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Comparison between Breast Feeding and Formula Feeding in Neonates with Idiopathic Hyperbilirubinemia

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ABSTRACT

Background: Breast-feeding had been linked to an increase in newborn jaundice during the first postnatal days. Unconjugated hyperbilirubinemia prolongation in breastfed infants is a typical and frequently occurrence of a physiological jaundice extension. Breast feeding and jaundice are strongly linked in healthy newborn newborns.

Aim of the work: This study aimed to improve outcome of neonates with idiopathic hyperbilirubinemia via doing comparison between breast-fed and artificial-fed infants with idiopathic hyperbilirubinemia.

Patients and methods: Our study included 150 neonates diagnosed with hyperbilirubinemia attending to Suez Canal University Hospital's Neonatal Intensive Care Unit. They were divided into group one included 50 neonates who received 75% of their feed as breast milk, group two included 50 neonates who received 75% of their feed as formula feeding (FF) and group three include 50 neonates who received both formula and breast feeding. Each neonate was subjected to complete history taking and examination.

Results: The mean serum bilirubin was higher among breast-fed infants than formula-fed infants at admission and after 2 days with statistically significant difference. Feeding frequency showed statistically significant weak negative correlation with bilirubin among formula-fed infants. Statistically significant negative correlation between bilirubin change after 2 days of admission in formula-fed infants and weight with bilirubin change among formula-fed infants.
Conclusion: Breastfeeding jaundice should be considered one of the most common causes of pathological jaundice, making lactational counseling throughout the antenatal and postnatal period to be an essential component of pathological jaundice care and prevention.

Keywords: Breastfeeding, Idiopathic hyperbilirubinemia, Infants, Jaundice.

INTRODUCTION

Jaundice is a prevalent condition in term and preterm neonates who are affected during the early neonatal period, with up to 60% of term and 80% of preterm infants. Approximately 60% of all term neonates exhibit clinical icter within 7 days of delivery, though less have pathogenic etiology **(1).** Physiologic jaundice is defined by total serum bilirubin levels of up to 6 mg/dL that decrease over the first week, whereas pathologic jaundice is defined by developing jaundice within 24 hours of birth, total serum bilirubin levels more than 17 mg/dl, serum conjugated bilirubin levels of more greater than 2 mg/dL, or greater than 20% of total serum bilirubin concentration **(2).**

Jaundice in breastfed infants often occurs between 24 and 72 hours after birth, peaks between 5 and 15 days later, and goes away by the third week. These infants have been noted to have higher bilirubin levels. Mild jaundice in breastfed neonates may appear 10–14 days after delivery or may return while the infant is still nursing **(3).** The incidence of hyperbilirubinemia was significantly reduced in neonates who were nursed 8 times per day than those who were breastfed 8 times per day, and more frequent breastfeeding is linked to lower serum bilirubin levels **(4).**

Newborns who are breastfed have greater bilirubin levels than newborns who had fed formula, frequently displaying bilirubin levels >12 mg/dL **(5).** An expected and frequent extension of physiological jaundice in healthy babies is prolonged unconjugated hyperbilirubinemia in breastfeeding infants. In healthy newborn newborns, there is a direct correlation between breastfeeding and jaundice **(6).** Thus, this study aimed to improve the outcome of neonates with idiopathic hyperbilirubinemia via doing comparison between breast-fed and artificial-fed infants with idiopathic hyperbilirubinemia and improving the practice of breast feeding of mothers.

Methods:

Our observational cross-sectional study was carried out in the Neonatal Intensive Care Unit in Suez Canal University Hospital through the period from December 2019 to December 2020 on neonates suffering from neonatal jaundice (indirect idiopathic hyperbilirubinemia).

Inclusion criteria: Neonates diagnosed with hyperbilirubinemia attending to Neonatal Intensive Care Unit in Suez Canal University Hospital and fulfilling the criteria of idiopathic hyperbilirubinemia.

Exclusion criteria: Newborns who had hemolysis, abnormal hemogram, abnormal reticulocyte count, complications such as sepsis or with direct hyperbilirubinemia and infection.

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We enrolled 3 groups of neonates with idiopathic jaundice, 150 infants were split into three groups: breastfed, formula-fed, and mixed fed infants (50 in each group) to detect frequency of idiopathic jaundice in each group and improvement in bilirubin level after days of follow up.

Every case had a comprehensive history taking, detailed physical examination, laboratory testing to determine serum bilirubin levels, C-reactive protein, complete blood counts (direct & indirect) (at admission then daily till discharge) and reticulocytic count. Measurement of serum bilirubin before nursing and after 2 days of phototherapy was done to detect the degree of decrease of bilirubin level.

Ethical approval:

An informed written consent obtained from parents of infants participating in the study. The study received approval from the Suez Canal University Hospital's Neonatal Intensive Care Unit's Ethical Council (n= RPNC-14). The Helsinki Declaration was followed throughout the study's conduct.

Statistics/data analysis

The computer was fed data, and IBM SPSS software package version 20.0 was used for analysis. Numbers and percentages were used to describe the qualitative data. After determining if the data were normal using the Kolmogorov-Smirnov test, the mean and standard deviation were used to characterize the quantitative data. At the 5% level, the results' significance was assessed. For the qualitative data for the two groups, the Monte Carlo test or Chi-Square test was employed.

The paired t test was used to evaluate pre- and post-changes for the same group for parametric variables, whereas the independent samples t-test was used to compare quantitative data between two groups if the data were normally distributed in both groups. The strength and direction of a linear link between two normally distributed continuous variables were ascertained using the Pearson product-moment correlation. For any of the used tests, results were considered statistically significant if p value ≤ 0.05.

RESULTS

Table (1) showed that the present study was carried out on 150 patients with their mean age at presentation 6.36 days, 52.7% were females. Maternal ages ranged from 17 to 37 years, 83.3% of them delivered by Cesarean section , 45.3% were ranked second, 76% are working mothers and 54.7% are low socio-economic status.

Table (1): Demographic characteristics of the studied neonates with idiopathic jaundice

Variables		n=150	%
Age at presentation/days	Mean ± SD	6.36±1.51	
	Min-Max	3.0-9.0	
Sex	Male	71	47.3
	Female	79	52.7
Maternal age /years	Mean ± SD	26.38±3.96	
	Min-Max	17.0-37.0	
Mode of delivery	Vaginal	25	16.7
	CS	125	83.3
order in family	1st	51	34.0
	2nd	68	45.3
	3rd	26	17.3
	4th	5	3.3
Occupation	Housewife	36	24.0
	Working mother	114	76.0
Socio economic status	Low	82	54.7
	High	68	45.3

Table (2) illustrated that 60.0% of the studied cases were full term (gestational age 38 weeks) and mean number of feedings was 8.67 ± 1.04 with maximum number 12 times. Mean weight of the studied infants was 3091.1 gm and 76.7% had diaper change frequency from four to six times. Mean weight gain was 61.39 ± 14.62 gm.

Table (2): feeding and clinical characters among neonates with idiopathic jaundice

		n=150	%
Gestational age /weeks	FT	90	60.0
	NT	60	40.0
Number of feedings	Mean ± SD	8.67 ± 1.04	
	Min-Max	(5.0-12.0)	
Type of feeding	Exclusive breast feeding	50	33.3
	Formula feeding	50	33.3
	mixed	50	33.3
Weight /gm	Mean ± SD	3109.3 ± 305.04	
	Min-max	2340-3850	
Diaper change frequency	<4	35	23.3
	4-6	115	76.7
Weight gain /gm	Mean ± SD	61.39 ± 14.62	
	Min-max	(35-88)	

NT: Near term **FT:** Full term

Table (3) demonstrated that there was no statistically significant difference between breast-fed, formula-fed & mixed-fed infants regarding age at presentation, mode of delivery and order in family. All the mothers of formula-fed infants are working mothers, and 82% of the mothers of infants with mixed feeding are working mothers.

Table (3): Comparison of socio-demographic characteristics between breast fed, formula fed and mixed fed neonates with idiopathic jaundice.

		Breast feeding n=50	Mixed n=50	Formula feeding n=50	Test of sig
Age at presentation/days	**Mean ± SD**	**6.26±1.64**	**6.10±1.62**	**6.72±1.18**	**F=2.32 P=0.102**
Mode of delivery	**Vaginal**	**6(12.0)**	**13(26.0)**	**6(12.0)**	**χ^2=4.70 p=0.1**
	CS	**44(88.0)**	**37(74.0)**	**44(88.0)**	
order in family	**1st**	**20(40.0)**	**16(32.0)**	**15(30.0)**	**MC P=0.30**
	2nd	**21(42.0)**	**23(46.0)**	**24(48.0)**	
	3rd	**8(16.0)**	**7(14.0)**	**11(22.0)**	
	4th	**1(2.0)**	**4(8.0)**	**0(0.0)**	
Occupation	**Housewife**	**27(54.0)**	**9(18.0)**	**0(0.0)**	**MC P<0.001***
	Working mother	**23(46.0)**	**41(82.0)**	**50(100.0)**	

MC: Monte Carlo test χ^2= Chi-Square test **F:** One Way ANOVA test ***statistically significant (if p<0.05)**

Table (4) showed that there was no statistically significant difference between studied groups regarding their weight, while weight gain illustrated statistically significant higher mean among mixed-fed followed by formula-fed and least was for breast-fed infants (72.82 ± 6.71, 63.60 ± 15.36 & 47.76 ± 6.43 respectively). Bilirubin at admission was significantly higher in breast-fed group followed by mixed feeding group & then formula feeding. Bilirubin after 2 days still significantly higher in breast-fed followed by formula-fed and then mixed feeding group. Percent of change of serum bilirubin showed higher percent among mixed-fed followed by formula-fed and least for breast-fed (41.54%, 39.24% & 33.62% respectively) which was statistically significant.

Table (4): Comparison of clinical and laboratory characters between breast-fed, formula-fed and mixed-fed infants

	Breast feeding n=50	Mixed n=50	Formula feeding n=50	Test of sig
Weight /gm Mean ±SD at birth	**3083.8±278.46**	**3059.9±364.52**	**3184.2±252.33**	**F=2.38 P=0.096**
Weight gain /gm Mean ± SD (Range)	**47.76±6.43**	**72.82±6.71**	**63.60±15.36**	**F=74.81 P<0.001***
Bilirubin at admission (mg/dl)	**17.16±1.14**	**16.20±1.21**	**16.36±1.09**	**F=10.02 P<0.001***
Bilirubin after 2 days (mg/dl)	**11.39±1.15**	**9.47±2.52**	**9.94±1.22**	**F=16.45 P<0.001***
test of sig	**t=30.42 p<0.001***	**t=25.35 p<0.001***	**t=34.03 p<0.001***	
Bilirubin change (mg/dl)	**5.77±1.34**	**6.73±1.88**	**6.42±1.33**	**F=5.14 P=0.007***
% of change of bilirubin at admission & after 2 days	**33.62%**	**41.54%**	**39.24%**	
Bilirubin value after phototherapy	**13.054±2.65**	**9.58±1.58**	**11.85±1.03**	**F=9.82 P=0.001***

F: One Way ANOVA test **t:** Paired t test ***statistically significant (if p<0.05) sig= significance

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Table (5) demonstrated that there was no statistically significant correlation between serum bilirubin, age at presentation and feeding frequency among breast-fed infants or gestational age ($p > 0.05$).

Table (5): correlation between bilirubin level and demographic characteristics and laboratory results among breastfed infants with idiopathic jaundice.

		Bilirubin at admission (mg/dl)	Bilirubin after days
Age at presentation/ days		0.08	-0.22
	p	0.07	0.123
Gestational age /weeks		-0.121	0.007
	p	0.401	0.96
Feeding frequency		-0.122	-0.02
	p	0.40	0.896

*Statistically significant (If $p<0.05$)

Table (6) illustrated that there was no statistically significant correlation found between serum bilirubin and age at presentation & gestational age. Feeding frequency showed statistically significant weak negative correlation with serum bilirubin among mixed-fed infants ($r=-0.283$, $p=0.04$).

Table (6): correlation between bilirubin level and demographic characteristics and laboratory results among mixed fed infants with idiopathic jaundice

		Bilirubin at admission (mg/dl)	Bilirubin after 2 days
Age at presentation/ days		0.074	-0.051
	p	0.610	0.725
Gestational age /weeks		-0.122	0.028
	p	0.400	0.847
Feeding frequency		-0.283	-0.118
	p	0.04*	0.416

*statistically significant (If $p<0.05$)

Table (7) demonstrated that there was a statistically significant weak positive correlation between serum bilirubin at admission and age at presentation ($p<0.05$) among cases with formula-fed.

Table (7): correlation between bilirubin level and demographic characteristics and laboratory results among formula-fed infants with idiopathic jaundice

		Bilirubin at admission (mg/dl)	Bilirubin after 2 days
Age at presentation/ days		0.313	0.179
	p	0.027*	0.213
Gestational age /weeks		0.13	-0.215
	p	0.367	0.133
Feeding frequency		0.099	0.119
	p	0.495	0.412

*statistically significant (If $p<0.05$).

Table (8) illustrated that there was weight gain in gram had statistically significant moderate positive correlation with bilirubin change among mixed-fed infants ($r=0.551$, $p<0.001$), respectively.

Table (8): correlation between bilirubin level change and demographic characteristics among mixed fed infants with idiopathic jaundice.

		Bilirubin change after 2 days of admission (mg/dl) in mixed fed
Age at presentation/ days		0.095
	p	0.513
Weight		-0.05
	p	0.73
Weight gain/gm		0.551
	p	0.001*
Frequency of feeding		0.204
	P	0.253

*statistically significant (If $p<0.05$)

Table (9) demonstrated that statistically significant weak negative correlation was detected for bilirubin change after 2 days of admission and HB (gm/dl).

Table (9): correlation between bilirubin level change and demographic characteristics and laboratory results among breast fed infants with idiopathic jaundice.

		Bilirubin change after 2 days of admission (mg/dl) in breast fed
Maternal age/ years		.218
	p	.128
Order in family		.046
	p	.753
Frequency of feeding		0.231
	p	0.09
Weight		-.133
	p	.358
Weight gain/gm		-.261
	p	.067

*statistically significant (If $p<0.05$)

Table (10) showed that there was no statistically significant correlation between bilirubin after 2 days of admission and age of presentation, frequency of feeding, weight and weight gain.

Table (10): correlation between bilirubin level change and demographic characteristics and laboratory results among formula-fed infants with idiopathic jaundice.

		Bilirubin change after 2 days of admission (mg/dl) in formula fed
Age at presentation/ days		0.068
	p	0.638
Frequency of feeding		0.124
	p	0.125
Weight		-0.271
	p	0.057
Weight gain/gm		0.214
	p	0.136

*statistically significant (If p<0.05)

DISCUSSION

The present study aimed to shorten the period of hyperbilirubinemia in breast-fed infants. Our study included 150 neonates diagnosed with hyperbilirubinemia who attended to the Pediatric Department of Suez Canal University Hospital. As regards mode of delivery, we found that 83.1% of the included neonates were delivered by CS. In accordance with our findings, **Temook and his colleagues** [(7)] compared to babies delivered normally, Cesarean section babies were more likely to experience jaundice**.** However, it's crucial to remember that some prenatal issues that result in jaundice are signs that a Cesarean section should be performed; as a result, it's likely that jaundice is not caused by the Cesarean section alone [(8)]**.** Mode of delivery also influences the severity of jaundice. Risk factors also include unnecessary delivery interventions like cesarean sections and the overuse of oxytocin during labor. Also, **Chang *et al.*** [(9)] reported that bilirubin level was higher among naturally delivered neonates, compared to those born by Cesarean section**.** However, our results disagree with the finding of **Boskabadi *et al.*** [(10)] who reported no connection between the mode of delivery and the frequency of jaundice. **Abdel-Aziz *et al.*** [(11)] revealed no connection ($p > 0.05$) between the infant's delivery method and the development of severe hyperbilirubinemia.

In the present study, 76.2% of the included neonates have diaper change frequency from four to six times. **Buiter *et al.*** [(12)] found that there was no correlation found between transcutaneous bilirubin levels and either cumulative stool output or newborn fecal fat. The intensity of newborn jaundice has been linked to a number of variables, including parity, weight loss, delivery method, gestational age, and mother characteristics including age and smoking. But it's important to understand that the numerous researches on these variables are inconclusive and occasionally even contradicting excretion [(12)]**.**

In the present study, comparison between formula-fed infants and breast-fed infants regarding weight gain illustrated statistically significant higher mean among formula-fed infants than among breast-fed (72.14 & 47.08, respectively). **El Sakka *et al.*** [(13)] found that with total serum bilirubin >12 mg/dL, the percentage of weight loss in the breast-fed group was higher (4.9%) compared to the formula-fed (1.9%) group. Additionally, there was a strong, positive, highly significant correlation between the level of bilirubin and the weight loss at the beginning of phototherapy. In a study done by **Huang *et al.*** [(14)], they claimed that weight loss was inversely correlated with gestational age and independently and substantially linked to exclusive breastfeeding. Hyperbilirubinemia and fasting have a well-established link that has been documented in both human and animal models. Also, **Hintz *et al.*** [(15)] validated the previously established links between weight loss and hyperbilirubinemia. Oral calorie intake was found to be inversely correlated with serum bilirubin levels, especially in neonates weighing less than 2000 g.

On assessment of serum bilirubin 2 days after admission, there was negative correlation between serum bilirubin and number of feedings that was significant negative correlation in formula-fed infants and non-significant negative correlation in breast-fed infants. Serum bilirubin levels rose as a result of the meconium taking longer to drain, according to **Gartner** [(6)]**.**

Supplementing with fluids might help treat severe hyperbilirubinemia. This is justified by indirect evidence that a significant number of infants with "idiopathic" hyperbilirubinemia have subclinical dehydration. Most newborns with severe hyperbilirubinemia receive just breast milk [(16)]. Dehydration can be brought on by consuming insufficient breast milk, breast milk with a high salt content, particularly in primiparous women, and inadequate sucking by a low birth weight infant. [(17)]**.**

Among the blood count variables reported to be risk factors in several investigations for the development of jaundice in neonates, the mean of hemoglobin, hematocrit, platelet count, and white blood cells was found to be significantly linked with hyperbilirubinemia [(18)]**.**

However, in the present study we found no correlation between serum bilirubin and hemoglobin, hematocrit and red blood corpuscles. Our findings concur with those of an earlier investigation, which found that the FF group responded better to phototherapy [(13)]**.** It was unclear why the breastfeeding group's response to phototherapy took longer than expected, but it appeared that pregnanediol and free fatty acids in breast milk inhibit the hepatic uridine diphosphoglucuronate and glucuronosyl transferase enzyme. Additionally, because large amounts of B-glucuronidase enzyme, which is also found in breast milk, reabsorb unconjugated bilirubin from the intestine at a higher rate, this enzyme cleaves the ester linkage of bilirubin glucuronide, making unconjugated bilirubin accessible for intestinal reabsorption [(15)]**.**

CONCLUSION AND RECOMMENDATIONS

We concluded that idiopathic hyperbilirubinemia is common in neonates. Increase caloric intake by mixing breast feeding with artificial formula in certain cases will help in reducing neonatal jaundice beside regular treatment with phototherapy. The best way to prevent idiopathic hyperbilirubinemia is to inform parents about these risk factors, encourage breastfeeding more frequently, abstain from early discharge, and avoid feeding with water or sugar water. Large-scale research is also required, both by the control group and for future research.

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