Epidemiology of Neonatal Hyperbilirubinemia in Niamey: about 146 Cases Collected at Issaka Gazobi Maternity Hospital

Mounkaila B[1], Oumarou Z[4], Farya Toukoua O[3], Hassane M[2]

1. Mounkaila Boutchi: Department of Applied Biological Science, Faculty of Health Sciences Abdou Moumouni University of Niamey-Niger.

2. Hassane Moumouni: Department of Basic Sciences, Faculty of Health Sciences, Abdou Moumouni University of de Niamey-Niger.

3. Farya Toukoua Oumarou: Department of Obstetrics Gynecology, Issaka Gazobi Maternity Hospital of Niamey-Niger.

4. Oumarou Zara: Neonatology department, Issaka Gazobi Maternity Hospital of Niamey-Niger

Abstract

Neonatal hyperbilirubinemia is a major morbidity and mortality factor, especially in a context of early exit of newborns. This study is aimed at determining the frequency of this pathology and characterizing its epidemiological aspects in the Neonatology Department at Issaka Gazobi Maternity Hospital in Niamey.

This is a descriptive and cross-sectional monocentric study, expanding over 5 months in the Neonatology Department. It involved newborns with local or generalized jaundice and hospitalized in the Neonatal Department.

The frequency of neonatal jaundice was 19.5%, with a gender ratio of 1.92. On average, mothers were aged 26.4 ± 4.2 years and almost half (46.4%) of them were under 25 years old. 64.3% were term births against 35.7% of preterm births. This was due to prophylactic caesarean section (32.3%), premature membrane rupture (17.7%), fetal suffering and severe pre-eclampsia 11.8% respectively. Etiologies of these jaundices were dominated by infections (39%), neonatal malaria (17.1%) and fetal-maternal incompatibility in the ABO/Rh system (15.7%). Development was good in 69.65% of cases against 10.7% of deaths.

Infections, neonatal malaria and maternal-fetal incompatibility are the main etiologies of neonatal hyperbilirubinemia in Niamey. Mortality rate related to this pathology is very high.

Keywords: *Hyperbilirubinemia, Neonates, Jaundice, Niamey.*

I. INTRODUCTION

Bilirubin is the product of the catabolism of hemoglobin and some hemoproteins. The specifities of bilirubin metabolism in the neonatal period justifies the frequency of severe jaundice occurrences during this period of life. Indeed, in newborns, hyperbilirubinemia results from the excessive production of unconjugated bilirubin associated with low elimination due to hepatic immaturity and high intestine reabsorption. The incidence of neonatal hyperbilirubinemia is around 60% in term infants and more than 80% in preterm infants, according to Watchko [1]. Neonatal hyperbilirubinemia remains therefore a major concern due to its neurotoxin effects which generate long term consequences [2]. This is a major factor of morbidity and mortality during the neonatal period [3], [4]. Pathological neonatal Hyperbilirubinemia tends to be related to severe hemolysis of infectious or immunological origin, or red cell enzyme deficiency [5]. Neonatal jaundice risk factors also include breastfeeding type, primiparity, mothers' young age, difficult labor, asphyxia at birth [6]. Despite its multiple risk factors, the real incidence of pathological neonatal jaundice is misunderstood at Issaka Gazobi Maternity Hospital, due to the absence of documented work. In addition, the current context of early exit of newborns at Issaka Gazobi Maternity Hospital has given impetus to the issue of severe hyperbilirubinemia diagnosis and management. To bridge this gap, this study is at determining the frequency of neonatal jaundice and characterizing the epidemiological aspects of hyperbilirubinemia in the Neonatology Department of Niamey.

II. PATIENTS AND METHODS

This is a descriptive, cross-sectional, monocentric study carried out over a period of 5 months (November 2015 to March 2016) in the neonatology department of the Issaka Gazobi maternity in Niamey.

A. Patients

1. Study Population

The study population includes all newborns hospitalized in the Neonatology Department

2. Sampling

The sample for this study included newborns with local or generalized jaundice during the period covered by this study.

3. Inclusion Criteria

Newborns with medical files containing all clinical information and a biological examination including at least a blood count, bilirubin levels, ABO/Rh blood typing of infants and mothers as well as direct Coombs test are covered by this study.

4. Non-inclusion criteria

Newborns referred to the Neonatology Department by others health facilities and those with no bilirubin levels and blood count in their examination files were excluded from this study.

B. Methods

1. Biological tests

Venous blood samples were taken from newborn heels and transferred into EDTA micro tubes for blood count purposes and into dry micro tubes without anticoagulant for the determination of bilirubin. Blood count was conducted within the hour following sampling on an Abbott Diagnostics "Cell Dyn 1800" type of automated cell counter. Anemia is determined when hemoglobin level is below 14g/dl in newborns.

For the bilirubin assay, the whole blood sample is centrifuged at 2500 rpm for 5 minutes to extract the serum. In the presence of diazotized sulphanilic acid and in alkaline media, bilirubin forms a red coloured compound whose intensity is proportional to the concentration of bilirubin in the sample. Conjugated bilirubin reacts directly in aqueous solution, while free bilirubin requires solubilization in DMSO before reaction. Bilirubins are measured at 405 nm with Cypress reagents using a Cypress Diagnostic Cyan Plus semi-automatic spectrophotometer. A serum bilirubin level above 150 mg/l is considered a threshold that may cause adverse effects in the newborn.

2. Data collection

Data were collected from the medical files of mothers and infant health cards and then transferred on pre-established individual survey forms.

3. Ethics

The study was approved by the National Scientific Committee and is free of any conflicts of interest. Parents who were involved in this study agreed by informed consent.

4. Studied Parameters

Parameters studied included mothers 'age and level of education , pregnancy term, delivery method, caesarian section reasons, sex of newborns, birth weight, total bilirubin levels, haematological parameters and exit methods.

5. Data Analysis

Data were entered and analyzed on EPI info 5.3.1. The STUDENT test was used to compare quantitative variable averages and chi-2 for qualitative variables. The significance level was set at $P < 5\%$.

III RESULTS

During the period under review, 146 newborns were eligible, and distributed in groups of 96 boys and 50 girls (sex ratio 1.92), with jaundice out of a total of 750 births, i.e. 19.5% of births during the same period.

The age of mothers was 26,4 ± 4,2 years with extremes ranging from 15 years to 44 years and almost half of them (46.4%) were aged between 15 and 24 years. Most of them were illiterate and housewives (58.9%).

Based on the term of pregnancy, 64.3% of newborns were term infants and 35.7% were preterm infants (35-37 SA). Newborns whose birth weight was below 2,500g represented 30.4%, while those with birth weights above 2,500g represented 12.50 % of cases. Caesarean deliver method was used in 60.7% of cases against 39.3% for vaginal delivery.

A. Reasons for Caesarian section

The main reasons provided included the prophylactic role of Caesarean section (32.3%), premature rupture of membranes (17.7%). fetal distress and Severe pre-eclampsia represented 11.8% of cases, each (Table I).

Table I: Reasons for C section

Reasons for Caesarian section	Number of cases	Percentage
Prophylactic caesarean section	11	32.3%
Premature membrane rupture	6	17.7%
fetal suffering	4	11.8%
Severe pre-eclampsia	4	11.8%
Suspicion of disunity	2	5.9%
Stationary Dilatation	2	5.9%
Poly malformation	1	2.9%
Oligohydramnios	1	2.9%
Retroplacental hematoma	1	2.9%
intra-uterine growth retardation	1	2.9%
Narrow heaps	1	2.9%

B. Etiologies of jaundices

Depending on the intensity of jaundice, 80.3% had frank icterus against 19.7% of subictus cases. Various etiologies are summarized in table II

Table II: Etiologies of jaundices

Etiologies of jaundices	Number of cases	Percentage
Neonatal infections	57	39%
Neonatal malaria	25	17.1%
Maternal fetal Incompatibility	23	15.7%
Physiological jaundice	15	10.3%
Prematurity	13	8.9%
Unknown Causes	13	8.9%
Total	146	100%

Neonatal infections represented the main etiology of monitored jaundices, followed by neonatal malaria.

C. Hemogram study

Anemia (Hb <14g/dl) was present in 17.9% of these newbornns, thrombocypenia in 10.7% and leukopenia in 1.8% of newborns (Table III).

Table III: Distribution of newborns by blood count

Hemogram		Number of cases	Percentage
White cells	Hyperleukocytosis	30	53.6%
	Normal	25	44.6%
	Leukopenia	1	1.8%
Hemoglobin	>14g/dl	46	82.1%
	<14g/dl	10	17.9%
Platelets	Thrombocytosis	7	12.5%
	Normal	43	76.8%
	Thrombocypenia	6	10.7%

D. Bilirubinemia depending on the term of pregnancy

The study shows that 53.8% of premature inants and 41.5% of term infants had hyperbilirubinemia above 150mg/l. Table IV summarizes the intensity of bilirubinzmia depending on the term of pregnancy.

Tableau IV: Intensity of bilirubinemia depending on the term of pregnancy.

Delivery	Intensity of bilirubinemia			
	<150 mg/L	Percentage	> 150 mg/L	Percentage
Term	55	58.5%	39	41.5%
Preterm	24	46.1%	28	53.8

E. Newborn exit method

Figure 1shows delivery methods for newborns at the Maternity. Almost 1 out of 10 newborns died from complications and in 18% of cases, the delivery method was not mentioned in medical files.

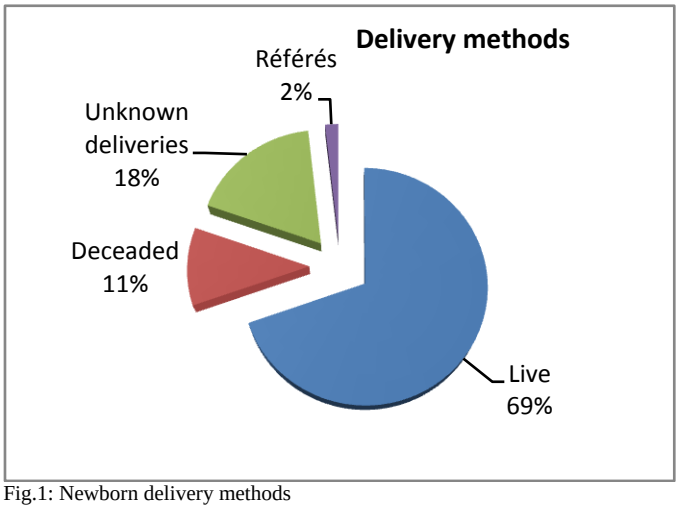

Fig.1: Newborn delivery methods

IV. DISCUSSION

During the period under review, neonatal jaundice was present in 19,5% of newborns at Issaka Gazobi Maternity Hospital. This result is significantly higher than those reported by Mutombo [7] in DRC and Olusanya [4] in Nigeria of respectively 4.9% and 6.7%. Our findings were however closer to those of Rasul [8] which stood at 22%. The frequency of neonatal jaundice occurrence also varies according to the stage of pregnancy. Indeed, Sarici [9] noted in their series that newborn jaundice was present in 10.5% and 25.3% respectively of full term newborns and preterm newborns. Variation in results observed accros studies would be attributable to selection criteria used, study environment and type, breastfeeding method, communities socio-cultural habits and genetic factors, including blood groups of variable frequency.

Gender distribution shows a high proportion of male newborns with a sex ratio of 1.92. A sex ratio of 1.8 in newborn jaundice was reported by Mutombo in DRC [7]. Predominance of male newborns led us to the hypothesis that males would be more fragile and therefore they would be more exposed to hyperbilirubinemia than females due to GPD deficit often observed in boys. This hypothesis is corroborated by Carolyn [6] and Tioseco [10] who also stressed that male sex was a risk factor associated with the occurrence of neonatal jaundice.

It was noted that the average age of mothers was 26.4 years and almost 87.5% were less than 34 years

old, including 46.43% who were under 24 years. In terms of education, 58.9% did not attend primary school. Similar results were reported by Olusanya in Lagos, Nigeria [4] with an average age of 28.0 ± 5.18 years and low level of education. Immature age, illiteracy and limited economic resources might be constraints which limit the number of prenatal consultations likely to detect on time neonatal jaundice risks.

Low birth weight (<2000g) was observed in our series in 30.40% of newborns, including 21.42% premature infants. Fetal suffering of all kinds as well as maternal fetal infections may justify the high proportion of low birth weight and premature childbirths.

Caesarean deliveries represented 60.7% of cases and the main reasons for this procedure included phrophylactic caesarean section (32.30%), RPM (17.70%), fetal suffering and Severe pre-eclampsia with 11.8% each. This high rate of caesarean section may be justified by the fact that this study was conducted in a reference maternity hospital where the majority of cases referred are emergencies. Among etiologies identified, neonatal infections were ranked first in 39% of case, followed by neonatal malaria in 19.20% of cases ABO/Rh incompatibility in 15.7% of cases. Infectious origin as the major cause of neonatal hyperbilirubinemia was also mentioned by Mutombo et al [7] in their series. For others authors, however, ABO/Rh incompatibility is the main cause of pathological hyperbilirubinemia etiologies [11], [12]. Other risk factors often mentioned in the literature include red cell constitutional abnormalities, mainly glucose-6-phosphate dehydrogenase deficiency [13], 14], [15]. Though we could not determine the activity of G6PD in our sample, previous studies showed high prevalence of this enzymopathy within our population [16], [17]. Thus, the high number of unspecified etiologies (6.8%) that we identified during this study might inter alia be related to this enzymopathy.

With regard to serum bilirubin, 53.8% of preterm newborns had developed severe hyperbilirubinemia above 150 mg/l contrary to term newborns (41.5%) (P=0,023). Preterm newborns are more likely to produce indirect bilirubin, though they are unable to excrete it. This high frequency of hyperbilirubinemmia justifies the introduction of tight and strict monitoring through the determination of transcutaneous bilirubin ;a non invasive method which is well correlated with serum essays [18]. In our study, anemia, thrombocytopenia and leukopenia were identified in 17.8%, 10.7% and 1.8% of cases. Cases of cytopenia, especially anemia, were noted by Isa et al. [19] particularly in the event of G6PD defficiency.

11% of cases had a fatal outcome. Cases of death were mentioned by Mutombo et al [7] and Hassan et al [20] with 9.16% and 0.7% respectively in their series. Several risk factors were underlined in our series, including inter alia poor conditions of mothers, their young age, absence of prenatal consultations and delayed management. We noted that in 18% of cases, the reason for exit was not mentioned in medical files. This might be justified by evasions and/or negligence in data collection. Mutombo [7] et al also noted 10 cases (8.33%) of exit by evasion or against medical opinion.

V. CONCLUSION

Neonatal hyperbilirubinemia is very common in our study. Infections, neonatal malaria and fetomaternal incompatibility are the main etiologies in our study. Prevention against these etiologies and early detection will reduce mortality. Attention should also be paid to early maternity leave, escapes and delays in the management of this pathology.

ACKNOWLEDGMENT

The authors extend their sincere thanks to the subjects who participated in this study

CONFLICT OF INTEREST

The authors declare having no conflict of interest regarding this article.

REFERENCES

[1] Watchko JF. Identification of neonates at risk for hazardous hyperbilirubinemia: emerging clinical insights. Pediatric Clinics of North America. 2009; 56, 671–687.

[2] Watchko JF. Hyperbilirubinemia and bilirubin toxicity in the late preterm infant. Clinics in Perinatology 2006; 33: 839-52;

[3] Hameed NN, Na'Ma AM, Vilms R and Bhutani VK. Severe neonatal hyperbilirubinemia and adverse short-term consequences in Baghdad, Iraq. Neonatology 2011; 100:57-63

[4] Olusanya BO, Akande A, Emokpae A and Olowe SA. Infants with severe neonatal jaundice in Lagos, Nigeria: incidence, correlates and hearing screening outcomes. Tropical Medicine and International Health. 2009; (14):301-10

[5] Phyllis A Dennery, DanieL S. Seidman, and David K. Stevenson. Neonatal hyperbilirubinemia. New England Journal of Medecine 2001;344(8)

[6] Scrafford CG, Mullany LC, Katz J, Khatry SK, LeClerq SC, Darmstadt GL and Tielsch JM. Incidence of and risk factors for neonatal jaundice among newborns in southern Nepal. Tropical Medicine and International Health, 2013;18(11): 1317-28

[7] Mutombo AK, Mukuku O, Kabulo BK, Mutombo AM, Ngeleka AM, Mutombo JD et al Ictères pathologiques du nouveau né à l'hôpital Bonzola de Mbuji-Mayi, République Démocratique du Congo. Pan African Medical Journal. 2014;19:302

[8] Rasul CH, Hasan A, Yasmin F. Outcome of Neonatal Hyperbilirubinemia in a Tertiary Care Hospital in Bangladesh. Malaysian Journal of Medical Sciences. 2010; 17(2): 40-44.

[9] Sarici SU, Serdar MA, Korkmaz A et al. Incidence, course, and prediction of hyperbilirubinemia in near-term and term newborns. Pediatrics. 2004; 113: 775–780.
[10] Tioseco JA, Aly H, Milner J, Patel K, El-Mohandes AA. Does gender affect neonatal hyperbilirubinemia in low-birth-weight infants? Pediatric Critical Care Medicine 2005; 6:171-4
[11] Alkhotani A, Eldin EEMN, Zaghloul A, Mujahid S. Evaluation of neonatal jaundice in the Makkah region. Scientific Reports. 2014; 4: 4802
[12] Esfandiarpour B, Ebrahimi H, Karkan MF, Farahmand N, Karambin MM. Neonatal exchange transfusion for hyperbilirubinemia in Guilan (the north province of Iran): a 3-year experience. Turkish Journal of Pediatrics. 2012; 54 (6): 626-631
[13] Kaplan M, Rubaltelli FF, Hammerman C, Vilei MT, Leiter C, Abramov A et al. Conjugated bilirubin in neonates with glucose -6-phosphate deshydrogenase deficiency. The Journal of Pediatrics. 1996, 128 (5):695-7
[14] Singh K, Singh P, Sagar M, Mehra V,Neki NS. Incidence, etiological risk factors and outcome of glucose-6 phosphate dehydrogenase deficiency (G6PD) among neonates presenting with hyperbilirubinemia in tertiary care hospital, Punjab. International Journal of Current Research in Medical Sciences. 2017; 3(3):62-71.
[15] Sinha R, Sachendra B, Syed VS, Nair L, John BM. To study the prevalence of glucose 6 phosphate dehydrogenase(G6PD) deficiency in neonates with neonatal hyperbilirubinemia and to compare the course of the neonatal jaundice in deficient versus non deficient neonates. Journal of Clinical Neonatology. 2017; 6: 71-4
[16] Daouda A, Mounkaila B, Maïguizo S, Moumouni Sina A, Sanogo I. G6PD deficiency: Study among 256 blood donors recruited at the blood transfusion center in Niamey. International Journal of Biotech Trends and Technology (IJBTT). 2016;16(1): 1-4
[17] Mounkaila B, Daouda A, Garba RM, Aridouane D. Neonatal glucose-6-phosphate dehydrogenase (G6PD) deficiency in Niamey. International Journal of Biotech Trends and Technology (IJBTT). 2016; 13(1): 12-14
[18] Surana AU, Patel S, Prasad R, Tilwani S, Saiyad A, Rathod M. Comparison of transcutaneous bilirubin with serum bilirubin measurements in neonates at tertiary care center in western part of india. International Journal of Contemporary Pediatrics. 2017; 4:1445-9.
[19] Isa HM, Mohamed MS, Mohamed AM, Abdulla A, Abdulla F. Neonatal indirect hyperbilirubinemia and glucose-6-phosphate dehydrogenase deficiency. Korean Journal of Pediatrics. 2017; 60(4):106-11
[20] Aletayeb H, Mohammad S, Masoud D, Aramesh Reza M, Arash Malakian; Hedayati Zeinab; Taheri Mehri. Outcome of Jaundice in neonates with ABO and Rh blood incompatibility and glucose-6-phosphate dehydrogenase deficiency. Biomedical Research. 2017; 28(8):3440-44.