to females. Fetal blood contains approximately 65 million erythrocytes per mm^3, which comprise a type of hemoglobin known as fetal hemoglobin, accounting for up to 90% of the normal hemoglobin in fetuses. After birth, this type is replaced by adult hemoglobin, and the number of erythrocytes decreases significantly, potentially reaching about 45 million erythrocytes per mm^3. This decrease is due to an increase in the rate of erythrocyte breakdown, resulting in elevated bilirubin concentrations and, consequently, neonatal jaundice. The gender of the newborn appears to contribute to the increased incidence of jaundice, as males are more likely to develop jaundice than females. This is attributed to the higher number of red blood cells in males compared to females. The current results align with previous findings **(Behrman *et al.*, 2000; Clemons, 2000)**. This discussion examines the influence of age on the incidence of neonatal jaundice in newborns. The results indicate that jaundice most frequently manifests within the first three days of life, consistent with the findings of **Bashir (2021)**, which reported an incidence of 93%. Furthermore, it was concluded that the majority of infections occurred on the first and second days of life. This increase in the incidence of neonatal jaundice during this early period is anticipated, particularly following the breakdown of red blood cells (RBCs). The enhanced erythrocyte degradation processes lead to elevated bilirubin levels, which are subsequently secreted in the bile. Consequently, the liver of a newborn does not reach full maturity until after birth, resulting in liver cells being unable to adequately process bilirubin. This mechanism elucidates the occurrence of neonatal jaundice and the prolonged survival of premature infants, whose livers are less developed than those of full-term infants **(Zilva *et al.*, 1999).** Alternatively, this phenomenon may be attributed to the diminished efficacy of the hepatic enzyme responsible for converting unbound bilirubin, produced by the breakdown of hemoglobin, into bilirubin bound to bile **(Manyal, 2004).** As confirmed by the findings of **Tirona *et al.* (2001),** maternal antibodies are generated against fetal red blood cells when these cells express a specific antigen. This phenomenon typically occurs when a child is born with either a positive or negative Rh factor, particularly in the context of a father with a positive Rh factor **(Tirona *et al.*, 2001)**. This

observation is consistent with statistical analyses indicating significant differences ($p > 0.05$) between blood groups and the severity of associated injuries. These results are corroborated by a prior study conducted by **Hossein (2011)**, which identified a statistically significant relationship between these variables. Furthermore, findings from **Taie-A *et al.* (2011)** suggest that there is no significant relationship between the blood groups of newborns and bilirubin levels. The incidence of incompatibility between maternal and fetal ABO blood groups, particularly when the maternal blood group is O and the newborn's blood group is A or B, occurs in approximately 15-20% of all pregnancies **(Murray & Roberts, 2007**). Infants born to mothers with blood group O should be closely monitored, with discharge from the hospital recommended after 72 hours. Routine umbilical cord blood tests are not advised for newborns whose mothers belong to Group O **(Yigit *et al.*, 2005).** Jaundice resulting from ABO incompatibility typically manifests after 24 hours of birth. In instances of significant jaundice or jaundice appearing within the first 24 hours, careful observation is essential. Table (6) illustrates that the predominant method of nutrition for affected infants was artificial feeding, aligning with the findings of **Bashir (2021),** which indicated that 52% of cases were sustained through artificial means. In contrast, only 4% of affected infants primarily received glucose water and breastfeeding. Additionally, 44% of infected infants relied on a combination of glucose-water feeding, breastfeeding, and artificial feeding. These results are consistent with the study conducted by **Hameed et al. (2013)**, which identified significant differences between the effects of artificial feeding and the severity of jaundice. However, these findings diverge from those of **Hassoun and Alaa (2011**), which reported no significant differences between these factors. Moreover, neonatal jaundice attributable to breastfeeding is occasionally observed. The results further demonstrate that the incidence of neonatal jaundice declines as newborns age. Through this study, it can be asserted that a relationship exists between the incidence of jaundice and the blood type of the newborn.

The findings revealed that the highest percentage of cases occurred in the O+ blood group, and an inverse relationship was observed between the ratios of blood groups and the Rh factor of both the mother and the newborn. Hemolytic jaundice may arise from incompatibility between maternal and fetal blood groups, particularly concerning the ABO and Rh factors. When maternal and fetal blood groups are incompatible, fetal blood may traverse the umbilical cord barrier prior to birth, resulting in hemolysis due to a robust immune response **(Sana *et al.*, 2016).**

Conclusions

The findings of the current study indicate the following: Hyperbilirubinemia is among the most prevalent conditions affecting newborns. Male sex exhibits a significantly greater influence than female sex on the incidence of hyperbilirubinemia, particularly concerning the frequency and severity of infections. A range of risk factors contributes to this condition in newborns, including breastfeeding, blood groups A and O, and male sex, all of which are associated with increased susceptibility to hyperbilirubinemia. Notably, the prevalence of these factors was highest in both the affected and control groups of infants

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