Early Neonatal Indirect Hyperbilirubinemia in Full Term Newborns and Types of Feeding

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ABSTRACT:

BACKGROUND:

Neonatal jaundice remains the most common and, perhaps, the most controversial problem in full-term newborns during the immediate postnatal period.

OBJECTIVE:

To evaluate the relationship between types of feeding and neonatal indirect hyperbilirubinemia in full term neonates in the first week of life.

METHODS:

In the period from the first of January 2008 to the first of August 2008, populations of 140 full term newborns admitted to the neonatal care unit in Children Welfare teaching Hospital in Medical City-Baghdad were studied. A serum bilirubin level >12.9 mg/dL was considered significant.

RESULTS:

Of the population studied, most newborns received supplementary feeding 73 (52.1%), followed by breast feeding 50(35.7%), while only 10(7.1%) and 7(5.0%) were on mixed and formula feeding, respectively. Ninety (64.3%) of the jaundiced neonates were males and 50(35.7%) were females with a male to female ratio of (1.8:1).

CONCLUSION:

This study revealed that, no significant association could be found between different types of feeding and indirect hyperbilirubinemia in full term newborns. Besides, giving water, dextrose water or formula with breastfeeding will adversely affect the volume of milk transferred to the baby and the volume of milk produced by the mother.

KEYWORDS: fullterm, neonate, indirect hyperbilirubinemia, feeding, jaundice

INTRODUCTION:

Hyperbilirubinemia is a common and, in most cases, benign problem in neonates. Jaundice is observed during the 1st wk of life in approximately 60% of term infants and 80% of preterm infants[1].

Neonatal jaundice remains the most common and, perhaps, the most controversial problem in full-term infants during the immediate postnatal period. There is an important debate on the role of breast feeding versus formula feeding in determining the number of infants with significant hyperbilirubinemia as well as influencing the peak serum bilirubin concentration in the first days of life[2,8].

Breastfeeding is the best choice for infant nutrition[6,7] however, breastfed infants have higher serum bilirubin concentrations than formula-fed infants [8], and 98% of the infants in a US kernicterus registry were breastfed [9].

Glucuronidase is a factor in neonatal jaundice, because it potentiates the enterohepatic circulation of bilirubin by deconjugating intestinal bilirubin conjugates, producing bilirubin that is better absorbed by the intestine [7]. After birth, the enterohepatic circulation of bilirubin delays bilirubin clearance [10].

Breast milk is rich in glucuronidase[11], whereas routine infant formula has negligible glucuronidase, and infants consuming such formula have less jaundice than breastfed infants[12]. Casein hydrolysate formula inhibits glucuronidase, and infants consuming such formula have less jaundice than infants receiving routine formula [12]. The major glucuronidase inhibitor in casein hydrolysate is l-aspartic acid [13].

Neonatal jaundice is related to breastfeeding in three primary clinical situations [14]:

1.Exclusively breastfed healthy term newborns during the first postnatal week.

2.Newborns that receive inadequate breastfeeding and have high concentrations of indirect bilirubin during the first postnatal week ("breast- nonfeeding" jaundice).

3.Breastfed infants who experience prolonged unconjugated hyperbilirubinemia (breast milk jaundice).

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Thus, initiation of breastfeeding in the first hour, followed by at least 10 to 12 breastfeeds per day for the first week or two without any water or other food supplementation, and using good positioning that assures effective milk transfer to the infant will minimize weight loss to less than 7% and maintain serum bilirubin levels well under those that would cause concern about risk for kernicterus [15,16].

Although phototherapy remained highly effective in controlling the hyperbilirubinemia, there is significantly less efficacy for breast-fed infants compared with the formula-fed and mixed-fed infants[17].

Aims: This study aimed to evaluate the relationship between the types of feeding, neonatal indirect hyperbilirubinemia in full term neonates in the first week of life, and the response to phototherapy.

PATIENTS AND METHODS:

In the period from the first of January 2008 to the first of August 2008, one hundred forty (140) full term newborns admitted to the neonatal care units in Children Welfare Teaching Hospital in Medical City-Baghdad, were studied.

Newborns presented with severe asphyxia, infections, abnormal direct serum bilirubin values and congenital malformations were excluded from the study. All newborns were in a continuous rooming-in setting (newborns were in their cots near their mothers' beds).

A full history was taken from their mothers including the sex, age at admission, onset of jaundice, mode of delivery, birth weight and type of feeding. Family history of neonatal jaundice, phototherapy, exchange blood transfusion and kernicterus were included in data collection. Breastfeeding refers to newborns who were exclusively breastfed with no supplementation of water or formula at any time. Supplementary feeding refers to newborns who were breastfed or formula fed and received additional supplements of water or glucose water. Formula feeding refers to newborns who were exclusively bottle- fed. Mixed feeding refers to newborns who were breastfed and formula fed at the same time.

For all newborns with hyperbilirubinemia, the important investigations included determination of total serum bilirubin concentration at admission (with direct and indirect bilirubin concentration), PCV,

blood group typing and Rh of the mother and the newborn, reticulocyte count, and G6PD activity assay were done.

Total bilirubin level for newborns with jaundice was measured by direct spectrophotometer of the serum in a microhematocrit tube. A bilirubin level of >12.9 mg/dL (221 µmol/L) was considered significant.

Serum bilirubin levels were monitored in newborns with jaundice twice to three times daily in subsequent days until a steady decrease was observed. The variables evaluated in this study were the following: Type of feeding (breastfeeding, formula feeding, mixed feeding and supplementary feeding); method of delivery (vaginal delivery, cesarean section); weight loss after birth in relationship to type of feeding; and maternal and neonatal risk factors for jaundice development (maternal diabetes and hypertension, neonatal gender, blood group systems of A, AB, B, and O [ABO] incompatibility, Rh incompatibility,G6PD,polycythemia,positive family history and the presence of Cephalhematoma).

The statistical analysis was done by using the Statistical Package for Social Sciences (SPSS, version 13) .Chi-Square Test ($\chi 2$) for 95% CI were calculated, when it's applicable. P-values were obtained by comparing each specific group of feeding with other groups. *P*-values of <0.05 were considered statistically significant.

RESULTS:

One hundred- forty newborns with indirect hyperbilirubinemia of more than 12.9 mg\dl were studied. Ninety (64.3%) were males and 50(35.7%) were females with a male to female ratio of (1.8:1). Significant association was found between indirect hyperbilirubinemia and sex (P=0.045).

For the type of delivery, one hundred (71.4%) of jaundiced newborns were delivered by normal vaginal delivery, while only 40(28.6%) were delivered by cesarean section. Statistically there was no significant association between indirect hyperbilirubinemia and delivery mode (P=0.419).

Sixty (42.9%) of newborns developed hyperbilirubinemia at the third day of life and 46(32.9%) at the second day of life.(Table-1)

Newborns received supplementary feeding were 73 (52.1%) followed by breastfeeding 50(35.7%), while only 10(7.1%) and 7(5.0%) were on mixed and formula feeding, respectively.(Table-2),

Newborns on mixed feeding showed the highest percentage of TSB levels above 20 mg\dl 7(70.0%) followed by supplementary type of feeding 47(64.4%).Breastfed newborns showed 29(58.0%) of TSB levels above 20 mg\dl whereas formula-fed newborns revealed the lowest percentage of TSB above 20 mg\dl 3(42.9%). Statistically, there was no significant association between the types of feeding and the TSB level (P values >0.05). (Table-3)

Birth weight was only known in 83(59.2%) of all the newborns studied. Of them, supplementary-fed newborns showed the highest percentage of weight

loss 22(52.4%) followed by breast fed 15(50.0%), then mixed fed 2(33.3%) ,then formula-fed 1(20.0%). Statistically, there was no significant association between the types of feeding and the weight loss since P values >0.05. (Table-4)

Significant weight loss (weight loss > 10% of the birth weight) was found in 6(40%) of breast fed newborns, 1(100%) of formula fed , 1(50%) of mixed fed and 6(27.3%) of supplementary fed. Since the samples were too small for statistical analysis, P-value was not obtained for this group.(Table-5)

Seventy two percent of breastfed newborns had known risk factors other than breast feeding for developing jaundice, (71.4%)of formula fed ,
(70.0%) of mixed-fed and(56.2%) of supplementary fed . (Table-6)

All newborns required phototherapy. Mixed fed newborns had the highest percent of exchange transfusion therapy 6(60.0%) compared to supplementary fed 43(58.9%) , formula fed 4(57.1%), and breast fed who showed the lowest percentage of exchange transfusion 26(52.0%). There was no significant statistical association between the types of feeding and the type of treatment since P values were > 0.05. (Table-7)

When compared to other types of feeding, breast fed jaundiced newborns required longer duration of phototherapy to decrease the bilirubin to safe levels (mean 71.44 hrs) then formula fed (65.71) , then supplementary (60.73), then mixed fed(60.20 hrs).

Mixed-fed newborns had the highest percentage of kernicterus 5(50.0%), followed by supplementary fed 30(41.1%), then breastfed 17(34.0%) , and the lowest was formula fed 2(28.6%). Statistically, there was no significant association between the types of feeding and the outcome (P-values were > 0.05).(Table-8)

Table 1: Onset of jaundice (in days) in relation to type of feeding

Onset of jaundice in days		Type of feeding				
		Breast feeding	Formula feeding	MIXED	Supplementary	Total
First day	No. and %	5(10.0%)	3(42.9%)	3(30.0%)	3(4.1%)	14(10.0%)
Second day	No. and %	19(38.0%)	22(8.6%)	4(40.0%)	21(28.8%)	46(32.9%)
Third day	No. and %	20(40.0%)	1(14.3%)	1(10.0%)	38(52.1%)	60(42.9%)
Fourth day	No. and%	4(8.0%)	.0%	.0%	5(6.8%)	9(6.4%)
Fifth day	No. and%	1(2.0%)	1(14.3%)	2(20.0%)	3(4.1%)	7(5.0%)
Sixth day	No. and%	1(2.0%)	.0%	.0%	3(4.1%)	4(2.9%)
	No. and%	50(100.0%)	7(100.0%)	10(100.0%)	73(100.0%)	140(100.0%)

Table 2: Distribution of the sample according to the type of feeding

	Frequency	Percent %
Breast feeding	50	35.7
Formula feeding	7	5.0
MIXED	10	7.1
Supplementary	73	52.1
Total	140	100.0

Table 3: Distribution of the sample according to the type of feeding in relation to the TSB level

Type of feeding		TSB			P-value
		Less than 20	Equal or more than 20	Total	
Breast feeding	Number and%	21(42.0%)	29(58.0%)	50(100.0%)	0.912
Formula feeding	Number and%	4(57.1%)	3(42.9%)	7(100.0%)	0.686
MIXED	Number and%	3(30.0%)	7(70.0%)	10(100.0%)	0.928
Supplementary	Number and%	26(35.6%)	47(64.4%)	73(100.0%)	0.889
Total	Number and%	54(38.6%)	86(61.4%)	140(100.0%)	

Table 4: Distribution of the sample according to the weight

weight		Type of feeding				
		Breast feeding	Formula feeding	MIXED	Supplementary	Total
Wt loss	Number and %	15(50.0%)	1(20.0%)	2(33.3%)	22(52.4%)	40(48.2%)
No wt loss	Number and %	15(50.0%)	4(80.0%)	4(66.7%)	20(47.6%)	43(51.8%)
Total	Number and %	30(100.0%0	5(100.0%)	6(100.0%)	42(100.0%)	83(100.0%)
P-value		0.936	0.483	0.762	o.774	

Table 5: Distribution of the sample according to the weight loss

Wt loss		Type of feeding				
		Breast feeding	Formula feeding	mixed	supplementary	total
Significant	No. and %	6(40%)	1(100%)	1(50%)	6(27.3%)	14(35%)
Not significant	No. and %	9(60%)	0(0%)	1(50%)	16(72.7%)	26(65%)
Total	No. and %	15(100%)	1(100%)	2(100%)	22(100%)	40(100%)

☆Significant wt loss refers to wt loss more than (10 %) from birth wt.

Table 6: Distribution of the sample according to the risk factors in relation to the types of feeding

Risk factors		Type of feeding				
		Breast feeding	Formula feeding	MIXED	Supplementary	Total
No risk factors	No. and %	14(28.0%)	2(28.6%)	3(30.0%)	32(43.8%)	51(36.4%)
ABO incompatibility	No. and %	13(26.0%)	.0%	1(10.0%)	19(26.0%)	33(23.6%)
RH incompatibility	No. and%	3(6.0%)	1(14.3%)	1(10.0%)	3(4.1%)	8(5.7%)
POLYCYTHEMIA	No. and %	.0%	.0%	.0%	2(2.7%)	2(1.4%)
CEPHALHEMATOMA	No. and %	1(2.0%)	1(14.3%)	.0%	.0%	2(1.4%)
G6PD	No. and %	1(2.0%)	.0%	1(10.0%)	1(1.4%)	3(2.1%)
Family History	No. and %	4(8.0%)	.0%	1(10.0%)	.0%	5(3.6%)
Gestational DM	No. and %	.0%	.0%	.0%	3(4.1%)	3(2.1%)
Gestational HPT	No. and %	.0%	.0%	1(10.0%)	.0%	1(.7%)
More Than One Risk	No. and %	14(28.0%)	3(42.9%)	2(20.0%)	13(17.8%)	32(22.9%)
Total	Number	50	7	10	73	140

Table 7: Distribution of the sample according to the type of treatment in relation to the type of feeding

Type of treatment		Type of feeding				
		Breast feeding	Formula feeding	MIXED	Supplementary	Total
phototherapy	No. and %	24(48.0%)	3(42.9%)	4(40.0%)	30(41.1%0	61(43.6%)
Exchange	No. and %	26(52.0%0	4(57.1%)	6(60.0%)	43(58.9%)	79(56.4%0
Total	No. and %	50(100.0%)	7(100.0%)	10(100.0%0	73(100.0%0	140(100.0%)
P-value		0.889	0.968	0.942	0.928	

Table 8: Distribution of the sample according to the outcome

Type of feeding						
Breast feeding	Formula feeding	MIXED	Supplementary	Total		
Kernicterus	No. and %	17(34.0%)	2(28.6%)	5(50.0%)	30(41.1%)	54(38.6%0
No kernicterus	No. and %	33(66.0%)	5(71.4%)	5(50.0%)	43(58.9%)	86(61.4%)
total	No. and %	50(100.0%)	7(100.0%)	10(100.0%)	73(100.0%)	140(100.0%)
	0.860	0.948	0.871	0.894		

DISCUSSION:

Several authors had reported an increase in the frequency of readily visible jaundice in the last 25 years, probably secondary to breastfeeding encouragement in the same period [18].

- One hundred forty newborn with indirect hyperbilirubinemia more than 12.9 mg\dl were studied. Onset of jaundice was mainly on the second and third day of life, this finding was the same as that observed by Giovanna Bertini (Italy) [18] and Glenn R. Gourley (Oregon) [19].
- This study demonstrated a statistically significant positive association between newborns with indirect hyperbilirubinemia of >12.9 mg/dL and male gender (P=0.047), a result similar to that of Giovanna Bertini (Italy) [18]. Conversely, no significant association was found with the mode of delivery and this result was not agreed with Giovanna Bertini [18] who suggested that infants born by cesarean section are stressed before birth and, therefore, induces conjugating enzymes before delivery.
- Our data showed that, newborns on feeding supplemented with water or dextrose water represented the largest group among other feeding groups (52.1%), this result was not found in other studies like Giovanna Bertini (Italy)[18], Shaul Dollberg (Israel)[20], Glenn R. Gourley (Oregon)[19] and Hintz SR (USA)[21] in which the types of feeding were mainly breast, formula and mixed feeding. This phenomena could probably be explained by: In our country, there is traditional administration of water or dextrose water by our people to their jaundiced newborns and Inadequate knowledge and misconceptions of NNJ in some doctors who encourage such practice.

Administration of water to newborns significantly reduce the frequency of milk feeding and increase serum bilirubin concentrations [22].Reduced volume of milk transfer to the infant will limit the caloric intake of the infant producing a state of partial starvation which can be expected to further increase the intestinal absorption of bilirubin in the newborn [22]. These reasons might explain the higher TSB levels (64.4%), higher percentage of weight loss (52.4%), higher exchange transfusion rates (58.9%) and higher percentage of kernicterus (41.1%) were found in this group when compared to breast or formula fed groups.

Compared to formula fed group, breast fed group was reported at higher percentage (35.7%), showed higher rates of bilirubin levels above 20 mg\dl (58.0%), showed higher percentage of weight loss (50.0%) and had higher frequency of kernicterus (34.0%). Despite these results, these findings were not of clinical or therapeutic consequence in this study (P>0.05). Similar results were reported by Hintz SR [21] but different results were recorded in studies done by Giovanna Bertini [18], Shaul Dollberg [20] and Glenn R. Gourley[19] who revealed significant clinical association between breast feeding and increased levels of indirect hyperbilirubinemia. A probable reasons for the higher rates of bilirubin and kernicterus in breastfed newborns in this study were that: 1.The presence of well-known risk factors for jaundice such as ABO incompatibility, Rh

incompatibility and Cephalhematoma in large numbers of breastfed newborns in our study (72.0%). This result was not consistent with the study of Giovanna Bertini [18] in which known risk factors were found in only (45-48%) of breast fed jaundiced newborns.

2.Inadequacy of milk intake due to poor breastfeeding practices. Support for this was that about 50.0% of breastfed newborns had weight loss, while only 20.0% of formula-fed neonates had weight loss due to the easier bottle feeding techniques and the larger amount of milk that can be given by a bottle. This was consistent with the study of Maisels[23] who suggested that even mild degree of dehydration in conjunction with breastfeeding has impacts on the severity of hyperbilirubinemia. Other studies demonstrated that lower serum bilirubin concentrations in breastfed infants are associated with weight gains comparable to or better than those of artificially fed infants [24,25]. Some studies showed that frequent Breastfeeding of at least 11 times per day, starting with the first day, have been associated with the lowest serum bilirubin concentrations on the third to sixth days of life[22,28].

Since healthy newborns can normally lose 10% of their birth weight during the first week of life, data were arranged to show which newborns had significant weight loss (weight loss >10%).As the samples were too small for statistical analysis, this subject was ignored in this study.

The duration of exposure to phototherapy was observed to be longer in breast fed group (mean 71.4 hrs) than other feeding groups. This result agreed with Tan K.L [17,27] who noticed that breast-fed infants still had the greatest weight deficit at the end of exposure; this relative "dehydration," although mild, might be a contributing factor in reducing the response to phototherapy.

Infants given mixed feeding (breast feeding plus formula feeding) showed the highest levels of bilirubin above 20 mg\dl (70.0%), the highest percentage of exchange transfusion (60.0%) and the highest percentage of kernicterus (50.0%) with weight loss observed in only (33.3%) of all the group studied. These results were similar to Maisels [23] who suggested that the easier bottle feeding will reduce the infant's suckling urge thus decreasing colostrum and breast milk intake , and there is also evidence that formula milk coats the gut differently than human milk and can interfere with the normal processes of excretion and hydration.:

CONCLUSION:

1. No significant association was found between types of feeding and indirect hyperbilirubinemia in full term newborns.
2. Breastfeeding can be a leading cause of neonatal jaundice if associated with greater weight loss following delayed initiation of or inadequate breastfeeding due to poor breast feeding practices.
3. Administration of water or dextrose water to the jaundiced newborns will adversely affect the volume of milk transferred to the babies leading to decreased caloric intake and starvation which further increase the bilirubin levels.
4. Giving formula feeding to breastfed newborns will interfere with the optimal breast feeding techniques leading to reduced milk produced by the mother thus limits caloric intake and increases bilirubin levels. 5. Breastfed newborns require longer duration of phototherapy to decrease the bilirubin to safe levels. So

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