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Neonatal Jaundice in Zaria, Northern Nigeria

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Summary

Werblinska B, Stankiewicz H, Oduloju MO, Atuchukwu CM and Fleming AF. Neonatal Jaundice in Zaria, Northern Nigeria. *Nigerian Journal of Paediatrics*, **1981; 8: 3.** The incidence of neonatal jaundice was only 2% of hospital deliveries in Zaria, but this was certainly a considerable underestimate. Twenty-four per cent of acutely ill new-born infants admitted to hospital were jaundiced. Of 40 consecutive jaundiced infants, 85% had infection, 40% weighed less than 200g between the third and tenth days of life and 33% were G–6–PD deficient. Causation of jaundice was multifactorial in almost all the patients; the most profound jaundice and the three deaths occurred in patients with three associated factors of infection, G–6–PD deficiency and low weight. Other causes included massive haematomas in 7·5% of the patients. ABO foeto-maternal incompatibility was a possible contributing factor in only two patients. It is concluded that antenatal care and supervised delivery with adequate facilities would prevent neonatal jaundice in most of our children.

Introduction

IN West Africa, jaundice is a common and often serious condition during the first ten days of post-uterine life. Awareness of the problem and criteria for diagnosis vary and the reported incidence among infants born in hospital ranges between 7 and 35%.[1] The commonest cause as reported by other workers is the inheritance of glucose-6-phosphate dehydrogenase (G–6–PD) deficiency. This enzyme is deficient in up to 50% of jaundiced patients,[1-5] the deficient enzyme being G–6–PD.[6] Infection is a common factor which triggers haemolysis in both the G–6–PD deficient and the G–6–PD normal infants born at home, but not in those delivered in a modern hospital.[7] Low birthweight is another associated factor present in 26% of patients in Ibadan.[7]

Foeto-maternal ABO incompatibility, another common causative factor, has been reported in up to 20% of patients.[1 3 4] The sera of 50% of group O Yoruba women recently delivered of ABO incompatible infants have been shown to contain immune anti-A or anti-B haemolysins, which are capable of crossing the placenta and lysing the red cells of infants *in utero*.[8] In contrast, haemolysis due to rhesus antibodies is rare because only about 3 to 6% of West Africans are rhesus (D) negative, and of these, only 2.5% are sensitized by their fourth pregnancy.[9]

Despite exhaustive investigations, the aetiology of jaundice remains unknown in about 30% of patients.[1]

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Neonatal jaundice has not been studied extensively in the savanna area of West Africa. The incidence of G–6–PD deficiency in males in Kano, northern Nigeria, is 20.6%.[10] The only study on neonatal jaundice in northern Nigeria was undertaken in Kaduna, but results on the role of G–6–PD deficiency were inconclusive because of difficulties in estimating enzyme activity.[11] The workers confirmed, however, the roles of infection and ABO incompatibility in neonatal jaundice.

The present study was undertaken in order to establish the aetiology of neonatal jaundice in Zaria where the population is predominantly Hausa. The other main tribal group is Yoruba who migrated from the south-west of Nigeria.

Patients and Methods

Jaundiced Infants

The study was performed at the Ahmadu Bello University (ABU) Hospital, Zaria, from February to May, 1975. There were 43 infants with serum bilirubin greater than 170 umol/l (10 mg/dl) in the first ten days of life. Thirty of these infants were delivered in the hospital and 13 were born at home and brought to the hospital because of severe illness. In no instance did a mother complain that her child was jaundiced. Data were incomplete on three infants, and the remaining 40 patients (19 males and 21 females) were compared with apparently normal control infants.

Control Infants

The great overcrowding of the labour and maternity wards in Zaria necessitated the discharge home on the first day, of all mothers and infants who were healthy after full-term normal delivery. This made it impossible to select wholly normal infants to serve as control. The only healthy infants who were in hospital up to the tenth day of life were those who were delivered by caesarian section because of maternal complications. Thirty-eight apparently healthy infants (14 males and 24 females), selected from those who were delivered by Caesarian section over the same period as the jaundiced infants were studied. They were matched with the jaundiced infants as closely as possible, for age and sex.

Weight

Birthweight was not recorded because some jaundiced infants were not seen until they were several days old. Nigerian babies are known to have lower mean birthweights than British or American babies; one of the best recorded series of Nigerian birthweights is from Igbo-Ora (112 km or 70 miles from Ibadan), where the mean birthweight of boys was 3,161.5g (± 464.2) and for girls 3,015.38 (±454.6).[12] These figures give 95% confidence limits of 2,233.1–4,089.98g for males and 2,106.1–3,924.5g for females. Experience in Zaria is similar, as 13.6% of all singletons born in hospital weighed less than 2,500g at birth.[13]

As infants normally lose up to 10% of their birthweight in the first three to five days of life,[14] it was decided to describe the three-to ten-day old infants in this study as being of "low weight" if they weighed less than 2,000g on admission. Similarly, the weights of the control infants were recorded at three to ten days, when they were included in the study.

Chemical methods

Serum bilirubin was estimated as described by Varley.[15] G–6–PD activity of red cells was measured quantitatively.[16] Results were interpreted from local standards as follows:

(*i*) G–6–PD activity less than 200mlu/ml of packed red cells indicated hemizygous male or homozygous female inheritance of deficiency,

(*ii*) activity 200–1100mlu/ml indicated intermediate or heterozygous inheritance of deficiency in females, and

(*iii*) activity above 1100mlu/ml was normal.

Haematology

Red cell indices and white cell counts were estimated by the Coulter ZF system. Reticulocyte counts, differential white cell counts, ABO blood grouping, rhesus typing, direct Coombs' test (DCT) and indirect Coombs' test (ICT) were performed by standard methods.[17] Significant haemolytic anti-A and anti-B antibodies in maternal serum were identified by the method of Worledge *et al.*[8]

Blood cultures were performed on all jaundiced but not on control infants.

Results

Hospital incidence, tribal origins and age

During the four-month period of study, there were 1,478 deliveries in the hospital, of which 30 infants (2%) developed neonatal jaundice. In the same period, 55 newborn infants were admitted to the Emergency Paediatric Unit, of whom 13 (24%) were jaundiced.

Twenty-two (55%) of the 43 jaundiced infants were Hausa, and six (15%) were Yoruba. Forty-one per cent of all deliveries in hospital were Hausa and 14% Yoruba, during the period of the study.

The diagnosis was made between the third and tenth days of life, and the commonest age at presentation was the fourth day (17 patients, 43%).

Aetiological factors

Low weight. Eighteen jaundiced and six control infants weighed less than 2,500g ($P < 0.01$); of greater significance, 16 (40%) jaundiced and none of the control infants weighed less than 2,000g ($P < 0.001$; Table I). The larger number of jaundiced than control infants weighing less than 2,000g was still significant when three pairs of twins were excluded from analysis ($P < 0.01$). Low weight was never the sole factor associated with jaundice.

TABLE I

Low weight, infection and G-6-PD deficiency in jaundiced and normal newborn infants in Zaria

		Controls	*Jaundiced*	*P**
Weight	2000g	6	16	< 0.001
	2001g+	38	24	
Weight (excluding twins)	2000g	0	10	< 0.01
	2001g+	38	24	
Infected		9	34	< 0.001
Not infected		29	6	
Males	G-6-PD deficient	0	7	< 0.05
	G-6-PD normal	14	12	
Females	G-6-PD deficient	1	6	< 0.05
	G-6-PD normal	23	15	
All	G-6-PD deficient	1	13	< 0.001
	G-6-PD normal	37	27	

*Following Finney *et al.*[21]

Infection. Thirty-four (85%) of the jaundiced infants were infected. In 23, there was septicaemia or bacteraemia demonstrated by blood cultures; the organisms isolated were *Staphylococcus aureus* (16 patients), *Streptococcus haemolyticus* (3 patients), *Klebseilla* (2 patients) and *Escherichia coli* (2 patients). *Staph. aureus* (3 patients), *Staph. albus* (one patient) and *Pseudomonas* (one patient) were isolated from septic lesions of skin or umbilicus. *Salmonella paratyphi C* was isolated from the stool of one patient. Five patients were considered to be infected because of the clinical observations of conjunctivitis (one patient), pus on the umbilicus (3 patients) and the combination of conjunctivitis, sepsis of skin and sepsis of umbilicus (one patient). Bacteriological culture did not yield specific organisms in these five patients.

Sepsis was the sole cause discovered in ten infants; it was seen in combination with low weight in 16 infants and G–6–PD deficiency in 12 infants (four infants having all three factors) (Figs. 1, 2).

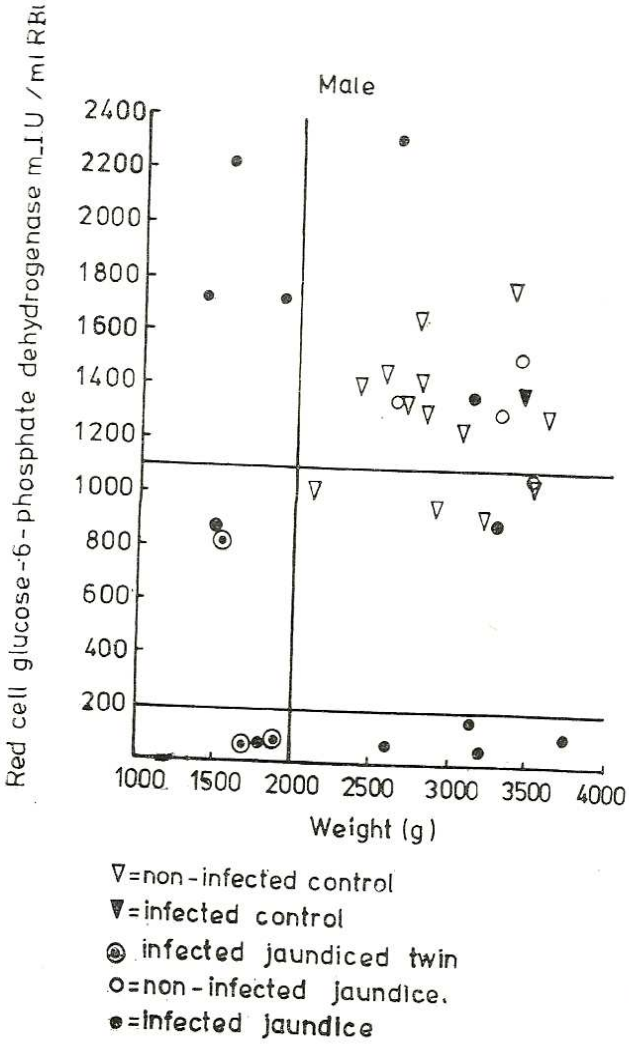

Fig. 1 Glucose-6-phosphate dehydrogenase activity, weight and incidence of infection in jaundiced and non-jaundiced male infants in Zaria.

Nine of the control infants showed mild superficial skin or umbilical infections, and the difference between the two groups (Table I) was significant ($P < 0.001$).

G-6-PD deficiency. Severe deficiency was observed in seven male and six female jaundiced infants, and in one control female infant. The frequency in the jaundiced infants (Table I) was higher in the two sexes ($P < 0.05$) and in all infants ($P < 0.001$). G-6-PD activity 800–1100mIu/ml occurred frequently in both sexes and in the jaundiced and control infants (Figs. 1,2). It would seem that the estimation as performed was not able to distinguish intermediate deficiencies in females.

G-6-PD deficiency was not the sole cause of the jaundice. Haemolysis appeared to be triggered by infection in 12 patients, of whom four were also low weight, and one was a case of possible ABO incompatibility.

Foeto-maternal incompatibility: The mothers of 24 jaundiced and 25 control infants were group O. Potential incompatibility was present in 8 jaundiced infants (two group A, six group B) and 6 control infants (two group A, four group B). The ICT and DCT were negative in all 14 infants. Two of the group O mothers of jaundiced infants had significant anti-B haemolysins which might have contributed to haemolysis. Two group O mothers of normal infants had anti-A haemolysins, but apparently unaffected group A infants. Three mothers of jaundiced and two of normal infants were rhesus (D) negative: only the two normal infants were rhesus positive and in both, the ICT and DCT were negative.

Other causes of jaundice: Three infants had massive haematomas; one infant was premature, had septicaemia, haematemesis and melaena, but in two, degradation of haemoglobin in the haematomas was the only apparent cause of jaundice.

No clear cause of jaundice was found in the three remaining infants. The mother of one had been taking herbal medicines during pregnancy because there was a history of neonatal jaundice in her family. Two of the infants had suffered hypoxia at birth, but this was the case in nine jaundiced and 13 non-jaundiced infants.

Serum bilirubin

The range of serum bilirubin in jaundiced infants was 170–524 umol/l (10.0–30.8mg/dl) with a mean of 252 umol/l (14.8mg/dl). The highest bilirubin concentrations were associated with multifactorial causation. Three of the four infants who were infected, of low weight and G-6-PD deficient, died. Kernicterus occurred in one low weight infant with mild sepsis and a bilirubin llvee of 505 umol/l (28.4 mg/dl). In

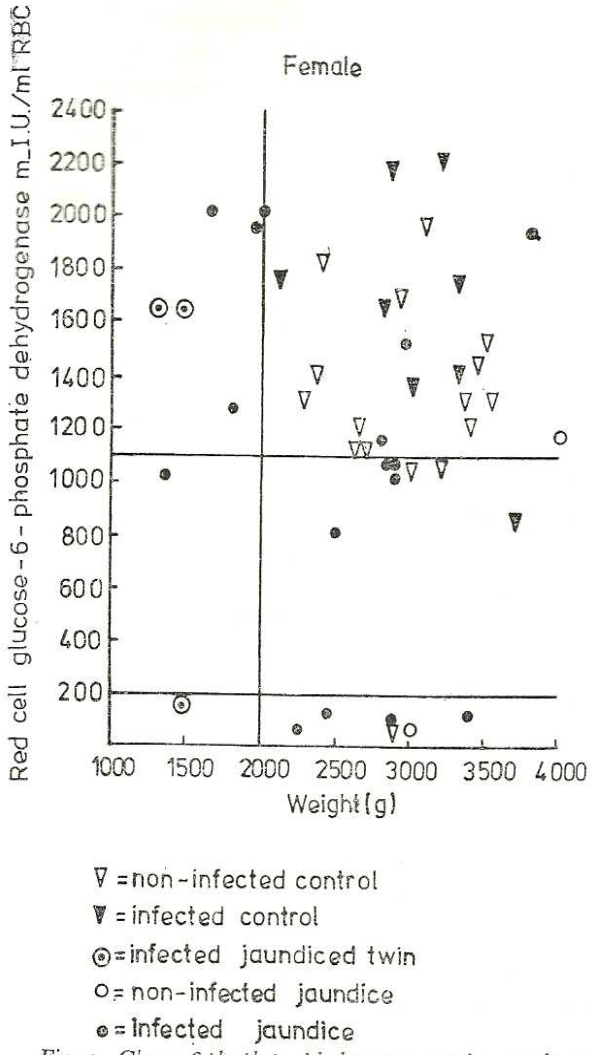

Fig. 2 Glucose-6-phosphate dehydrogenase activity, weight and incidence of infection in jaundiced and non-jaundiced female infants in Zaria.

control infants, the range was 10–102 umol/l (0.6–6mg/dl), with an average of 46.7 umol/l (2.7mg/dl).

Anaemia in the Newborn

The lowest Hb recorded in the control infants was 12.6g/dl. Six jaundiced infants had Hb. 8.0–12.5g/dl, associated with multifactorial neonatal jaundice in five and massive haematoma in one. The jaundiced infants showed evidence of a macrocytic anaemia with a reticulocytosis (Table II). None showed abnormalities of haemoglobin synthesis except sickle-cell trait in five infants. None had malaria.

Maternal haematology

The mothers of the control infants were slightly anaemic (Table III), probably due to blood-loss at Caesarian section. One mother had Hb.SC disease.

Treatment and Outcome

Five infants with serum bilirubin above 300 umol/l (18mg/dl) were treated by exchange blood transfusion, which was repeated once in one patient. The infant with a massive haematoma and anaemia was transfused with concentrated red cells. Treatment of the remaining infants included phototherapy, antibiotics and otner supportive measures.

Thirty-five infants recovered without complications. One infant was removed from hospital by his parents when he had improved, but before treatment was completed. The infant with kernicterus was treated with exchange blood transfusion, and she showed no neurological abnormality at six weeks of life, but was anaemic (Hb. 9.6g/dl). Three infants died: they were all low weight twins, with G–6–PD deficiency and sepsis.

Discussion

The triad of sepsis, low weight and G–6–PD deficiency accounted for 35 (88%) of 40 consecutive patients with neonatal jaundice in Zaria. Infection dominated the picture in 34 infants (85%) and this was regretably true both of women delivered at home and in the hospital. Sepsis was seen in Ibadan in association with G-6-PD deficiency in 56% of patients and in association with ABO incompatibility in 23% of patients with neonatal jaundice born at home,[7] but infection played no significant role in the causation of jaundice amongst infants born in hospital in Ibadan.[1] The hospital in Ibadan is spaceous and modern, whereas the hospital in Zaria is old and

TABLE II

Haematological Values in Jaundiced and Control Newborn Infants in Zaria

Investigation	*Control Infants*			*Jaundiced Infants*			*t*	*P*
	N	*Mean*	*SD*	*N*	*Mean*	*SD*		
Hb (g/dl)	38	17.2	2.1	39	15.9	3.4	2.028	<0.05
PCV	38	0.51	0.07	39	0.47	0.10	2.101	<0.05
MCHC (g/dl)	38	33.5	1.4	39	33.6	1.7	—0.516	NS
RBC (x 10^{12}/l)	31	5.39	0.77	25	4.64	0.84	3.438	<0.01
MCH (pg)	31	31.8	2.9	25	35.2	3.5	—3.467	<0.01
MCV (fl)	31	95.3	7.8	25	101.9	6.7	—3.385	<0.01
Reticulocytes (%)	31	3.5	3.0	29	5.6	4.5	—2.013	<0.05
WBC (x 10^9/l)	38	8.77	3.99	39	7.99	5.01	—0.756	NS
Neutrophils (x 10^9/l)	37	3.27	2.00	38	4.01	3.71	—1.079	NS
Lymphocytes (x 10^9/l)	37	4.66	2.40	38	3.42	1.88	2.487	<0.05
Monocytes (x 10^9/l)	37	0.43	0.46	38	0.37	0.44	0.577	NS
Eosinophils (x 10^9/l)	37	0.24	0.21	38	0.12	0.15	1.944	NS

TABLE III

Haematological Values of the Mothers of Jaundiced and Control Newborn Infants in Zaria

Investigation	*Mothers of Control Infants*			*Mothers of Jaundiced Infants*			*t*	*P*
	N	*Mean*	*SD*	*N*	*Mean*	*SD*		
Hb (g/dl)	38	9.7	1.8	37	10.8	2.1	—2.429	<0.05
PCV	38	0.30	0.05	37	0.32	0.07	—1.513	NS
MCHC (g/dl)	38	32.9	1.6	37	33.2	1.5	—1.067	NS
RBC x (10^{12}/l)	30	3.61	0.85	25	3.84	0.98	—0.919	NS
MCH (pg)	30	27.2	4.16	25	28.5	3.4	—1.224	NS
MCV (fl)	30	80.0	8.7	25	85.6	9.5	—2.227	<0.05
Reticulocytes (%)	20	3.5	1.9	21	4.1	4.2	—0.598	NS
WBC (x 10^9/l)	38	9.12	3.80	37	8.46	3.66	0.766	NS
Neutrophils (x 10^9/l)	38	6.31	3.30	36	5.87	3.22	0.580	NS
Lymphocytes (x 10^9/l)	38	2.22	0.87	36	2.10	0.88	0.590	NS
Monocytes (x 10^9/1)	38	0.24	0.27	36	0.25	0.22	—0.175	NS
Eosinophils (x 10^9/1)	38	0.33	0.33	36	0.31	0.30	0.273	NS

grossly overcrowded in the labour, maternity and nursery wards.

The second most common factor associated with jaundice in Zaria was low weight (16 infants or 40% less than 2,000g). The role of low weight was somewhat larger in Zaria than in Ibadan,[7] and was probably a reflection of the generally lower standard of living and antenatal care available in Zaria.

G-6-PD deficiency occurred in 13 patients (33%) in Zaria. This frequency was probably lower in relative terms only to that reported from Ibadan (61% in males and 34% in females), because of the much greater importance of sepsis in Zaria. Six females and seven male infants were G-6-PD deficient in the Zaria series, whereas it would be expected that males would be seen four times more commonly because of the mode of inheritance. The proportion of G-6-PD deficient females with neonatal jaundice was greater than expected in Accra and Ibadan.[1 3 7] It is possible that the homozygous inheritance in the female results in more severe haemolysis than the hemizygous inheritance in males,[18] or that the expression of deficiency is so severe in some female heterozygotes as to cause neonatal jaundice.

Neither low weight nor G-6-PD deficiency was seen as a solitary cause of jaundice in Zaria. Both were always observed in patients with sepsis, with one exception who was G-6-PD deficient and possibly complicated by haemolysis from ABO incompatibility. The most severe jaundice and the three deaths were seen in patients with all three causative factors. Low birthweight is associated with an immature immune system and a high incidence of infection. It has been suggested that G-6-PD deficiency also predisposes to infections, including viral hepatitis, pneumococcal infections and typhoid.[19] However, over-representation of G-6-PD deficiency amongst hospital patients with these infections could be the result of more complications, including haemolysis and jaundice, rather than to an increased susceptibility.

The presence of high agglutinin titres and significant titres of anti-A or anti-B haemolysins in maternal serum may be taken as presumptive evidence that haemolysis and jaundice in the infant are due to ABO incompatibility.[8 20] These criteria were met in only two jaundiced infants, but they had other causes of haemolysis and the criteria for incompatibility were met also in two control infants. It is possible that ABO incompatibility will emerge as an important cause of jaundice in the Zaria population once sepsis has been controlled and better standards of observation and treatment of patients become possible. Rhesus incompatibility was not detected in this series.

Haematoma was the fourth commonest cause of jaundice; trauma and haemorrhagic disease leading to large haematomas are rare causes of jaundice in the newborn elsewhere.

The reported incidence of neonatal jaundice in Zaria was 2% of hospital admissions and in Ibadan, 35%. The low observed incidence in Zaria was certainly due to overcrowding necessitating the discharge of women and infants from hospital within a few hours of delivery if neither showed complications, whereas all newborn infants were observed for one week in Ibadan before discharge from hospital.[1] Another factor is the awareness of jaundice by the mothers: neonatal jaundice was diagnosed more often in Yoruba than in Hausa in Kaduna, which is about 80km (50miles) south of Zaria,[11] and this was probably the consequence of the Yoruba making greater demands for hospital attention. The Yorubas were not over-represented in Zaria, possibly because of a reluctance to attend the excessively overcrowded Emergency Paediatric Unit.

The present study has shown that neonatal jaundice in Zaria results from largely preventable causes:

(i) *Adequate antenatal care:* Maternal sepsis can be prevented or treated. Drugs known to precipitate haemolysis in G-6-PD deficiency can be avoided. Many causes of premature delivery can

be prevented. Birth trauma will be reduced by anticipating difficult deliveries. ABO and rhesus incompatibility can be anticipated.

(*ii*) *Supervised delivery and puerperium:* The prevention of sepsis at this stage would reduce the incidence of neonatal jaundice in Zaria more than any other single factor. For this, adequate buildings and well qualified staff are essential.

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