NEONATAL SCREENING IN HONG KONG AND MACAU

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Abstract. For the implementation of the neonatal screening program, the following factors have to be considered for the selection of conditions to be screened and evaluation of outcome. These include the factors pertaining to public health impact, availability and acceptability of the screening system, and other social issues involved in the implementation. In the context of Hong Kong, Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency and Congenital Hypothyroidism (CHT) have been highlighted in the early 1980s for consideration. A territory wide program for screening these conditions was started in 1984. Since then, over 99% of all newborns in Hong Kong was screened. Of these, around 70% were delivered in public hospitals, and the remaining were from private hospitals. Pre-screening education was emphasized, and 95% of pregnant ladies received information about this screening program from the Maternity and Child Health Centers run by the Department of Health, Hong Kong. For those who were born in public hospitals, the incidence of CHT was 1 in 2404 (269/646,580), while that of G6PD deficiency was 4.5% in male newborns and 0.3% in female newborns. This paper highlights details of the screening program, including its outcome evaluation. In Macau, CHT screening has not been started. Instead, G6PD deficiency screening commenced in 1977 in one of the two major hospitals where most newborns are delivered. Methodology and results of this program are presented.

NEONATAL SCREENING IN HONG KONG

Hong Kong is a major city with a sizable population of 6.8 million in the year 2000. One of the major public health issues in the 1960s and 1970s was hyperbilirubinemia. In 1965, the number of neonatal deaths from kernicterus was well beyond 350. It was estimated that about 50% of these neonatal deaths were the direct result of glucose-6-phosphate dehydrogenase (G6PD) deficiency. The high incidence of this enzyme deficiency was well documented among this population (Chan *et al*, 1964; Yue and Strickland, 1965; Lai *et al*, 1968). With the advent of better medical care, including the introduction of exchange transfusion and phototherapy, the number of neonatal morbidity and mortality due to this cause had dramatically decreased in the early seventies. It was also realized at that time that hyperbilirubinemia in newborns could be significantly aggravated by the consumption of some Chinese herbs, which were prescribed to newborns in an attempt to remove the so called "Placental Toxins". During this period, healthcare professionals started to educate the public against the continuation of such practices. In addition, close proximity to mothballs and camphor, which was commonly applied to the clothing of newborns for hygienic purposes, was found to be associated with increased hyperbilirubinemia. This practice was also strongly discouraged. Such intensive campaigns to change practices of neonatal care contributed to further decrease G6PD associated mortality and morbidity in the 1970s. However, the annual neonatal mortality from kernicterus was still in the range of dozens during this period. At the start of the 1980s, in an attempt to further tackle this problem, pilot studies were conducted to study the feasibility of neonatal screening for this condition in Hong Kong. In addition, it was also recognized that congenital hypothyroidism (CHT) was also of significant prevalence among newborns in Hong Kong. Preventive measures were considered vital to salvage optimal development of patients suffering from this condition. A combined screening program for both G6PD deficiency and CHT appeared to be a logical proposition (Lo *et al*, 1996; Lo and Lam, 1996).

From the start, it was recognized that in the implementation of such a program, the entire system of events, including professionals and public education, proper sampling procedures, quality assured laboratory assays, comprehensive follow up assessments and counseling and outcome evaluations of the whole program, had to be considered. Subsequent to this feasibility study, the territory wide screening program was started in 1984, covering not only G6PD deficiency but also CHT. Such combination was found to be highly cost-effective.

Education

Pre-screening education of the whole population was conducted via different channels. Since almost 95% of pregnant ladies attend the Maternal and Child Health Centers run by the Department of Health, transmission of knowledge of these conditions were conducted during the antenatal visits. Healthcare professionals in these centers underwent training to assure competence in offering these educational sessions. This was facilitated by the production of pamphlets and audiovisual materials. The fact that the program was meant to be screening in nature instead of being diagnostic was emphasized, and information was offered in such a manner as to be non-conducive to anxiety. In addition, promotion materials were distributed via the public media.

Sampling

Since the result of G6PD activity had to be available within the first few days of life for proper management of affected neonates, placental cord blood was employed as the sample for study for both G6PD deficiency and CHT. It was considered inappropriate under this system to employ filter blood spot collected on day 5 or beyond as the sample of screening, since the critical time for intervention for hyperbilirubinemia would be missed. Initially, a comparison study was performed to evaluate whether the Fluorescence Spot test or whole blood specific enzyme activity should be performed for G6PD. It was found that the former had problems of sensitivity and technician bias. Hence, it was decided that the latter test would be employed for this purpose. The arbitrary cut off point was set at 25% of the mean G6PD activity, below each subject were considered to be deficient. For CHT, cord blood Thyroid Stimulating Hormone (TSH) was assessed. Elevation of TSH beyond 15 international units per litre was used as criteria for recalling individuals for further assessment.

Recall assessment and counseling

Neonates suspected to be suffering from either G6PD deficiency or Congenital Hypothyroidism were recalled by trained genetic nurse counselors. Counseling was provided, and reassessments of the newborns were conducted either at the Clinical Genetic Service or in Pediatric departments in hospitals where the neonates were delivered. For confirmed cases of G6PD deficiency, a packet of public information was provided to the parents. They were advised to seek further medical care during the critical neonatal period should jaundice or any symptoms presented. For suspected cases of CHT, further investigation including biochemical and radiological studies were performed. Upon confirmation of CHT, thyroxine replacement would be started during the first three weeks of life.

Results and evaluation

From year 1984 to 2000, a total of 646,580 newborns delivered in public hospitals were offered the whole screening procedures. This represented about 70% of all newborns in Hong Kong. The remaining 30% of newborns delivered in private hospitals in Hong Kong were offered free of charge laboratory screening investigations for these two conditions. In the latter situation, pre-testing education, recall assessment and counseling were conducted by private obstetricians or pediatricians. Overall, more than 99% of newborns in Hong Kong was screened. The incidence of G6PD deficiency was found to be 4.5% in males and 0.3% in females. Since the implementation of this program, the number of neonatal deaths related to hyperbilirubinemia had significantly decreased to an average of less than one per year. Issues relating to counseling of this condition had been thoroughly examined (Li *et al*, 1999). It was found that parents in general accepted this condition well and submitted that their future reproductive decisions were not adversely affected. In addition, telephone counseling was considered adequate and effective as a mode of counseling. As for CHT, the incidence was found to be 1 in 2404 (269/646,580). The Male to Female ratio of CHT was 1 to 1.84. Of these, 6.9% of babies had thyroid agenesis, 4.96% had ectopic thyroid, and the remaining 43.9% had normal thyroid scan. Average time of commencing thyroxine replacement was at the third week of life. At reassessment at three years of age, it was found that 23% of confirmed CHT patients could be taken off thyroxin replacement. This latter group was considered to be suffering from transient hypothyroidism (Sham and Lam, 1996). The occurrence of such a high incidence of transient hypothyroidism may be related to the borderline iodine deficiency in existence in Hong Kong. Subsequent follow up of children under treatment for hypothyroidism revealed normal intelligence compared with the general population.

NEONATAL SCREENING IN MACAU

Macau had a population of about 0.45 million in the year 2000. For the past decades, deliveries were mostly conducted in two major hospitals (one run by government and the other by the private sector). With similar geographical and ethnic characteristics as those found in Hong Kong, diseases of public health significance were also similar. However, for various reasons, CHT screening had not been started, while G6PD screening was conducted in one of the two hospitals (KW Hospital).

Such screening was provided on a fee for service basis. Similar to Hong Kong, placental cord blood was employed instead of filter spot as the sample. Screening was conducted by methaeomoglobin reduction test instead of fluorescence spot test or whole blood specific enzyme activity. From January 1st 1977 to 31st December 1998, a total of 51,117 samples were collected. Of these, 519 were found to be deficient in G6PD. The total incidence of G6PD deficiency was 1.15%. Of these, male incidence was found to be 1.1% (563/51,117) and female was 0.05% (27/51,117). It was suggested that the lower incidence of G6PD deficiency found in this programme may be due to subtle population difference from those of Hong Kong, or, more plausibly, technical reasons.

CONCLUSION

G6PD deficiency has been a major public health problem in Southern China, as witnessed in Hong Kong and Macau. Social and cultural factors had compounded a relative high incidence of this condition behind this phenomenon. While significant advances in medical care and health promotion efforts had contributed to decrease in morbidity and mortality associated with this condition, implementation of the screening programmes had further decreased these complications. As for CHT, neonatal screening had uncovered an unsuspected high incidence of transient hypothyroidism, which in turn led to the awareness of relative iodine deficiency in the population in Hong Kong. The latter finding would have major public health implications.

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