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Risk Factors and Incidences for Neonatal Hyperbilirubinemia in Erbil-City: A Cross-Sectional Study

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Abstract

Neonatal hyperbilirubinemia is a common condition in newborns, defined by increased bilirubin levels usually manifested as jaundice. In the present review, the incidence of neonatal hyperbilirubinemia and its risk factors will be discussed in Erbil, Kurdistan Region of Iraq. A cross-sectional study was done on 100 full-term neonates admitted into three hospitals from January to April 2023. The analysis identified maternal factors such as age, mode of delivery, and type of anesthesia in relation to neonatal factors of mode of feeding, gestational age, and blood type. In this regard, the mode of feeding and type of anesthesia used at birth showed a strong association with hyperbilirubinemia but not with maternal age, blood group, and Rh factor. In particular, this will be crucial in avoiding serious consequences, especially for prematurely born infants. Further investigations are recommended with larger sample sizes in order to study other possible risk factors. In conclusion, the study shows that feeding habits and delivery anesthetics strongly influence newborn hyperbilirubinemia. Although maternal age, educational level, and Rh factor were not statistically significant, and the need of early screening and focused therapy to minimize poor outcomes, especially in high-risk neonates such preterm newborns. To identify more risk variables and improve newborn care, bigger studies are necessary.

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1. Introduction

Neonatal hyperbilirubinemia is a condition characterized by increased amounts of bilirubin in the blood, which can be alarming. This condition is considered one of the most common health concerns affecting newborns worldwide, regardless of geographical location or ethnicity. Hyper-bilirubinemia commonly manifests itself in the form of jaundice, which is characterized by a yellowish discoloration of both the skin and the sclera, the white portion of the eyes. This yellowish hue is due to the deposition of bilirubin, which is essentially a waste product resulting from the normal breakdown process of the body's red blood cells [1]. Approximately 60% of full-term infants, as well as around 80% of preterm infants, show signs of jaundice during the initial week after birth. Among these infants, a small percentage, roughly 2%, experience severe hyperbilirubinemia that necessitates medical treatment and intervention [2]. In cases of severe hyperbilirubinemia, there can be significant complications that arise, one of which is kernicterus. This is a rare but extremely serious condition that has the potential to result in irreversible brain damage, posing a serious threat to the affected infant's health and development [3]. Many factors are known to influence the development and onset of neonatal hyperbilirubinemia. According

to Watchko 2016, one of the major causative agents for this condition is the immaturity of the newborn liver to process bilirubin efficiently. It is important to note that neonates possess a bigger mass of red blood cells co-existing with a much shorter lifespan of these cells compared to adults, therefore leading to a higher production of bilirubin in the neonate body. This fact, coupled with the still-developing hepatic system, results in the characteristic increase in blood levels of bilirubin [4]. Additionally, factors such as gestational age, maternal health conditions, and the method of feeding can influence the risk of developing hyperbilirubinemia [1].

While exclusive breastfeeding, particularly in the first days following delivery, has been associated with an increased risk of hyperbilirubinemia, such a condition can result from poor feeding that can lead to both a lack of fluids and the calories that a newborn requires to thrive and be healthy [5]. It must be considered, however, that when effective and frequent breastfeeding takes place, it can prevent severe hyperbilirubinemia since the stimulation provided helps to create bowel movements that effectively eliminate bilirubin from the body. It also needs to be understood that genetic elements are also a significant factor in this condition; for example, patients with G6PD deficiency have a significantly higher risk of developing a problem of this nature, especially in ethnic groups where the deficiency is more common [6]. While jaundice is usually regarded as a benign condition, it is not always of a harmless nature. In fact, it can signify several critical, potentially serious conditions when this condition persists beyond the neonatal period, as evidenced by the statements made by [7]. More specifically, neonatal jaundice that persists for greater than 14 days in full-term infants could indicate the presence of serious health issues, such as biliary atresia and other forms of hepatic dysfunctions, as stated by Merritt & Palmer in 2017. As such, determining the risk factors that are linked to neonatal jaundice becomes a priority since identification will allow for the development of effective early intervention and prevention methods against the manifestation of severe and adverse outcomes. This current comprehensive study will be vastly informed on the prevalence of neonatal hyperbilirubinemia in Erbil City, the Kurdistan Region of Iraq. It also seeks to find out and analyze various associated risk factors contributing to this condition. Elucidation of various risk factors is very important because it would go a long way in contributing to an improvement in neonatal care practices and reducing the overall incidence of complications related to hyperbilirubinemia in this particular region.

2. Materials and Methods

In accordance with the data which was collected by the approving letter No. 31.215. This research was conducted on one hundred term neonates who were diagnosed with hyperbilirubinemia and were admitted to the neonatal critical unit of the Rapparin Teaching Hospital for Children, Maternity Hospital, and Zheen Private Hospital during the months of January and April 2023 within the scope of this cross-sectional study. The normal level of bilirubin is:

Total Bilirubin: In neonates, it should be less than 10 mg/dl or 171 µmol/L, whereas in infants over the age of one month, it should be between 0.3 and 1.2 mg/dl or 5.1 and 20.5 µmol/L Cobas e 411 analyzer was used for this experiment respectively. In neonates, the B-normal range for G6PD activity is 10.15–14.71 U/g Hb, whereas in adults, it ranges from 6.75–11.95 U/g Hb. , quantitative enzyme test following the directions given by the maker (Biolabo, France). The size of the sample was one hundred, and it was gathered from newborns in three different hospitals located in the city of Erbil. The data collection process consisted of a predesigned and pretested questionnaire that was used to collect demographic information. This information included blood group, maternal age, educational level, the various periods of pregnancy, delivery technique, medical condition, forms of anesthetic, family history, and virus screen. The method of data collection consisted of, under sterile and aseptic circumstances, the removal of three milliliters of gel tube venous blood by means of a three milliliter disposable syringe in the appropriate manner, followed by the shipment of the blood to the laboratory for TSB level monitoring using a Cobas e411 analyzer. All of the findings were stored until they were subjected to statistical analysis.

2.1. Ethical consideration

Prior to the collection of the sample, the test and method were described to each and every family, and the optimum blood collection was carried out.

2.2. Statistical analysis

All of the data were gathered and processed with the help of the SPSS program for statistical analysis version 26, which was used to calculate descriptive statistical analysis (frequency and percentage). In order to evaluate the degree of correlation between the variables, inferential statistical analysis, namely Chi-square and Fisher's exact tests, was used. If the P-value is less than or equal to 0.05, then the null hypothesis is rejected, and the P-value is regarded to be statistically significant.

3. Results

The findings of of the study research provide insights into additional characteristics of mothers and probable variables that may increase the incidence of newborn jaundice. Results: The data consists of information about the distribution of maternal age, the duration of pregnancy, educational levels, delivery details (including whether anesthesia was used), blood group type with Rh factor, and family history. This data is useful for gaining a better understanding of neonatal hyperbilirubinemia, including its causes, diagnosis, and management options. The majority of mothers (53.3%) were between the ages of 28 and 35, followed by a range of ages between 20 and 27 (38.3%). Only 8.4% of moms in this age group were between the ages of 36 and 43. Approximately 53.3% of the pregnancies were carried to full term, while roughly 25.2% were past term. There were 20 pregnancies that occurred before the expected time, which accounted for 21.5% of the total. Maternal educational attainment: 37.4% of the mothers had a diploma. Thus, the proportion of those with elementary education was 29%, while those with a bachelor's degree accounted for 19.6%. Within the sample, 11.2% of women had moms who did not get any formal education, while fewer than three percent had mothers with a master's degree. 51.4% of the women did not get anesthetic during delivery. Regional anesthesia was administered in 28% of the patients, while 3.7% received epidural anesthesia. 16.8% of the instances had deliveries performed while the patient was under general anesthesia. The most prevalent blood group among the moms was blood type O, accounting for 36.4% of the total. This was followed by blood group A at 28%, blood group B at 23.4%, and blood group AB at 12.1%. The majority of the moms, 90.7%, had a positive RH factor, whereas a small percentage, 9.3%, had a negative RH factor, as seen in Table 31.

Table 3.1: The frequency and percentage of several characteristics of women included in the research. These variables include maternal age, pregnancy terms, educational level, anesthesia kinds, blood group, and Rh factor.

Mother's Characteristics	N	Percentage
Maternal Age group (Years)		
36-43	9	8.4
20-27	41	38.3
28-35	57	53.3
Terms of pregnancy		
Full-Term: Pregnancy that has lasted between 37 and 42 weeks.	57	53.3
Post-Term: Pregnancy that has lasted beyond 42 weeks.	27	25.2
Pre-Term: Table 3-1: characteristics of mothers and probable lasted beyond 42 weeks.	23	21.5
Educational Level		
Uneducated	12	11.2
Primary	31	29
Diploma	40	37.4
Bachelor	21	19.6
Master	3	2.8
Types of Anesthesia		
None	55	51.4
Regional	30	28
Epidural	4	3.7
General	18	16.8
Mother BG		
O	39	36.4
A	30	28
B	25	23.4
AB	13	12.1
Mother-BGRh		
Positive	97	90.7
Negative	10	9.3

There was a nearly equal distribution between natural deliveries (52.3%) and cesarean sections (47.7%) as shown in Figure 3.1.

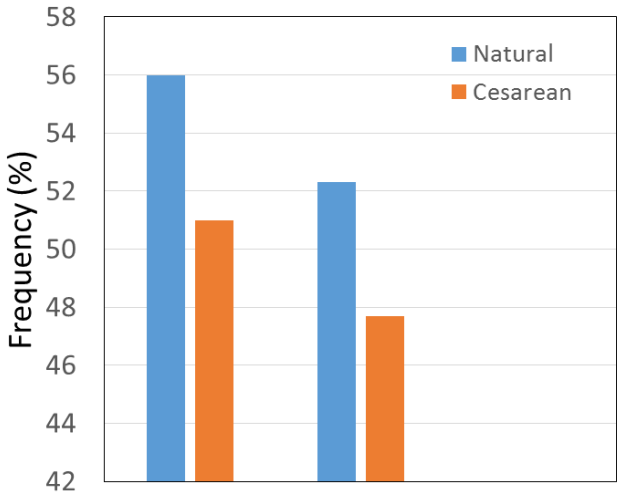

Figure 3.1. Shows the percentage of the delivery Methods.

Figure 3.1. Shows the percentage of the delivery Methods/ put below the figure. The majority of mothers (74.8%) had no family history of diabetes or hypertension. A small percentage had a family history of diabetes (6.5%), hypertension (14.0%), or both hypertension and diabetes (4.7%) as shown in Figure 3.2.

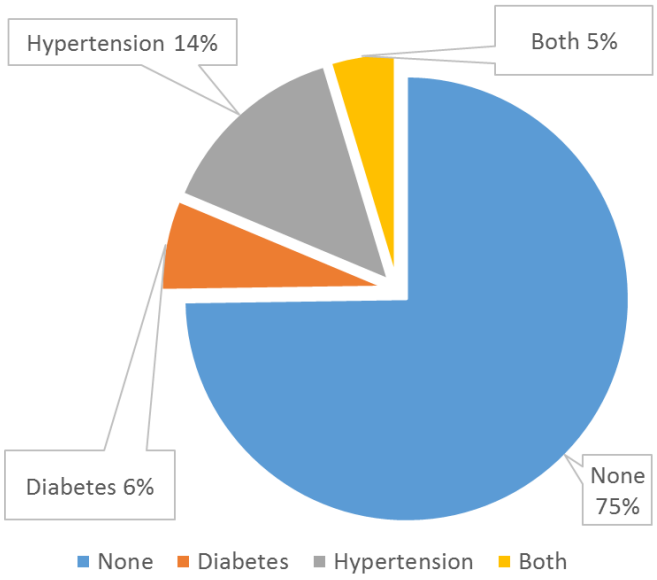

Figure 3.2. Indicates the percentage of the family history (Hypertension & Diabetes).

The prevalence of jaundice was: 74.8%, between 7-11 days postpartum, 9.3% between 2-6 days, and 15.9% between 12-16 days. This study illustrates that most neonates developed jaundice in the first 5 days following birth at 86.0%, while other neonates developed jaundice between 6 - 9 days at 14.0%. The distribution of newborn weight was mostly categorized as normal weight, 77.6% underweight by 15.9%, and extremely underweight by 6.5%. The most common blood type among neonates was group O: 34.6%. Other blood types are A: 32.7%, B: 23.4%, and AB: 9.3%. Of the babies, 89.7% had a positive Rh factor, whereas 10.3% had a negative Rh factor. From Table 3.2, it is observed that breastfeeding was the major method of feeding, which accounted for 50.5% of the cases, while both breast and formula feeding were almost equal at 49.5%. Table 2 shows the characteristics of the newborns are described,

including age, gender, with or without jaundice, weight, blood group, Rh factor, feeding mode, and TSB levels.

Table 3-2: Frequency and percentage of several characteristics of women

Newborn's Characteristics	Frequency	Percentage (%)
Newborn Age Days		
2-6	10	9.3
7-11	80	74.8
12-16	17	15.9
Age of Jaundice Days		
2-5	92	86.0
6-9	15	14.0
Weight of Neonate		
Severe Underweight	7	6.5
Underweight	17	15.9
Normal Weight	83	77.6
Birth-BG		
O	37	34.6
A	35	32.7
B	25	23.4
AB	10	9.3
Birth-BGRh		
Positive	96	89.7
Negative	11	10.3
Feeding Mode		
Breast Feeding	54	50.5
Both	53	49.5

The distribution of gender among newborns was almost equal, with 51.4% females and 48.6% males as shown in Figure 3.3.

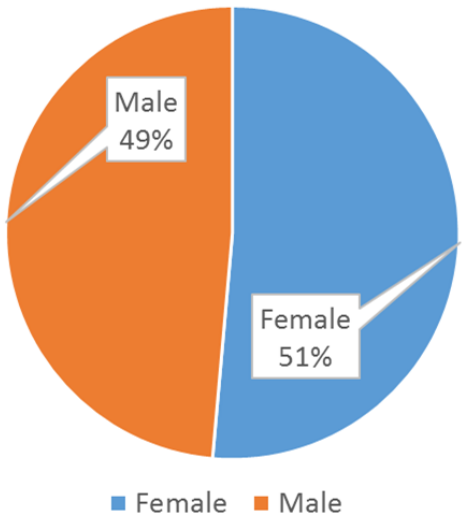

Figure 3.3: The distribution of gender among newborns.

In the study, most newborns (68.2%) exhibited total serum bilirubin (TSB) levels that indicated the presence of jaundice. On the other hand, 31.8% of the newborns had TSB levels within the normal range, as shown in Figure 3.4.

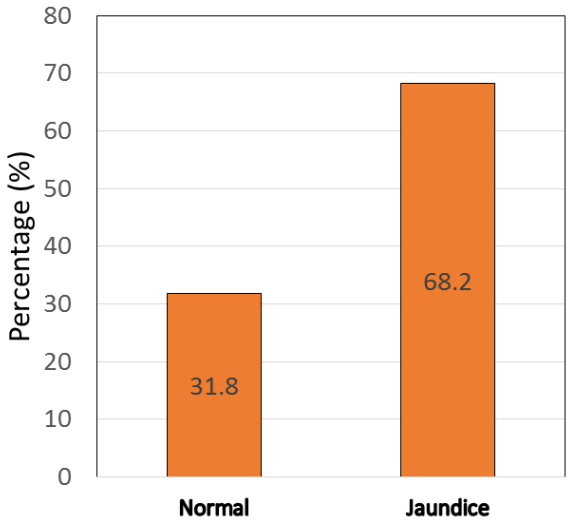

Figure 3.4. Reveals the percentage of Total Serum Bilirubin among Newborns.

In fact, such a study aimed at analyzing the correlation between TSB levels and various maternal and infant characteristics was conducted in the context of neonatal hyperbilirubinemia. The table attached herein served useful in providing data for an in-depth analysis of such correlations. From such a careful analysis, the research showed that no statistical significance correlation existed between the age of the mother and total serum bilirubin levels, as evidenced by the p value of 0.226. The results from this study show clearly that advanced maternal age does not have a noticeable effect on the incidence or prevalence of neonatal hyperbilirubinemia. In this regard, the study found from an extensive research that the different stages of pregnancy, such as full-term, post-term, and pre-term, are not correlated with statistically significant differences in TSB levels as the p-value was 0.222. From these results, it can be deduced that full-term, post-term, or pre-term pregnancy has no significant effect on the overall incidence of neonatal hyperbilirubinemia. The broad research carried out in this domain indicated that there was no statistical significance in the level of education among mothers and the levels of TSB, as the p-value was 0.623. This leads to the belief that the level of education attained by mothers does not seem to be a statistically significant determinant or factor that influences the incidence of newborn hyperbilirubinemia-a medical condition characterized by high levels of bilirubin in the blood of newborn babies. Secondly, the research also pointed out that there was no statistically significant association between the delivery technique, whether natural childbirth or through cesarean section, and the TSB levels, as the p-value was 0.137. These findings show that the specific mode of delivery used at birth does not appear to have an effect on either the occurrence or prevalence of hyperbilirubinemia among newborns. The study performed revealed a statistically significant association between the differing types of anesthesia used during the delivery process, including none, regional, epidural, and general anesthesia, and the bilirubin levels, as measured in terms of total serum bilirubin (TSB), derived from the newborns themselves, as evidenced by the derived p-value of 0.011 demonstrating the statistical significance of this association. Further study is needed to more clearly articulate the exact biological and physiological mechanisms underlying this identified association between type of anesthesia and levels of bilirubin in newborns. This study did not find any significant correlations; that is, no significant or meaningful relationships were established between the mother's blood group categories O, A, B, and AB, along with the presence of the Rh factor positive or negative, and the levels of TSB in the newborns. The p-values derived from the analysis were 0.76 for the mother's blood group and 0.893 for the combination of mother's blood group and Rh factor, indicating quite explicitly that these particular variables have no substantial or noteworthy influence on causing hyperbilirubinemia among neonates. No statistically significant correlation was found or established between the different classes of family history, which are nil, diabetes mellitus, hypertension, and the category of both hypertension & diabetes, and the levels of total serum bilirubin recorded in the study ($p = 0.545$). These findings strongly suggest that the history or presence of certain medical conditions within the family does not contribute or play a significant or major role in determining the incidence of neonatal hyperbilirubinemia. The multivariate analysis conducted in the current study indicated that there was a statistically significant relationship between neonatal age in three distinct categories of age-2 to 6 days, 7 to 11 days, and 12 to 16 days - and TSB levels at $p=0.040$, respectively. This key finding now points out that infant age is a crucial determinant that significantly affects the timing of development of neonatal hyperbilirubinemia, and thus, an infant's age should also be one of the parameters considered in determining the risk for the development of neonatal hyperbilirubinemia. A wide investigation conducted on the relation between

gender at birth, whether female or male, and the levels of TSB demonstrated no significant statistical relevance, as reflected by the p-value of 0.660. Thus, it seems that gender at birth is not one of the major determining factors that could affect the incidence of hyperbilirubinemia among newborns. Although the hypothesis presented within this investigation failed to reach statistical significance, as reflected by the p-value of 0.085, the study still recommended a possible relationship that could occur between the age of the beginning of jaundice between the age brackets of 2-5 days and 6-9 days, respectively, and the related levels of TSB reflected. Further study is needed to understand the finding fully and its wider implications. As confirmed through this research, with a p = 0.435, no statistically significant relationship or correlation exists between the infant weights grouped into severe underweight, underweight, normal weight, and overweight categories and the levels of TSB present. Such findings have proven that the weight of the infant during delivery has no significant bearing or impact on the incidence or severity of neonatal hyperbilirubinemia, or high levels of bilirubin in newborns. The investigation conducted into the matter revealed that no statistically significant correlations could be ascertained between the various birth blood groups, which include O, A, B, and AB, nor between the Rh factor, whether positive or negative, and the levels of total serum butyrate (TSB). Furthermore, the comprehensive statistical analysis yielded a p-value of 0.077 for birth blood glucose and a p-value of 0.921 for birth-blood glucose, and thus these particular variables exert very little impact upon the occurrence of newborn hyperbilirubinemia. A statistically significant correlation was found and established between the different modes of feeding, such as exclusive breastfeeding and the combination of breastfeeding and other feeding modalities, and the levels of total serum bilirubin measured in infants, p = 0.001. From the information and data provided in Table 3.3, it is quite implicit that the mode of infant feeding plays a decisive role in determining the incidence and occurrence of neonatal hyperbilirubinemia. Furthermore, Table 3.3 also shows the association existing among total serum bilirubin level related to both maternal and newborn characteristics.

Table 3.3. The association among total serum bilirubin and mother's characteristic and newborn characteristics.

Mother and Newborn Characteristics	TSB Levels		P-Value
	Normal	Jaundice	
Maternal Age (Years)			
20-27	11 (23.9%)	35 (76.1%)	0.226
28-35	22 (35.5%)	40 (64.5%)	
36-43	4 (57.1%)	3 (42.9%)	
Different Terms of Pregnancy			
Full-Term	24 (36.4%)	42 (63.6%)	0.222
Post-Term	5 (15.2%)	28 (84.8%)	
Pre-Term	8 (32.0%)	17 (68.0%)	
Educational Level			
Uneducated	3 (15.8%)	16 (84.2%)	0.623
Primary	9 (29.0%)	22 (71.0%)	
Diploma	13 (32.5%)	27 (67.5%)	
Bachelor	7 (30.4%)	16 (69.6%)	
Master	1 (25.0%)	3 (75.0%)	
Delivery Method			
Natural	16 (27.1%)	43 (72.9%)	0.137
C/S	20 (34.5%)	38 (65.5%)	
Types of Anesthesia			
None	13 (23.2%)	43 (76.8%)	0.011
Regional	14 (42.4%)	19 (57.6%)	

Epidural	0 (0%)	6 (100%)	
General	3 (21.4%)	11 (78.6%)	
Mother BG			
O	16 (43.2%)	21 (56.8%)	0.76
A	9 (34.6%)	17 (65.4%)	
B	2 (10.0%)	18 (90.0%)	
AB	2 (25.0%)	6 (75.0%)	
Mother-BG Rh			
Positive	26 (31.0%)	58 (69.0%)	0.893
Negative	3 (30.0%)	7 (70.0%)	
Family History			
None	23 (34.3%)	44 (65.7%)	0.545
Diabetes Mellitus	1 (14.3%)	6 (85.7%)	
Hypertension	5 (33.3%)	10 (66.7%)	
Hypertension & Diabetes	0 (0%)	2 (100%)	
Newborn Age (Days)			
2-6	1 (10.0%)	9 (90.0%)	0.04
7-11	20 (29.9%)	47 (70.1%)	
12-16	8 (57.1%)	6 (42.9%)	
Gender of Birth			
Female	14 (29.8%)	33 (70.2%)	0.66
Male	15 (34.1%)	29 (65.9%)	
Age of Jaundice (Days)			
2-5	23 (28.7%)	57 (71.3%)	0.085
6-9	6 (54.5%)	5 (45.5%)	
Weight Neonate			
Severe Underweight	1 (20.0%)	4 (80.0%)	0.435
Underweight	3 (20.0%)	12 (80.0%)	
Normal Weight	25 (35.2%)	46 (64.8%)	
Birth-BG			
O	14 (43.8%)	18 (56.3%)	0.077
A	11 (35.5%)	20 (64.5%)	
B	2 (10.0%)	18 (90.0%)	
AB	2 (25.0%)	6 (75.0%)	
Birth-BG Rh			
Positive	26 (31.7%)	56 (68.3%)	0.921
Negative	3 (33.3%)	6 (66.7%)	
Feeding Mode			
Breast Feeding	7 (15.2%)	39 (84.8%)	0.001
Both	22 (48.9%)	23 (51.1%)	

4. Discussion

The findings indicate that neonatal hyperbilirubinemia is an etiologically complex and multifactorial condition due to various variables related to the mother and the newborn. The first variable was maternal age with reference to the incidence of hyperbilirubinemia. The findings therefore support those by Watchko, J. F. (2016)[6], which state that maternal age may be one of the contributing factors, although the exact mechanism(s) have not been sufficiently clarified. In our study, mothers aged 28-35 years had a slightly lower incidence of infants with elevated bilirubin levels compared to younger and older mothers. While this trend is not statistically significant, it is an interesting pattern that deserves more detailed scrutiny, particularly in terms of maternal health and prenatal care. The other important variable was the mode of delivery, which did not show any significant association with hyperbilirubinemia in the context of our study. This result is in good agreement with the findings from the study by Kim, and Park (2022) [5], where it was deduced that cesarean delivery is not a strong risk factor for hyperbilirubinemia, which is compared to the previous beliefs on the subject. However, in this present study, the anesthesia type used in delivery was found to be associated with high levels of bilirubin, especially for those cases involving general anesthesia as a mode of pain management. This agrees with and supports the work of previous studies, such as that of Maisels and McDonagh in 2008 [1], which advanced the theory that anesthesia may affect the neonates' liver function. However, the exact physiological processes by which this may occur still require further study and research for complete elucidation. The result showed identified various ways in which feeding practices contribute to neonatal jaundice, which may occur in the newborn. It was noted that the exclusively breastfed infant, without supplementation, was more likely to develop hyperbilirubinemia -an elevation of bilirubin in the blood- than those who were both breastfed and received formula feeding as part of their diet. This finding is supported by the body of literature, which includes those studies that Scrafford et al. conducted in 2013 and Chen *et al*, in2015 [8,9]. These studies reveal that despite the fact that breastfeeding has numerous benefits, poor feeding practices predispose an infant to a condition of jaundice. In relation, it is important to establish that early initiation of breastfeeding and frequent feeding schedules are important in preventing newborn infants from experiencing dehydration, while this practice also enhances the passage of bilirubin through the infants' stool process [7]. Basically, it requires a careful balancing to ensure adequate calorie intake while still enjoying most of the benefits of exclusive breastfeeding. This introduces another critical consideration in the effective management of neonatal jaundice. Surprisingly, there was no significant relation in the study between neonatal hyperbilirubinemia and maternal educational level or even maternal blood group and the Rh factor. This contradicts the findings of some earlier studies. Blood group incompatibility, for example, was identified by Scrafford, *et, al.* [8] as one of the notable risk factors that could result in severe jaundice among newborn babies. However, no such association was observed in this study, it could either be the small sample size or the dissimilarity in the population's genetic and socioeconomic characteristics mentioned by AAPSH (2022) [2]. Larger studies are required to look into these variables. The research clearly determined gestational age as a critical determinant of health outcomes among infants, specifically observing that preterm infants have a decidedly greater incidence of hyperbilirubinemia. Such observations are in strong agreement with earlier findings by Dennery et al. back in 2001 [10], indicating similar trends. It needs to be emphasized that, typically, preterm infants have relatively immature liver function and hence are inherently more susceptible to higher levels of bilirubin. This being the case, the dire need for specialized monitoring and careful attention with regard to their handling is heightened, due to the crucial necessity of averting serious complications such as kernicterus, as by Merritt and Palmer 2017 [3]. Finally, our wide research clearly established a statistical significance between the age of onset of jaundice and the levels of TSB among the affected persons. To be precise, infants who developed the onset of jaundice within the first couple of days of their life were found to be significantly at risk of recording high levels of total serum bilirubin, which is an indication of an urgent call for early screening, coupled with appropriate measures aimed at taking remedial actions on time. This assertion rings well with the works of Maisels and McDonagh, 2008 [1], that stipulate early detection and proper management of hyperbilirubinemia as critical in averting potential damages that may occur. It is to be therefore underscored at this point that our research has underlined the neonatal hyperbilirubinemia, influenced by a range of factors in practice, such as feeding practices, use of anesthesia, and gestational age of the neonate, all playing crucial and significant roles in this condition. Whereas our findings indeed have agreed with much of the literature on this subject, they also shed light on areas where further

research could be warranted. In particular, this relates to the regional variation that may still occur both with regard to risk factors for neonatal hyperbilirubinemia and subsequent outcomes for the affected infants.

5. Conclusions

Neonatal hyperbilirubinemia is a multidimensional factor, and this study established a there is association between neonatal hyperbilirubinemia and the mode of feeding and general anesthesia use during delivery in Erbil City. However, other factors like maternal age, education level, blood group, and Rh type showed no significant associations in this study. Nevertheless, early detection and management are always crucial, especially in high-risk groups like preterm babies.

6. Recommendations

1. Early Screening: Standardized screening for jaundice needs to be implemented, especially in preterm babies.
2. Feeding advice: Advise on appropriate breastfeeding and the dangers of feeding.
3. Anesthesia advice: Discuss anesthesia in problematic pregnancies
4. Public awareness: The risk factors for jaundice must be better disseminated to raise awareness and allow for early detection.
5. Future research: Further studies with larger series are needed to look into other risk factors.

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