Kernicterus and G6PD Deficiency—a Case Series from Oman

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Summary
The relationship between glucose-6 phosphate dehydrogenase (G6PD) deficiency and jaundice in the newborn period is well recognized. However, there is concern about the increasing incidence of kernicterus being reported worldwide, especially due to unrecognized G6PD deficiency and early discharge from hospital after birth. We report a case series of kernicterus from a set-up where the high prevalence rate of G6PD deficiency is known. Fourteen cases of kernicterus were seen during a time period of 6 years, 71 per cent of them had G6PD deficiency. Recent literature is reviewed and possible preventive measures in the light of current information and practices are suggested.

Introduction
The relationship between jaundice in the newborn period and G6PD deficiency is now well recognized. Of late, concern has been raised about the possible resurgence of kernicterus in the Western world due to less aggressive treatment of jaundice and also from unrecognized G6PD deficiency. Kernicterus due to G6PD deficiency is preventable, provided jaundice is detected early and adequate interventions are instituted promptly. High rates of G6PD deficiency is well known in the Middle Eastern population. However, despite the awareness of the high prevalence rate of G6PD deficiency and the availability of facilities for treating jaundice, a number of newborns are still developing kernicterus. It is a matter of concern from a public health point of view, considering the devastation it causes not only to the individual infant but to the family and the society at large. The main reasons for this seems to be the lack of a screening programme, unpredictability of the onset and course of jaundice, rapidity in rise of bilirubin levels, and an early discharge from the hospital after birth without proper follow-up of the high risk baby. The problem is compounded by the lack of educational programmes meant for the target population.

Here is a case series of 14 term babies with kernicterus, the majority of whom had G6PD deficiency. Available medical literature is reviewed and measures for detection and prevention of high bilirubin levels are discussed.

Materials and Methods
Records of all babies with significant jaundice (serum bilirubin (SBR) level > 250 µm/l) admitted to our unit from January 1995 to March 2001 were reviewed. A total of 4048 babies were admitted during this period; 258 (6.3 per cent) of these had significant jaundice and 87 (33.7 per cent) of these 258 babies had G6PD deficiency. G6PD status is currently tested only when jaundice is clinically detected in the newborn period, or in older children and adults presenting with anemia. Over a 3-year period from 1998 to 2001, 17,619 samples were tested in all age groups at the Royal Hospital and 3751 (21.2 per cent) were found to have no G6PD activity (Table 1).

Kernicterus developed in 14 babies accounting for a prevalence rate of 2.24/year. Table 2 shows the clinical profile of these babies. Four (28.5 per cent) babies died; 13 of these were term babies. The mean birth weight was 3020 (range 2200–4250) g. Ten out of the 14 (71.4 per cent) babies had G6PD deficiency and nine of them were males. The mean age at peak of jaundice was 5 days. The time period between detection of jaundice clinically to the peak bilirubin levels is short (Fig. 1). The mean highest SBR level noted was 532 (range 377–782) µm/l. There was a history of henna application in three babies just prior to the onset of jaundice with G6PD deficiency. No other triggering factors were noted. The hemoglobin levels did not show any appreciable drop nor was there any significant increase in reticulocyte counts (Fig. 2). This puts hemolytic process as the cause for jaundice in doubt.

All these babies were discharged home within 48 h of birth and were apparently healthy and free of jaundice. The G6PD status was not known in any of the babies at the time of discharge home. All the
babies were on exclusive breastfeeds at the time of discharge.

**Discussion**

The data presented reveals a relatively high prevalence rate of kernicterus in our set-up. One-third of the cases with significant jaundice had G6PD deficiency; it accounted for 70 per cent of the cases of kernicterus. In view of the fact that almost all these babies were perfectly normal when discharged home and that brain damage could have been prevented easily if they had presented early makes it a matter of concern.

Glucose-6 phosphate dehydrogenase deficiency is the commonest disease producing enzyme disorder of human beings. Although not all G6PD deficient babies develop jaundice, it is difficult to predict which one is likely to be a victim, due to several variables involved. Hemolysis does not seem to be the main process in the causation of jaundice in newborns. This is evident from our series also. As such, merely recommending the avoidance of triggering factors of hemolysis does not serve to prevent jaundice. The rapidity with which the SBR levels rise and the relatively late onset of jaundice (around the 4th or 5th day of life) makes it difficult for any public health measures to be instituted.

The World Health Organization recommends that neonatal screening should be performed on cord-blood samples in populations where G6PD deficiency is common (i.e., where it affects more than...
3–5 per cent of males). In Oman, G6PD deficiency is seen in 18 per cent of the population (25 per cent in males and 10 per cent in females) as per the National Genetic Blood Disorder Survey 1998. Screening should be combined with an education campaign. The Centre for Disease Control and Prevention (CDC) recommends that infants discharged less than 48 h after delivery should be examined by a health provider within 2–3 days for routine follow-up and for jaundice assessment. The awareness of G6PD deficiency must entail surveillance for jaundice until at least the 4th to 5th day of life. Parents of babies who are known to be G6PD deficient, and health workers, should be trained to detect jaundice early.

The prevention of the development of significant jaundice in G6PD-deficient neonates was hitherto considered to be impossible. However, over the past decade a series of controlled trials by a group of workers have shown the efficacy of tin protoporphyrin (Sn-PP) and mesoporphyrin (Sn-MP) in reducing the rate of bilirubin production. The action of tin is independent of the cause for jaundice. Trials in G6PD-deficient babies have shown promising results. In one study a single dose of tin mesoporphyrin (Sn-MP) at 6 mmol/kg given at birth was shown to avoid the requirement for phototherapy in 76 per cent of babies. Long-term treatment with
Sn-MP has been attempted in adolescents with Crigler–Najjar type 1, with no major side-effects.\textsuperscript{13} If safety issues could be confidently addressed, metalloporphyrins perhaps could most usefully be applied prophylactically in at-risk populations, as suggested by Cooke.\textsuperscript{14} Whether it is appropriate for all babies, or at least those found to be G6PD deficient, to receive one single dose of tin protoporphyrin or mesoporphyrin at birth (similar to vitamin K being given at birth for the prevention of hemorrhagic disease of the newborn) is worth contemplating. Perhaps a large population-based study could address this issue.

In conclusion, this paper shows a relatively high prevalence rate of kernicterus due to jaundice caused by G6PD deficiency in our setting. This being a preventable problem, it is necessary that screening programmes are introduced and public health measures such as education, surveillance and training measures are instituted.

References