

CHALLENGES OF MANAGING PATIENTS WITH INHERITED METABOLIC DISORDERS IN A DEVELOPING COUNTRY

Phyllis B Acosta, Robin Sabo

Ross Products Division, Abbott Laboratories, Columbus, Ohio, USA

Abstract. The main problems encountered in managing patients with inherited metabolic disorders (IMDs) are inadequate numbers of clinicians and scientists with experience in IMDs, ill-equipped laboratory facilities, lack of funding, and lack of a well-organized plan. Other challenges that must be faced in developing countries include basic health care, birthing centers, and funding. The community environment including a clean water supply and appropriate waste disposal may also be problems. A stable communication system is necessary, as well as the means of paying for these systems. Analyses of local foods, at least for protein and energy, are required to utilize local materials in the diet. The home environment must also be considered. Adequate housing, clothing, and fuel are essential to help prevent frequent infections that may lead to serious illness or death of patients with IMDs. Adequate parental education is necessary along with adequate finances to purchase equipment to measure a prescribed diet and any necessary foods. Specialized medical, public health, community and home environments all contribute challenges of managing patients with IMDs in developing countries.

INTRODUCTION

Newborn screening is a public health program that prevents developmental and physical disabilities. In order to detect patients with inherited metabolic disorders (IMDs), universal newborn screening is essential. It is clear that children in developing countries in the Asia-Pacific area suffer from IMDs (Lee *et al*, 1999; Ozalp *et al*, 1986; 1990; Surarit *et al*, 1999; Wasant *et al*, 1999a,b,c; Wasant 1995; Zakhia *et al*, 1995) including: galactosemia, isovaleric acidemia, maple syrup urine disease (MSUD), mitochondrial fatty acid oxidation defects, methylmalonic acidemia (MMA), phenylketonuria (PKU), and others. Detecting these 'silent' disorders cannot be achieved by selective screening of already affected infants and children. Many challenges must be faced in managing patients with an IMD in a developing country. As an example, the main problems reportedly facing physicians attempting to manage patients with IMDs in Thailand are inadequate numbers of clinicians and scientists with experience in IMDs, ill-equipped laboratory facilities, lack of funding, and the lack of a well-organized plan (Wasant, 1995). There are other obstacles that must also be overcome but this paper will focus on those listed above.

CHALLENGES

Inadequate numbers of health care professionals

It is a demonstrated fact that throughout the Asia-Pacific area, health care professionals such as nurses,

laboratory technicians, pharmacists, and dietitians are lacking. In South Asia there is 0.4 physician/1,000 people and overall there is 1.5 physicians to 1000 people in East Asia and the Pacific contrasted to 1.1 physicians/1,000 people in Chile, 1.7 physicians/1,000 people in the UK, and 3.5 physicians/1,000 people in Germany where universal newborn screening is conducted (WHO, 1998; World Bank, 2001).

Lack of funding for basic and public health care

Some indices by which health care funding is measured include: (1) per capita health expenditures, (2) percentage of deliveries attended by trained personnel, (3) maternal mortality, (4) percentage of infants < 2,500 g at birth, (5) percentage of infants attended by trained personnel, (6) infant and child mortality, (7) percentage of infants immunized, and (8) vitamin A supplementation of infants and children. In all South Asia, the total per capita health expenditure was \$19 and in East Asia and the Pacific \$43, compared to \$4,306 in the US (World Bank, 2001). The percentage of infants weighing < 2,500 g at birth in East Asia and the Pacific was 59% in 2000 and 45% in South Asia, contrasted to 6% of infants in industrialized countries (UNICEF, 2000).

Infant and child mortality was very high in Cambodia where fewer trained health care personnel were available, than in some other Asian countries (Fig 1) (World Bank, 2000). By contrast, in the US there were 7 infant deaths per 1,000 live births and 8 deaths per 1,000 live births for

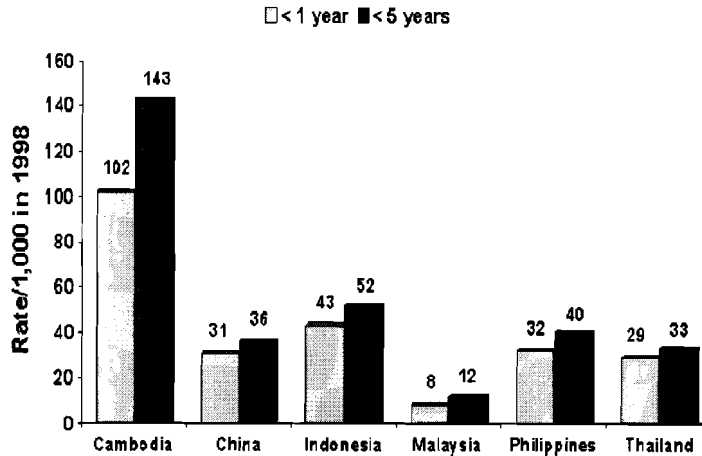


Fig 1. Comparison of infant and child mortality in selected Asian populations.

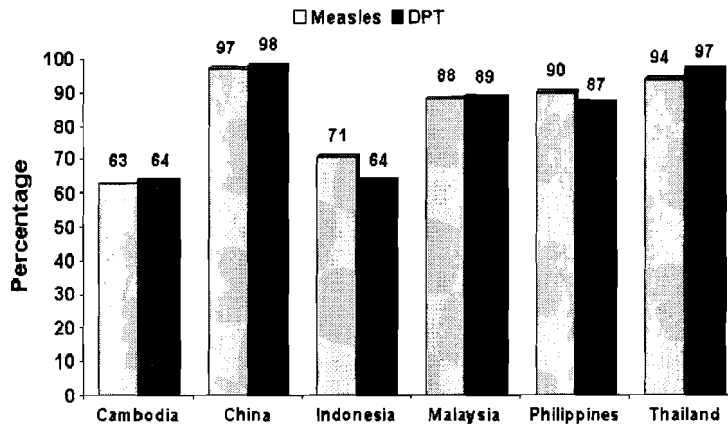


Fig 2. Percentage of infants (<12 months) immunized for measles and DPT in 1999 in selected Asian populations.

children < 5 years in 1999.

The percentage of immunized infants is also an indication of health spending priorities. Fig 2 graphically shows that Asian countries generally have good immunization rates (WHO, 1999). They compare well to the US where 96% of infants were immunized for DPT and 92% were immunized for measles.

Blindness resulting from severe vitamin A deficiency has also long been a problem in South Asia and East Asia and the Pacific. Currently, it is estimated that 1.0 million of the 1.5 million blind children in the world live in Asia (Hornby *et al*, 1999) and each year, there are 350,000 new

cases of blindness due to vitamin A deficiency (Thylefors, 1992). South Asia continues to have a high percentage of children who may become blind due to vitamin A deficiency. Many of these blind children will die within a year, partly due to severe malnutrition (UNICEF, 2000).

Community environment

Characteristics of a community are important for long-term management of patients with IMDs. Because organic acidemias depress the immune system (Hutchinson *et al*, 1985) and infection leads to catabolism (Wolf and Keusch, 1999). A safe water supply and safe waste disposal are essential for patient management. While

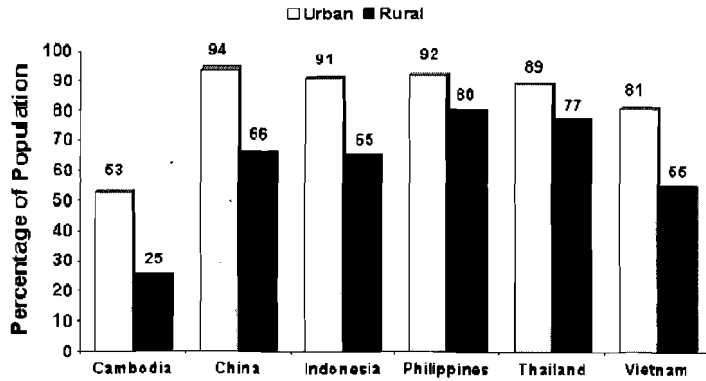


Fig 3. Percentage of population with 'safe' water supply in selected Asian countries.

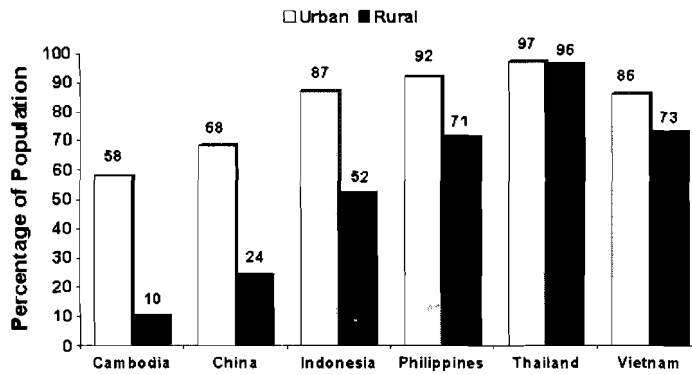


Fig 4. Percentage of population with safe waste disposal in selected Asian countries.

urban areas have made considerable progress in providing a safe water supply to the population, rural areas in many developing countries still have a significant percentage of the population with unsafe water (Fig 3).

Safe waste disposal has improved over the last 10 years, but in both Cambodia and China, a large percentage of the urban population and an even higher percentage of the rural population have unsafe waste disposal (Fig 4) (WHO, 2000).

Other characteristics of a community important to management of patients with IMDs include a

communication system, infrastructure (such as roads), and knowledge of the major nutrients in local foods. A rapid method of communicating results of newborn screening and monitoring is essential to quality care of patients with an IMD. The telephone, e-mail and telefax are often the means of communication in industrialized countries, but as can be seen in Fig 5, the number of people with telephones varies from 0.2% to 19.8% in some Asian countries (World Bank, 2000). Other methods of rapid communication would need to be developed in order to provide ongoing results of newborn screening and monitoring.

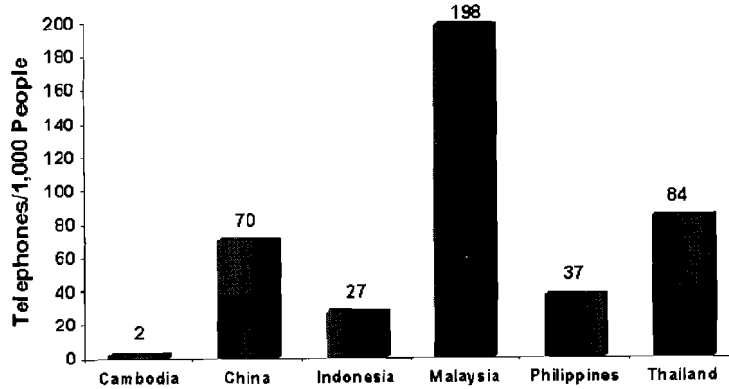


Fig 5. Telephones per 1,000 People in selected Asian countries (1998).

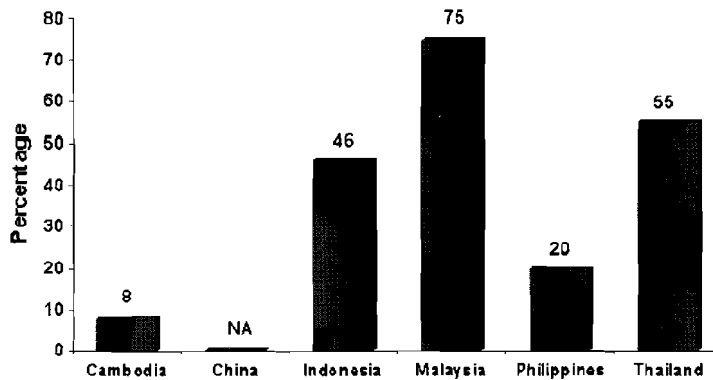


Fig 6. Paved roads as a percentage of total roads in selected Asian countries.

If adequate roads were available, IMD health care professionals could more easily travel to villages from more urban areas to monitor patients. Fig 6 (World Bank, 2000) describes the percentage of total roads paved in several Asian countries. In some countries, transportation would require specialized vehicles.

Home environment

Since food is the basis for treatment of many different IMDs, knowledge of composition of local foods, especially protein, energy, amino acids, carbohydrates, and fat composition would be helpful. Otherwise, “trial and error” becomes the approach to determining what local foods and appropriate amounts may be used in a

prescribed diet. The home environment presents many challenges to long-term management. In South Asia, East Asia and the Pacific, the GNI per capita in 1999 was \$440 and \$1,010 respectively (World Bank, 2001), and 42% of the population lives on < \$1/day in South Asia and 19% in East Asia and the Pacific (UNICEF, 2000). The lack of family funding to provide adequate food, clothing, shelter, can be related to the percentage of children stunted in growth. Moderate and severe stunting is defined as below minus 2 standard deviations from median height for age of the reference population (UNICEF, 2000). In South Asia, 52% of children are stunted and in East Asia and the Pacific, 36% of children are stunted compared to 2% in the US.

Table 1. Approximate wholesale cost* per patient for medical food for selected inherited metabolic disorders by age of patient

Disorder	per capita wholesale cost, US\$			
	(0 < 1 yr)	(1 < 4 yrs)	(4 < 7 yrs)	(7 < 11 yrs)
Phenylketonuria (PKU)	1,064	1,669	1,779	1,862
Branched chain ketoaciduria (maple syrup urine disease, MSUD)	2,054	3,221	3,443	3,594
Urea cycle enzyme defects	730	1,095	1,146	1,198

* Based on WHO recommendations for protein intake - 75% of recommended protein from medical food for phenylketonuria and maple syrup urine disease, 50% for urea cycle enzyme defects.

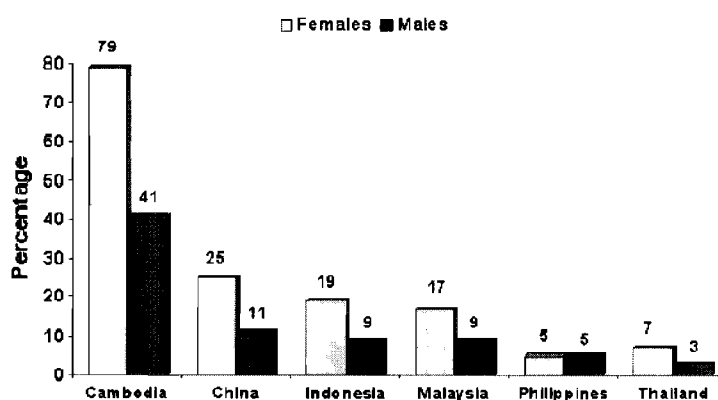


Fig 7. Percentage of population > 15 years who are illiterate (divided by sex) in selected Asian countries.

One of the challenges of providing medical foods to children with IMDs is shown in Table 1. To supply medical food for an infant with PKU, the cost is \$1,064/year. Monitoring of the diet by measuring appropriate blood analytes would add to the cost of managing the patient.

Administration of a prescribed diet for a child with an IMD requires that the mother or caregiver be able to carefully follow written directions. Of 98 families with PKU in Turkey, about 17% of mother's were illiterate (Demirkol *et al*, 1994). In Cambodia (World Bank, 2000) 79% of females ≥ 15 years of age were illiterate (Fig 7). In China, Indonesia, and Malaysia, female illiteracy was similar to that in Turkey. Illiteracy requires that health care givers design innovative approaches to teach parents how to manage the diet, often without refrigeration, measuring equipment, safe water supply, or a safe site for food storage.

Cultural mores

In many Asian countries, two generations often live in the same household and the grandmother, rather than the mother, may be the predominant caregiver. The experience of the grandparents in feeding and rearing several children may be the deciding factor in how their grandchildren are fed. Thus, family education must span more than one generation and may need to be supplied in the form of cartoons and pictures and repeated often.

CONCLUSIONS

At least one person (Velazquez, 1994) has recommended no newborn screening for IMDs, other than hypothyroidism, in a developing country. However, GNI of a country, per capita income of individuals, public funding

available for health care, level of education of individuals in the country and public health infrastructure are more likely to determine when universal newborn screening for selected disorders will begin within a country. As the GNI increases, more funding should become available for basic public health programs in maternal and child health, of which newborn screening should be a part. Increases in GNI should also lead to improvements in communication, housing, waste disposal, and roads. With improved GNI, the number of health care professionals should increase along with an improved literacy rate. With improved literacy and education, parents may see the benefits of a newborn screening program and work with health care professionals to promote national public health screening, retrieval, diagnosis, and long-term management programs. In the interim, in order to determine which IMDs have a high incidence in a developing country, screening of selected patients (developmentally disabled, patients with seizures, metabolic acidosis, failure-to-thrive, hepatomegaly, neurodegenerative disorders, hypoglycemia, sepsis of undetermined origin, etc) should be ongoing if funds are available.

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