Epidemiology of Neonatal Jaundice at the University Hospital of the West Indies

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ABSTRACT

Objective: *To describe the epidemiology of neonatal jaundice at the University Hospital of the West Indies (UHWI).*

Methods: *A retrospective review of all neonates at the UHWI with clinically significant jaundice between January 1, 2006 and June 30, 2007 was performed. Demographic, clinical and laboratory data were collected. Descriptive analyses were performed.*

Results: *The incidence of clinically significant neonatal jaundice at the UHWI was 4.6% for the study period. There were 103 male (61%) and 67 (39%) female infants. The aetiology of jaundice in the infant was attributed to ABO incompatibility in 59 (35%), infection in 30 (18%), prematurity in 19 (11%), G6PD deficiency in 8 (5%), Rhesus incompatibility in 6 (3.5%) and no cause was identified in 16 (9%) infants. There was a low incidence (26%) of screening for G6PD deficiency although it was the most common aetiology for infants presenting from home. Nine (5%) neonates required exchange blood transfusion. Infants admitted from home had a significantly higher mean total bilirubin value at presentation, a significantly higher mean peak bilirubin level and presented significantly later than those who were admitted from the postnatal ward (*$p < 0.001$*). One patient was discharged with a diagnosis of bilirubin encephalopathy but defaulted from follow-up. Two neonates died but from causes unrelated to neonatal jaundice. Sixty-two patients (37%) were followed-up post discharge; 50% had hearing tests done, all tests were normal. Sixty-one (98%) infants had normal development at the time of the study; one patient had impaired motor development but this infant also had a myelomeningocoele.*

Conclusion: *To further reduce morbidity associated with neonatal jaundice at the UHWI, there should be increased screening for G6PD deficiency; current systems in place for follow-up and monitoring of infants discharged from hospital prior to 72 hours must also be expanded and strengthened.*

Keywords: Neonatal jaundice

Epidemiología de la Ictericia Neonatal en el Hospital Universitario de West Indies

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RESUMEN

Objetivo: *Describir la epidemiología de ictericia neonatal en el Hospital Universitario de West Indies (UHWI).*

Métodos: *Se llevó a cabo una revisión retrospectiva de todos los recién nacidos con ictericia clínicamente significativa, en UHWI entre el 1^{ero} de enero de 2006 y el 30 de junio de 2007. Se recogieron datos demográficos, clínicos y de laboratorio. Se realizaron análisis descriptivos.*

Resultados: *La incidencia de la ictericia neonatal clínicamente significativa en UHWI fue de 4.6% para el periodo en estudio. Había 103 recién nacidos varones (61%) y 67 (39%) hembras. La etiología de la ictericia en los neonatos se atribuyó a la incompatibilidad de ABO en 59 (35%), infección en 30 (18%), prematuridad en 19 (11%), deficiencia de G6PD en 8 (5%), e incompatibilidad de Rhesus en 6 (3.5%). No se identificó ninguna causa en 16 (9%) de los recién nacidos. Hubo una baja incidencia (26%) de tamizaje para la deficiencia de G6PD, aún cuando ésta es la etiología más común en el caso de los infantes provenientes de casa. Nueve (5%) recién nacidos requirieron cambio de sangre mediante trans-*

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fusión. Infantes ingresados desde sus casas presentaban un valor promedio de bilirrubina total significativamente mayor en el momento de su hospitalización, así como un nivel pico promedio de bilirrubina significativamente más alto, y se presentaron significativamente más tarde que aquellos ingresados directamente de las sala de atención postnatal ($p < 0.001$*). Un paciente fue dado de alta con un diagnóstico de encefalopatía bilirrubínica, pero no se presentó a las sesiones de seguimiento. Dos recién nacidos murieron, pero por causas no relacionadas con la ictericia neonatal. Sesenta y dos pacientes (37%) tuvieron seguimiento luego del alta; al 50% se les realizó pruebas de audición; todas las pruebas arrojaron resultados normales. Sesenta y un infantes (98%) presentaban un desarrollo normal en el momento del estudio. Un paciente tenía discapacidad del desarrollo motor, pero también presentaba un mielomeningocele*

Conclusión: *A fin de lograr una reducción de la morbosidad asociada con la ictericia neonatal en UHWI, debe realizarse un tamizaje de la deficiencia de G6PD. Asimismo, es necesario ampliar y fortalecer los sistemas actuales establecidos para el seguimiento y monitoreo de los infantes dados de alta del hospital antes de las 72 horas.*

Palabras claves: ictericia neonatal

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INTRODUCTION

Neonatal jaundice affects 60% of full-term infants and 80% of preterm infants in the first three days after birth. Although transient, the condition accounts for up to 75% of hospital readmissions in the first week after birth (1).

Palmer and Drew, in a review of jaundiced newborn infants in Australia over a ten-year period found that prematurity was the most common aetiological factor (20%), followed by ABO erythroblastosis (7%), sepsis (3%), Rhesus erythroblastosis (3%), bruising (2%) and glucose-6-phosphate dehydrogenase (G6PD) deficiency [0.5%] (2). Dawodu *et al* in their study also found that prematurity was the most common aetiological factor along with ABO haemolytic disease, accounting for 26% each, this was followed by the group in which there was no identifiable cause (24%). Glucose-6-phosphate dehydrogenase deficiency accounted for 9%, breastmilk jaundice for 6% and Rhesus isoimmunization for a further 1% (3). Martin *et al* in Antigua and Barbuda found the most common cause for hyperbilirubinaemia in their study to be idiopathic (71%), this was followed by sepsis in 16%, prematurity 9%, ABO incompatibility 3% and Rhesus isoimmunization in 1% (4).

Neonatal jaundice was studied in Jamaican neonates in 1963; ABO/Rh incompatibility, prematurity and maternal diabetes were the only significant underlying factors reported to predispose to neonatal hyperbilirubinaemia (5). Subsequent studies in Jamaican neonates (1972, 1979) showed similar results while identifying G6PD as a significant cause of jaundice in neonates with moderate to severe neonatal hyperbilirubinaemia (6, 7). In a similar study done in Trinidad (1987), 44% of the cases were due to ABO incompatibility, with G6PD accounting for 21% of the cases (8).

There have been no recent studies from the English-speaking Caribbean done in the area of neonatal jaundice and few have looked at the outcome of these infants. This study aimed to describe the epidemiology of neonatal jaundice at the University Hospital of the West Indies (UHWI) over an 18-month period.

SUBJECTS AND METHODS

This is a retrospective, descriptive study looking at all neonates with a discharge diagnosis of unconjugated hyperbilirubinaemia between January 1, 2006 and June 30, 2007 at the UHWI. Cases were identified from the neonatal unit log books; however, on review of the individual charts, any case that did not require medical intervention was excluded. Demographic, clinical and laboratory data were extracted from the individual charts using a data extraction sheet. For five of the patients, patient files could not be retrieved; however, baseline demographic data were collected from the labour ward, the Newborn Special Care Nursery and the laboratory. The demographics of these five patients were no different from the study population.

Case definition

For the purpose of this study, clinically significant neonatal jaundice (unconjugated hyperbilirubinaemia) was defined as any unconjugated bilirubin level requiring investigation and medical intervention. Medical intervention was defined as the need for phototherapy, exchange blood transfusion or both.

Exclusion criteria

Neonates who had neonatal jaundice but did not require medical intervention and neonates who had a direct serum bilirubin level greater than 20% of the value of their total serum bilirubin level were excluded from the study.

Statistical analysis

Descriptive analyses were performed. Differences between groups were determined using Chi-square tests for categorical

variables and student's *t tests* for continuous variables. Statistical significance was taken at the level $p < 0.05$. Analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 12.

Ethical approval

The University of the West Indies/University Hospital of the West Indies, Faculty of Medical Sciences Ethics Committee granted approval for this study to be conducted.

RESULTS

During the study period, January 2006 to June 2007, 170 neonates fulfilled inclusion criteria for this study. There were 3561 live births at UHWI during this period. One hundred and sixty-two (4.6%; 45.5 per 1000 live births) had clinically significant unconjugated hyperbilirubinaemia; the other 8 infants in the study were admitted from other hospitals. There were 103 (61%) males and 67 (39%) females. Sixty-five (38%) patients were admitted from the labour ward, 62 (37%) from the postnatal ward, 35 (20%) from home and 8 (5%) were admitted from other hospitals.

Maternal age ranged from 16 to 46 years with a mean of 29.4 ± 6.3. The majority of the mothers (91) were primiparous (54%). Maternal demographics are shown in Table 1.

Table 1: Maternal demographics of neonates with clinically significant unconjugated hyperbilirubinaemia at the UHWI 2006–2007

Variable	Frequency %
Parity	
Para 0	91 (54)
Para 1–2	67 (39)
Para 3–6	12 (7)
Previous infant treated for hyperbilirubinaemia	7 (4)
Oxytocin induction/augmentation	26 (15)
Misoprostal induction	40 (24)
Prolonged rupture of membranes (PROM)	16 (9)
Spinal anaesthesia	57 (34)
Hypertensive disorders	46 (27)
Diabetic disorders	23 (14)
Sickle cell disease	6 (4)

The majority of mothers had blood group O (66%). There were 20 (12%) Rhesus negative mothers, but only 4 (3%) had positive indirect Coombs test (IDCT). Neonatal demographics are shown in Table 2. The majority of infants were male (61%). The mean gestational age was 36.2 ± 3.1 and ranged from 24 to 41 weeks. Birthweight ranged from 670 g to 4830 g with a mean of 2696 ± 799. There were seven (4%) infants with a low five minute Apgar score (score < 7), however, only one patient had documented evidence of hypoxic ischaemic encephalopathy.

Eighty-nine (52%) infants were exclusively breastfed, 36 (21%) were supplemented/formula fed and 44 (26%) were receiving *nil* orally. Those who were getting *nil* orally were mainly admitted to the neonatal unit for reasons other than hyperbilirubinaemia. Infants who were exclusively breastfed had a significantly higher mean admission 350.7 ± 77.2 µmol/L and peak bilirubin 370.7 ± 66.7 µmol/L level than infants who were getting supplementation 233.4 ± 113.1 µmol/L and 316.73 ± 47.6 µmol/L respectively, $p < 0.01$. Nineteen (11%) infants were dehydrated on admission, 6 (32%) were hypernatraemic. Fifteen (79%) of the dehydrated infants, which included all infants with hypernatraemia, were exclusively breastfed, 9/15 (60%) of these infants were admitted from the postnatal ward. All infants with hypernatraemia also had evidence of weight loss on admission.

Table 2: Demographics of neonates with clinically significant unconjugated hyperbilirubinaemia at the UHWI 2006–2007

Variable	Frequency %
Male	103 (61)
Female	67 (39)
Term gestation	98 (58)
Preterm gestation	72 (42)
Vaginal delivery	112 (66%)
Caesarean section	58 (34%)
Forceps delivery	6 (4%)
Vacuum delivery	2 (1%)
Presentation at delivery	
Cephalic	158 (93)
Breech	10 (6)
Face	1 (1)
Cephalohaematoma	4 (2)
Excessive bruising	10 (6)

The mean ± SD age of admission was 1.8 ± 2.4 days. Neonatal jaundice was noted on day 1 to 2 in most cases (119; 70%) [Table 3]. One hundred and fifty-five neonates (91%)

Table 3: Admission characteristics of neonates with clinically significant unconjugated hyperbilirubinaemia at the UHWI 2006–2007

Variable	n	Frequency (%)
Day of life jaundice first noted	169	
Day 1		45 (27)
Day 2		74 (43)
Day 3–4		45 (26)
Day 5–6		5 (3)
Duration of stay on the postnatal ward (hours)	102	
< 24		15 (15)
24–48		48 (47)
> 48		39 (38)
Day of peak bilirubin level	170	
Day 1–2		20 (12)
Day 3–4		70 (41)
Day 5–6		57 (34)
Day 7–9		17 (10)
Day 10–15		6 (3)

had bilirubin levels done on the day of life that jaundice was first noted. Eighty-two of the102 patients (81%) who stayed on the postnatal ward had bilirubin levels checked on that ward. The peak bilirubin was seen on days 3 to 4 in 70 (41%) infants. The mean ± SD day of life of peak bilirubin level was 4.7 ± 2.1. All patients received phototherapy; duration of phototherapy ranged from 1 to 14 days with a mean of 3.0 ± 1.8 days. Nine (5%) neonates required exchange blood transfusion. There were no complications of phototherapy or exchange blood transfusion.

Haemoglobin levels ranged from 8.5 – 21.8 g/dL with a mean of 14.5 ± 2.3 g/dL. The peak total bilirubin ranged from 171 to 598 μmol/L with a mean of 340.3 ± 67.6. There were 62 (38%) infants with blood group O and 97 (59%) with blood groups A or B; 48 (29%) infants had positive Direct Coombs test (DCT).

Table 4 highlights the causes of neonatal jaundice in this study. Fifty-nine (35%) of the cases were caused by ABO incompatibility; 38 (64%) of these were DCT positive. Only 44 infants (26%) were tested for G6PD deficiency: 8 (18%) of these infants were G6PD deficient, seven of whom were male, giving a 5% incidence for the study population. Of the 16 patients diagnosed with idiopathic jaundice, only 3(19%) were tested for G6PD deficiency. Of the 103 male cohort, only 33 (32%) were tested for G6PD deficiency. ABO, Rhesus and minor blood group incompatibility were most commonly noted on day 1 to 2 of life. Fifty-two (88%) of the cases of ABO incompatibility occurred on day 1 to 2 of life while 5 (83%) of Rhesus incompatibility occurred on the same days.

Table 4: Aetiology of clinically significant unconjugated hyperbilirubinaemia in neonates at the UHWI 2006–2007

Aetiology	Frequency (%)
ABO incompatibility	59 (35)
Presumed sepsis and pneumonia	24 (14)
Prematurity only	19 (11)
Idiopathic	16 (9)
Infant of a diabetic mother	10 (6)
Dehydration	8 (5)
G6PD deficiency	8 (5)
Excessive bruises	7 (4)
Culture positive infection only	6 (4)
Rhesus isoimmunization	6 (4)
Minor group incompatibility	4 (2)
Cephalohaematoma	3 (1)

Infants admitted from home had a significantly higher mean total bilirubin level at presentation 388.4 ± 69.4 μmol/L and a significantly higher mean peak total bilirubin level 399.3 ± 62.6 μmol/L than those who were admitted from the postnatal ward 316.8 ± 77.6 μmol/L and 348.4 ± 61.5 μmol/L respectively ($p < 0.001$). The mean day of life jaundice first noted in infants admitted from home 2.1 ± 1.0 was not significantly different from those admitted from the postnatal ward (1.8 ± 0.9). However, the infants admitted from home presented significantly later 5.6 ± 2.9 days compared to those admitted from the postnatal ward 2.5 ± 1.1 days ($p < 0.001$). Fifty-nine per cent of the infants admitted from home were discharged from the postnatal ward between 24 to 48 hours; 41% were discharged after 48 hours. Twenty-six (74.3%) had bilirubin estimated on the postnatal ward before discharge. Glucose-6-phosphate dehydrogenase deficiency was the most frequent aetiology in those admitted from home (7; 20%). Of the 35 infants admitted from home, only 8 (23%) were visited by nurses from the UHWI domiciliary services prior to admission to hospital.

Nine infants (5%) received exchange blood transfusion. A male preponderance 7 (78%) was noted in the infants who required exchange blood transfusion. Four of the 9 infants (44%) had jaundice on day one of life. The other five infants had jaundice on day two to three of life. The day-of-life on admission for the cases of exchange blood transfusion ranged from day one to day six. ABO incompatibility was the cause of jaundice in 3 (33%) of the patients who received exchange blood transfusion.

One patient was discharged with a diagnosis of bilirubin encephalopathy but no follow-up assessments were documented. There were two deaths, but these were related to extreme prematurity and not directly to jaundice. Sixty-two patients (37%) were followed-up at the outpatient clinic at UHWI. Thirty (50%) had hearing tests done and they were all normal. Sixty-one (98%) had normal development at the time of the study; one patient had impaired motor development but this infant also had a myelomeningocoele.

DISCUSSION

This retrospective study encompassed 18 months of admissions to the Newborn Special Care Unit at the UHWI, Jamaica. During the study period, the incidence of neonatal jaundice requiring intervention was 4.6%. This is similar to the incidence documented for Italy (5%), India (6.5%) and Antigua and Barbuda [7.1%] (9, 10, 4).

There was a general male preponderance in this study (60%), which is in accordance with other reports (4, 10, 11). Males represented 78% of infants who received exchange blood transfusion. This concurs with research from China (12). At UHWI, ABO incompatibility (35%), infection (19%) and prematurity (11%) were more common causes of hyperbilirubinaemia than Rhesus isoimmunization (4%). This differs from previous studies from Jamaica (5, 6, 7). These results may be an indication of the success of the widespread use of anti-D gamma globulin in preventing Rhesus isoimmunization. The incidence of Rhesus isoimmunization of 4% at UHWI is lower than the 12% incidence found in Trinidad in 1986 (8). This lower incidence, however, is seen in more recent studies done in other countries such as Croatia (2.8%) and India [2.9%] (13, 10). The incidence of ABO isoimmunization of

35% in the present study is lower than that found in Trinidad in 1986 (44%), however, it is higher than more recent studies from India (6.1%) and Italy [13%] (8, 9, 10).

In the present study, only 26% of the infants were tested for G6PD deficiency; 18% of those tested were G6PD deficient giving a 5% incidence for the entire study population. The majority of these infants were male. This, however, represents a gross under-estimation of the true incidence as so few infants were tested. In Trinidad, an incidence of 21% for G6PD deficiency was seen in infants with hyperbilirubinaemia (8). Gibbs and Gray found an incidence of 20.5% for G6PD deficiency in a group of infants with neonatal jaundice at the UHWI in 1978 (7). In that study, G6PD deficiency was detected in 16 (69.6%) of a group of 23 neonates who had unexplained moderate to severe jaundice. The findings suggested that G6PD may be an important cause of neonatal jaundice in our setting. In this study, only 19% of the infants with unexplained jaundice and 33% of the male infants were tested for G6PD deficiency. Given the male gender bias for hyperbilirubinaemia and G6PD deficiency, it is paramount that G6PD testing be done on all male infants who have neonatal jaundice requiring medical intervention. Based on our results, screening for G6PD deficiency in any infant with clinically significant jaundice is not done as frequently as warranted.

Jamaica followed the recommendations of the Innocenti Declaration in support of breastfeeding and has adopted the Baby-Friendly Hospital Initiative since 1996. The present study demonstrated that infants who were exclusively breastfed had higher mean admission and peak total bilirubin levels than infants who were supplemented. This association between jaundice and breastfeeding is in keeping with that documented in other studies (10, 11, 14, 15).

Seventy-nine per cent of infants who were dehydrated on admission were being exclusively breastfed. All of the infants with hypernatraemic dehydration had evidence of weight loss. Weight loss has been cited as a risk factor for hyperbilirubinaemia in other studies, as a function of decreased caloric and fluid intake (9, 15). Sixty per cent of the infants who had dehydration and were exclusively breastfed were admitted from the postnatal ward. This may indicate that monitoring of breastfeeding on the postnatal ward may not be as rigorous as is necessary. Therefore, the recognition of infants with difficulty breastfeeding in the first 48 hours of life and the implementation of breastfeeding support and supplementation if medically indicated needs to be more aggressive on the postnatal ward.

Fifty-nine per cent of the infants admitted from home were discharged from the postnatal ward between 24 and 48 hours and the remaining infants were discharged after 48 hours. Seventy-five per cent of the infants admitted from home had received bilirubin estimation prior to discharge, yet infants admitted from home presented at a later stage in their disease process and with higher bilirubin levels. Of the infants admitted from home, only 23% were visited by nurses from the domiciliary services prior to admission to hospital. Therefore, a more thorough screening process prior to discharge from the postnatal ward and review once discharged may be warranted to identify infants at risk of developing clinically significant jaundice. Either a longer postnatal stay (> 72 hours) or an early review may decrease the number of infants being readmitted from home at a later stage of their disease process and with higher bilirubin levels. (14, 16)

In our experience, phototherapy was safe and effective and exchange blood transfusion was also a safe intervention. Follow-up, though limited, revealed minimal adverse neurological complications; however, only 50% of the infants had hearing assessment done. This is not acceptable as high bilirubin levels increase the risk of hearing impairment and all the infants should have had at least one hearing assessment done. From our findings, we recommend that all babies need to be closely monitored for jaundice in the first weeks of life with provision made for early follow-up of infants who are discharged before 72 hours of life. There should be heightened monitoring of the establishment of appropriate breastfeeding on the postnatal ward to prevent dehydration in newborn infants and mothers should not be discharged until adequate breastfeeding has been established. Routine G6PD deficiency screening in all infants with clinically significant jaundice in our population should be instituted.

To further reduce morbidity associated with neonatal jaundice at the UHWI, there should be increased screening for G6PD deficiency and current systems in place for follow-up, and monitoring of infants discharged from hospital prior to 72 hours must be expanded and strengthened.

REFERENCES

1. Britton JR, Britton HL, Beebe SA**.** Early discharge of the term newborn: a continued dilemma. Pediatrics 1994; **94:** 291–5.
2. Palmer DC, Drew JH. Jaundice: a 10-year review of 41,000 live born infants. Aust Paediatr J 1983; **19:** 86–9.
3. Dawodu A, Qureshi MM, Moustafa IA, Bayoumi RA. Epidemiology of clinical hyperbilirubinaemia in Al Ain, United Arab Emirates. Ann Trop Paediatr 1998; **18:** 93–9.
4. Martin TC, Shea M, Alexander D, Bradbury L, Lovell-Roberts Li. Did exclusive breastfeeding and early discharge lead to excessive bilirubin levels in newborns in Antigua and Barbuda? West Indian Med J 2002; **51:** 84–8.
5. Miller CG, Milner PF, Sue SL. Neonatal jaundice in Jamaican children [Abstract]. West Indian Med J 1963; **12:** 142.
6. Gibbs WN, Gray R. Glucose-6-phosphate dehydrogenase (G6PD) deficiency and neonatal jaundice in Jamaica [Abstract]. West Indian Med J 1972; **21:** 160.
7. Gibbs WN, Gray RH. Glucose-6-phosphate dehydrogenase (G6PD) deficiency and neonatal jaundice in Jamaica. Br J Haem 1979; **43:** 263–74.
8. Dillon-Remy MT, Manning-Alleyne P, Stewart V, Bratt D, Charles W. Neonatal jaundice at Port-of-Spain General Hospital [Abstract]. West Indian Med J 1987; **36 (Suppl):** 28.
9. Bertini G, Dani C, Tronchin M, Rubaltelli F. Is breastfeeding really favoring early neonatal jaundice? Paediatrics 2001; **107:** published ahead of print.
10. Narang A, Gathwala G, Kumar P. Neonatal jaundice: An analysis of 551 cases. Indian Pediatr 1997; **34:** 429–32.
11. Tiker F, Hande G, Hasan K, Aylin T, Berkan G. Extreme hyperbilirubinemia in newborn infants. Clin Paediatrics 2006; **45:** 257–61.
12. Chen LY, Lo YS, Lu CC, Tsai LT. Clinical studies of neonatal hyperbilirubinaemia treated with blood exchange transfusion [Abstract]. Gaoxiong Yi Xue Ke Xue Ze Zhi 1990; **6:** 556–64.

13. Dzinovic A, Heljic S, Maksic H, Hrnjic Z. Neonatal hyperbilirubinaemia: evaluation and treatment [Abstract]. Med Arch 2002; **56 (Suppl):** 44–5.
14. Ip S, Chung M, Kulig J, O'Brien R, Sege R, Glicken S et al. An evidence-based review of important issues concerning neonatal hyperbilirubinemia. Pediatrics 2004; **114:** 130–53.
15. Maisels MJ, Gifford K, Antle CE, Leib GR. Jaundice in the healthy newborn infant: A new approach to an old problem. Pediatrics 1988; **81:** 505–11.
16. American Academy of Pediatrics, Subcommittee on Hyperbilirubinemia. Clinical practice guidelines: Management of hyperbilirubinemia in the newborn infant 35 or more weeks of Gestation**.** Pediatrics 2004; **114:** 297–316.