

Impact of Breast Milk Biochemistry on Neonatal Jaundice: Insights from a Cross-Sectional Study in Jos, Nigeria

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Abstract

Background: Exclusive breastfeeding is globally promoted as a preventive health measure. However, an increasing incidence of jaundice among exclusively breastfed neonates has been observed. In Jos, Nigeria, anecdotal evidence suggests a rise in jaundice cases among breastfed infants during their first week of life. This study investigates the relationship between neonatal jaundice and the biochemical composition of maternal breast milk in Jos, Nigeria. **Objective:** To evaluate the role of maternal milk protein status and other milk constituents in the development of neonatal jaundice among exclusively breastfed full-term infants. **Methods:** This cross-sectional study involved 152 participants, comprising of 76 neonates (38 jaundiced and 38 healthy controls) and their corresponding 76 mothers at Jos University Teaching Hospital. Biochemical analyses were conducted on maternal breast milk (albumin, proteins, casein, fat, lactose, enzymes) and infant serum (bilirubin, albumin, proteins, enzymes). Statistical analysis was performed using Mann-Whitney tests with significance set at $p \leq 0.05$. **Results:** Maternal breast milk from mothers of jaundiced infants showed significantly lower protein (0.73 ± 0.07 g/100ml), albumin (0.62 ± 0.04 g/100ml), and casein (1.6 ± 0.12 g/100ml) levels compared to controls ($p < 0.05$). Serum albumin and alkaline phosphatase levels were also significantly lower in jaundiced infants ($p < 0.05$). Elevated unconjugated bilirubin (10.70 ± 0.98 mg/100ml) was the predominant form of bilirubin in jaundiced neonates, accounting for 93% of total bilirubin levels. No significant differences were observed in carbohydrate or fat content of breast milk between groups. **Conclusion:** The study highlights a potential link between lower maternal milk protein levels and the occurrence of neonatal jaundice. Interventions aimed at enhancing maternal nutrition and promoting

more frequent breastfeeding may mitigate the risk. Further research should explore additional maternal and neonatal factors contributing to this condition.

Keywords

Neonatal Jaundice, Breast Milk Composition, Maternal Nutrition, Bilirubin, Lactation, Exclusive Breastfeeding

1. Introduction

Exclusive breastfeeding is widely recommended by health organizations as the optimal method of infant feeding due to its nutritional and immunological benefits [1]. Breast milk provides essential nutrients for the growth and development of an infant during the first six months, offers immunological protection against illnesses like diarrhea and pneumonia, and supports long-term health by reducing the risk of chronic conditions such as obesity and diabetes [2]. However, neonatal jaundice, a condition marked by elevated serum bilirubin levels, is more frequently observed in breastfed infants than formula-fed counterparts, due to factors such as suboptimal milk intake, lower caloric intake, and increased enterohepatic circulation of bilirubin, which can lead to elevated bilirubin levels [3]. Studies and clinical guidelines highlight that more than 80% of newborns experience some degree of jaundice, with breastfed infants being more susceptible, and exclusive breastfeeding showing a stronger association with hyperbilirubinemia compared to formula feeding [3]-[6]. Similarly in Nigeria, a study carried out at Our Lady of Apostle Hospital in Jos found that the incidence of neonatal jaundice was 11.7% among live births from 2019 to 2021 [7]. Also, a study carried out at the University College Hospital in Ibadan found that breastfeeding was associated with a two-fold increase in jaundice, and confirmed breastfeeding as an independent factor associated with increased jaundice [8]. Breastfeeding jaundice, can lead to severe complications such as bilirubin encephalopathy if unmanaged [9], this is caused by factors such as inadequate milk intake and increased enterohepatic circulation of bilirubin [3] [10]. The other type of neonatal jaundice, is the less common breast milk jaundice, which typically arises later, around the second week of life [11]. Breastfeeding jaundice is a common neonatal condition globally, which occurs in the first weeks of life, affecting up to 60% of term infants, with higher prevalence among breastfed babies due to factors like suboptimal feeding and delayed bilirubin clearance [3] particularly among breastfed infants.

The etiology of breastfeeding jaundice is multifactorial, involving physiological bilirubin metabolism, nutritional factors, and maternal milk composition. This condition, is associated with inadequate feeding practices and delayed excretion of meconium [10]. Globally, 13% of breastfed neonates experience significant jaundice, and severe cases can lead to complications like kernicterus. In sub-Saharan Africa, neonatal jaundice contributes significantly to morbidity, with Nigeria

reporting 35% - 60% of neonatal hospital admissions linked to jaundice. Cultural practices, inadequate maternal nutrition, and delayed breastfeeding initiation exacerbate the issue, particularly in resource-limited settings like Jos, Nigeria. The exact prevalence of breastfeeding jaundice exhibits variability. Localized studies are vital to addressing these challenges and developing targeted interventions.

Despite the prevalence of breastfeeding jaundice, there remains a gap in understanding the biochemical interactions between maternal milk components and neonatal bilirubin clearance. This study aims to investigate the relationship between jaundice in exclusively breastfed neonates and the biochemical composition of the breast milk of mothers in Jos, Nigeria, providing localized insights into this global issue.

2. Methodology

2.1. Study Design and Setting

This cross-sectional study was conducted at Jos University Teaching Hospital, Nigeria, focusing on neonates aged 2 - 10 days and their mothers. The study compared biochemical parameters in the breast milk of mothers of jaundiced infants (study group) with those of healthy controls.

2.2. Study Population

A total of 152 participants, made of 76 mother-infant pairs were recruited, comprising 38 jaundiced infants and their mothers, and 38 healthy controls. Inclusion criteria were full-term neonates exclusively breastfed from birth, delivered via normal vaginal delivery, and free from known causes of jaundice such as ABO incompatibility, infection, or maternal drug use.

2.3. Data Collection and Analysis

Blood samples were collected from infants, and breast milk was expressed manually by mothers. Biochemical parameters, including total proteins, albumin, casein, alkaline phosphatase, and α -amylase activity, were measured using standard spectrophotometric methods. Statistical analysis was performed using Mann-Whitney tests, with significance set at $p \leq 0.05$.

2.4. Ethical Considerations

The study protocol was approved by the Jos University Teaching Hospital Ethics Committee. Written informed consent was obtained from all participants.

3. Results

Table 1 shows the result from the maternal breast milk in the study group. The mean albumin concentration was significantly lower in the breast milk of mothers of jaundiced infants (0.73 ± 0.07 g/100 mL) compared to mothers of control infants (1.11 ± 0.08 g/100 mL; $p < 0.05$). Similarly, casein levels were significantly lower in the breast milk of mothers of jaundiced infants (0.62 ± 0.04 g/100 mL)

compared to mothers of control infants (0.87 ± 0.06 g/100mL; $p < 0.05$). Total protein concentrations were significantly reduced in the breast milk of mothers of jaundiced infants (1.60 ± 0.12 g/100mL) versus control mothers (2.05 ± 0.16 g/100mL; $p < 0.05$). No significant difference was observed in α -amylase activity between the two groups (135.50 ± 3.92 g·h⁻¹·L⁻¹ in control versus 123.66 ± 4.47 g·h⁻¹·L⁻¹ in jaundiced mothers; NS). Alkaline phosphatase activity did not differ significantly between the two groups (10.78 ± 2.50 IU in control versus 9.75 ± 1.44 IU in jaundiced mothers; NS). The fat content of breast milk showed no significant difference between the groups (5.19 ± 0.70 g/100mL in control versus 4.82 ± 0.46 g/100mL in jaundiced mothers). Lactose levels were similar between the two groups (3.15 ± 0.09 g/100mL in control versus 2.92 ± 0.10 g/100mL in jaundiced mothers; NS). Glucose and fructose concentrations were not significantly different (2.21 ± 0.07 g/100mL in control versus 2.04 ± 0.07 g/100mL in jaundiced mothers). Maltose concentration also showed no significant difference (3.37 ± 0.10 g/100mL in control versus 3.12 ± 0.11 g/100mL in jaundiced mothers; NS), this indicates consistency in disaccharide content across the two groups.

Table 1. Breast milk albumin, casein, total proteins concentrations, α -amylase activity, alkaline phosphatase activity, fat, lactose, glucose, fructose, and maltose concentrations of mothers of babies recruited in JUTH in jos metropolis.

Parameter	Albumin (g/100 mL)	Casein (g/100 mL)	Total Protein (g/100mL)	α -Amylase Activity (g h ⁻¹ L ⁻¹)	Alkaline Phosphatase Activity (IU)	Fat (g/100 mL)	Lactose (g/100 mL)	Glucose and Fructose (g/100 mL)	Maltose (g/100 mL)
Mothers of Control Infants (Mean \pm SD, n)	1.11 \pm 0.08 [11]	0.87 \pm 0.06 [11]	2.05 \pm 0.16 [11]	135.50 \pm 3.92 [11]	10.78 \pm 2.50 [11]	5.19 \pm 0.70 [8]	3.15 \pm 0.09 [11]	2.21 \pm 0.07 [11]	3.37 \pm 0.10 [11]
Mothers of Jaundiced Infants (Mean \pm SD, n)	0.73 \pm 0.07 [27]	0.62 \pm 0.04 [25]	1.60 \pm 0.12 [26]	123.66 \pm 4.47 [24]	9.75 \pm 1.44 [27]	4.82 \pm 0.46 [16]	2.92 \pm 0.10 [19]	2.04 \pm 0.07 [19]	3.12 \pm 0.11 [19]
Statistical significance	p < 0.05	p < 0.05	p < 0.05	NS	NS	NS	NS	NS	NS

NS: Not significant. Values are presented as mean \pm standard deviation with the sample size in brackets (n). Significant differences ($p < 0.05$) were observed between mothers of control infants and mothers of jaundiced infants for albumin, casein, and total protein concentrations.

The results on infants are presented in **Table 2**. Albumin levels were significantly lower in jaundiced infants (4.73 ± 0.13 g/100mL) compared to control infants (5.19 ± 0.13 g/100mL; $p < 0.05$). No significant difference was observed in globulin levels between the two groups (5.72 ± 0.95 g/100mL for control vs. 4.78 ± 0.68 g/100mL for jaundiced infants; NS). This indicates that immune-related proteins are not altered in jaundiced infants. Total protein levels showed no significant difference between control (10.91 ± 1.03 g/100mL) and jaundiced infants (9.26 ± 0.79 g/100 mL; NS). α -Amylase activity was not significantly different between control (7.14 ± 3.37 g·h⁻¹·L⁻¹) and jaundiced infants (5.47 ± 2.34 g·h⁻¹·L⁻¹; NS). This suggests that starch-digesting enzyme activity in infants is unaffected by jaundice. Alkaline phosphatase activity was significantly lower in jaundiced infants (13.37 ± 1.05 IU) compared to control infants (19.27 ± 1.66 IU; $p < 0.05$). Total bilirubin levels were markedly higher in jaundiced infants (11.57 ± 1.05

mg/100mL) compared to control infants (2.38 ± 0.35 mg/100mL; $p < 0.05$). Likewise, conjugated bilirubin was significantly higher in jaundiced infants (0.87 ± 0.13 mg/100mL) compared to controls (0.45 ± 0.22 mg/100mL; $p < 0.05$). Unconjugated bilirubin was significantly higher in jaundiced infants (10.70 ± 0.98 mg/100mL) compared to controls (1.93 ± 0.33 mg/100mL; $p < 0.05$).

Table 2. Serum albumin, globulins and total proteins concentrations, α -amylase activity, alkaline phosphatase activities, total bilirubin, conjugated bilirubin and unconjugated bilirubin concentrations of infants attending JUTH in jos metropolis.

	Albumin g/100ml	Globulin g/100ml	Total protein g/100ml	α -Amylase activity (g h ⁻¹ l ⁻¹)	Alkaline phosphatase activity [IU]	Total bilirubin mg/100ml	Conjugated bilirubin mg/100ml	Unconjugated bilirubin mg/100ml
Total control infants	5.19 \pm 0.13 [11]	5.72 \pm 0.95 [11]	10.91 \pm 1.03 [11]	7.14 \pm 3.37 [7]	19.27 \pm 1.66 [11]	2.38 \pm 0.35 [11]	0.45 \pm 7.22 [11]	1.93 \pm 0.33 [11]
Total jaundiced infants	4.73 \pm 0.13 [17]	4.78 \pm 0.68 [17]	9.26 \pm 0.79 [17]	5.47 \pm 2.34 [12]	13.37 \pm 1.05 [19]	11.57 \pm 1.05 [20]	0.87 \pm 0.13 [20]	10.70 \pm 0.98 [20]
Statistical Significance	*p < 0.05	NS	NS	NS	*p < 0.05	*p < 0.05	*p < 0.05	*p < 0.05

NS: Not significant. Values are presented as mean \pm standard deviation with the sample size in brackets (n). Significant differences ($p < 0.05$) were observed between control infants and jaundiced infants for albumin, casein, and total protein concentrations.

4. Discussion

The findings of this study suggest that low protein content in maternal breast milk contributes to the development of jaundice in exclusively breastfed neonates. Proteins such as albumin play a critical role in bilirubin transport and clearance; thus, inadequate protein intake may exacerbate hyperbilirubinemia. Casein, a major milk protein, plays a crucial role in nutrient delivery and digestion; lower levels could impact infant nutrition and growth. The finding of this study aligns with the study carried out by Robinson, *et al.* [12]. Also, the overall reduction in protein concentration may reflect a lower protein supply to the jaundiced infants, potentially influencing their nutritional status and recovery. The result of this study agrees with previous studies that show that low protein intake by the mother can affect the infant [13]-[15]. The observed slight reduction in serum alkaline phosphatase activity supports the conclusion that this jaundice is physiological rather than pathological [16]. The study highlights significant reductions in albumin, casein, and total protein concentrations in the breast milk of mothers of jaundiced infants compared to control mothers. These findings may suggest a possible nutritional adaptation or alteration in milk composition associated with infant jaundice. However, other parameters, such as enzyme activities, fat, and sugar concentrations, remained unaffected, indicating a selective change in breast milk composition. Further studies could explore the underlying mechanisms and potential clinical implications for infant health and nutrition.

From the results of the analyses carried out on the infants, the reduced albumin may impact bilirubin transport and metabolism, as albumin binds to unconjugated bilirubin in the blood [17]. This reduction could exacerbate hyperbilirubinemia in jaundiced infants. However, despite the reduction in albumin levels,

the total protein level remains relatively stable, possibly due to compensatory levels of globulin or other proteins. There was a significant decrease in ALP levels. This agrees with the work of Semler, *et al.* [18] This enzyme is very important for bone growth and mineralization and might indicate a reduced metabolic activity in jaundiced infants, potentially due to compromised liver function. Elevated total bilirubin in infants observed in this study was also confirmed in another study [19], which reflects the defining characteristic of jaundice, with elevated bilirubin levels indicating impaired liver function or increased hemolysis. High unconjugated bilirubin levels were observed in the jaundiced infants, which is supported by Westenberg, *et al.* [20]. This indicates the predominant issue in jaundice, as unconjugated bilirubin is a direct result of the inability of the liver to conjugate bilirubin efficiently.

Management strategies should prioritize improving maternal nutrition to enhance breast milk quality and encourage frequent breastfeeding to promote bilirubin excretion. These interventions are consistent with global recommendations and have shown efficacy in reducing breastfeeding jaundice. From the pattern of the results obtained in this study, it shows that there is need for Maternal supplementation recommendations, which aligns with global breastfeeding guidelines by ensuring optimal maternal nutrition to support breast milk production and quality. Maternal supplementation helps prevent nutritional deficiencies that could hinder milk production, supporting the recommendation for exclusive breastfeeding for the first six months. Studies have shown that maternal intake of certain vitamins and minerals, such as vitamins A, D, B1, B2, and C, can positively influence the composition of breast milk [21]. Adequate maternal nutrition through supplementation ensures sufficient milk production, which is crucial for frequent breastfeeding and reducing conditions like breastfeeding jaundice. Additionally, maintaining a well-balanced diet and taking recommended supplements can help mothers meet the increased nutritional demands during lactation [22]. Maternal supplementation is especially important in low-income or resource-limited settings to address nutritional gaps and improve breastfeeding outcomes [23]-[25]. Global guidelines discourage formula use in the first six months, and maternal supplementation enhances the quality of breast milk, reducing the need for artificial alternatives [1] [26]. In essence, maternal supplementation supports the goals of exclusive breastfeeding by ensuring both maternal health and optimal infant nutrition.

In Nigeria, neonatal jaundice affects 35% - 60% of hospitalized neonates, with breastfeeding jaundice being a major contributor [8] [27]-[29]. Similar findings in Kenya report a 28% prevalence, linked to delayed breastfeeding initiation and inadequate feeding practices [30]. In China, a lower prevalence is attributed to better maternal nutrition and lactation support [31]. Reports in Europe and North America showed that in the United States, 20% - 30% of neonates experience jaundice, often managed through early and frequent breastfeeding and effective health-care interventions [32]. In the United Kingdom, neonatal jaundice is indeed a common condition, with reports indicating that around 60% of term babies and

80% of preterm babies develop jaundice in the first week of life with educated mothers being more likely to recognize early signs of jaundice and seek timely medical intervention, which can significantly reduce the risk of complications [33]. Breastfeeding jaundice prevalence varies globally, influenced by maternal nutrition, breastfeeding practices, and healthcare infrastructure. Low-resource settings like Nigeria show higher prevalence due to inadequate maternal nutrition and limited lactation support, highlighting the need for targeted interventions. The increase in conjugated bilirubin suggests some degree of liver processing, but not enough to prevent accumulation of total bilirubin [4].

5. Conclusions

This study highlights the potential contribution of maternal breast milk protein levels to neonatal jaundice in exclusively breastfed infants. Improving maternal nutrition and breastfeeding practices could mitigate the risk of jaundice, supporting better neonatal outcomes. Further research with larger sample sizes and broader biochemical analyses is needed to validate these findings and inform targeted interventions.

Actionable Recommendations for Healthcare Providers and Mothers could involve: encouraging breastfeeding initiation within the first hour and exclusive breastfeeding for six months; advise mothers on balanced diets and supplements like vitamin D and omega-3 fatty acids to improve milk quality; assess feeding frequency, infant weight, and support proper latch and positioning; provide targeted guidance for at-risk mothers, such as those with poor nutrition or socioeconomic challenges; educate families on jaundice signs, recommend frequent breastfeeding, and offer timely medical interventions. And for the mothers, recommendations include: begin breastfeeding within the first hour and practice exclusive breastfeeding for six months; maintain a nutritious diet and consider supplements as advised by healthcare providers, feed on demand to ensure adequate milk intake and reduce jaundice risk; consult healthcare providers for assistance with breastfeeding challenges; and be alert for jaundice symptoms and seek medical advice if needed. These recommendations aim to enhance breastfeeding outcomes, improve maternal and infant health, and reduce complications like breastfeeding jaundice.

Study Limitation

The relatively small sample size, may not fully represent the larger population and limits generalizability. Additionally, the cross-sectional design precludes long-term follow-up of the infants to observe how the biochemical parameters evolve over time or if the jaundice resolved or persisted. External factors such as maternal diet and other environmental influences on breastmilk composition could not be extensively explored.

Ethical Approval

The research protocol for this study was approved by the Medical and Health

Ethics Committee of Jos University Teaching Hospital, Jos. Ref: JUTH/CT/ADM/127/VOL.IV/761.

Consent to Participate

Informed consent and assent were obtained from the parents after the research protocols was communicated in the language best understood by the parents.

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Authors' Contributions

This study was carried out in collaboration between all authors. Author Olomu A. Segun conceptualized and designed the research work. Author Okolo S. Nnuaku. Co-supervised the work. Authors Samuel Y. Gazuwa, Kiri H. Jaryum Jane Rose Oche and Olorunyomi A. Olumuyiwa reviewed the manuscript. All authors partook in the analysis, interpretation of data obtained. All authors read and approved the final manuscript.

Conflicts of Interest

All the authors hereby declare that we have no conflicting interests on this study.

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