

Organising Services for IMD in Thailand: Twenty Years Experience

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Abstract

The study of inherited metabolic disorders (IMD) in Thailand is in its infancy when compare with developed countries. Prior to 1987, majority of these disorders were clinically diagnosed since there were only a handful of clinicians and scientists with expertise in inborn errors of metabolism, lack of well-equipped laboratory facilities and government support. In developing countries, inherited metabolic disorders are not considered a priority due to the prevalence of infectious diseases such as HIV infection and congenital infections. A multicentre survey conducted in 1994 and 2001 revealed the existence of numerous cases of IMD from all over the country. Case reports and publications on IMD in Thai (and international) medical journals in past 20 years had undoubtedly raised its awareness among Thai paediatricians and scientists. In 2001, the Genetic Metabolic Centre was first established in Siriraj Hospital Faculty of Medicine, Thailand. Numerous new cases of IMD had been identified since then.

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Introduction

Milestones of IMD in Thailand

The study of inherited metabolic disorders in Thailand started in 1987. Majority of IMD were clinically diagnosed since there were only a handful of clinicians and scientists with expertise in IMD. There was also a lack of governmental interest and support due to the high prevalence of infectious diseases and congenital infections. However a multicentre survey conducted between 1994 to 2001 revealed the existence of numerous cases of IMD from all over the country. Research collaborations with United States and Japanese experts and scientists were initiated since 1989.

The First Decade (1987-1997)

Majority of IMDs were clinically diagnosed, since there were no laboratory facilities available in Thailand. In May 1990, only 1 Thai delegate (the author) attended the 5th International Congress of IEM held in Asilomar, California, United States. In June 1993, the First Asia-Pacific Regional Meeting (APRM) of the International Society on Neonatal Screen (ISNS) was held in Sapporo, Japan. Experiences from these 2 international meetings had made a great impact on the development of IMD in Thailand. In July 1994, the First Asia-Pacific Conference on Medical Genetics

was held in Bangkok, Thailand, supported by Mahidol University and International Center for Medical Research (ICMR), Kobe University, School of Medicine, Japan. Subsequently, there was a multicentre study for IMD initiated from 1994 to 1998 to collect data and explore the prevalence of IMD.^{1,2}

From 1993 to 1997, a pilot project on Newborn screening was started at Siriraj Hospital, Mahidol University in Bangkok.³ In November 1995, the 2nd APRM of ISNS was held in Hong Kong. The following year, 1996, the Department of Medical Science, Ministry of Public Health (MOPH), Thailand initiated a pilot project in newborn screening in Thailand.^{4,5}

The Second Decade (1997-2007)

In 1998, the 3rd APRM of the ISNS was organised in Chiang Mai, Thailand and was attended by more than 200 people. The objective of the meeting was to raise awareness of IMD and to educate Thai physicians (paediatricians & obstetricians) and to help nurses understand the importance of newborn screening.

From 1998 to 2000, gas-liquid chromatography/ mass spectrometry (GC/MS) was first introduced in Thailand through collaborations with Japanese scientists which led

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to previously undiagnosed organic acid disorders.^{7,8,21} Collaborations with US scientists (1993 to 2002) for tandem mass spectrometry also led to identification of newly diagnosed fatty acid oxidation disorders.^{6,8} In 2003, the first Thai textbook on IMD, a collective data on IMD as well as 15 years' of experience of IMD referrals to Siriraj Hospital was completed.⁹

In 2003, the IX International Congress on IMD (ICIEM) held in Brisbane, Australia; 2 papers on urea cycle disorders and 1 oral presentation titled "IMD in Thailand – Siriraj Experience" were presented. In 2005 – the First Genetic Metabolic Symposium was held in Bangkok to raise awareness of IMD among Thai paediatricians.

The X ICIEM was held in Chiba, Japan, in September 2006. The author of this paper was invited to be one of the local organising committee and invited speakers in "IEM in Asia" Symposium. Twenty-five newly reported cases on IMD in Thailand were presented. The 6th ISNS meeting was held in Awaji Island, Tokushima, Japan and a poster "PKU infant from newborn screening at Siriraj Hospital" was presented. The invited lecture titled "Newborn Screening in Thailand: Challenges and Opportunities" was also presented. From 2005-2008, numerous publications on molecular characterisation of IMDs in Thai patients were accomplished.¹³⁻¹⁸

Establishment of Genetic Metabolic Centre in Thailand

Research collaboration with Chulabhorn Research Institute in Bangkok since 1998 has also helped us in the area of amino acid analysis, enzyme assays and mutation analysis from which almost 20 publications were published based on pioneering works on IMD in Thailand.^{2,11,13-18}

In 2001, the Genetic Metabolic Centre was established at Siriraj Hospital Faculty of Medicine, the first of its kind in Thailand, with assistance from JICA (Japanese Intergovernmental Cooperation Agency) which provided Gas-liquid Chromatography-Mass Spectrometry (GC/MS) and technology transfer, together with funding from Chaofa-Maha Chakri Pediatric Building for High-Performance Liquid Chromatography (HPLC). Numerous new cases of IMD had been identified since then.

Multicentre Study of IEM (2001 to 2004)^{1,2,6-8,10,11}

The following IMDs were identified: (i) *Carbohydrate disorders* – galactosemia, glycogen storage diseases (GSD type I, GSD type II, GSD type III), fructose^{1,6} bisphosphatase deficiency; (ii) *Amino acid disorders* – PKU, hyperphenylalaninemia, tyrosinemia type I, MSUD, homocystinuria, albinism, NKH; (iii) *Urea cycle disorders* – ALD, OTC, ASD, unidentified UCD; (iv) *Organic acid disorders* –

Research Collaborations

(a) Research Collaborations with the United States (1987-1997)^{1-3,6,8,12}

Prof Edwin Kolodny (NYU)	Lysosomal enzyme assays
Dr Edwin Naylor (McGee Women's & Children, PA)	Tandem mass spectrometry (TMS)
Dr George Thomas (Johns Hopkins)	Amino acid analysis (AA)
Prof Hugo Moser (Kennedy Krieger Institute)	Peroxisomal disorders
Dr Robert Guthrie (New York)	Newborn screening (NBS)
Prof Saul Brusilow (Johns Hopkins)	Urea Cycle Disorders (UCD)
Dr Holmes Morton (Lancaster, PA)	Maple Syrup Urine Disease (MSUD)
Prof Vivian Shih (Boston, MA)	Amino acid analysis (AA)

(b) Research Collaborations with Japan (1997-2007)^{2,3,7,8,21}

Dr Toshiaki Oura (Osaka)	Newborn screening
Dr Hiroshi Naruse (Tokyo)	Newborn screening
Prof Isamu Matsumoto (Kanazawa)	Gas-Liquid Chromatography and Mass Spectrometry
Prof Seiji Yamaguchi (Shimane)	Tandem mass spectrometry
Prof Keiko Kobayashi (Kagoshima)	Mutation analysis (Citrullinemia)
Assoc Prof Toshihiro Shinka (Kanazawa)	Gas-Liquid Chromatography and Mass Spectrometry
Assoc Prof Kenji Hara (Fukuoka)	Gas-Liquid Chromatography and Mass Spectrometry

IVA, MMA, PA, alkaptonuria, multiple carboxylase deficiency (MCD); (v) *Mitochondrial disorders* – MCAD, translocase deficiency, carnitine deficiency; (vi) *Peroxisomal disorders* – RCDP, Zellweger, primary hyperoxaluria type I; (vii) *Lipidosis* – Niemann-Pick type I, Gaucher, Sandhoff, GM₁ gangliosidosis; (viii) *Mucopolysaccharidosis* – Hurler, Hurler - Scheie, Scheie, Hunter, Sanfilippo, Morquio, Maroteaux-Lamy, Sly, unidentified MPS; (ix) *Disorder of Purine Metabolism* – Lesch - Nyhan; (x) *Disorder of Copper Transport* – Menkes; (xi) *Leucodystrophies* – X-linked ALD, others; (xii) *Others* – lipoprotein lipase deficiency, hyperlipoproteinemia, porphyria, cystinuria, methemoglobinuria, HMG CoA lyase deficiency.

Newborn Screening Programme in Thailand

A national neonatal screening programme has been implemented into public health infrastructure by the Ministry of Public Health (MOPH) since 1996. At present, approximately 80% to 90% of all newborns are being screened for congenital hypothyroidism (CH) and phenylketonuria (PKU).^{19,20} However, many problems still exist due to a lack of systematic and holistic approach which include a lack of adequate follow-up, genetic counselling and problems with medical management. A national committee has recently been established in 2006 and problems are being solved.

Summary

Inherited metabolic disorders in Thailand is in its developing stage; however there was marked improvement in the past 20 years from clinical to biochemical diagnoses and more recently to the molecular level. There is also an increase in the number of well-trained clinical geneticists and biochemists who have taken a keen interest in the area of IMD. Though we have difficulties presenting the epidemiological data of each IMD and Thailand is not free from the prevalence of infectious diseases and congenital infections; the future of IMD in Thailand is certainly progressing well.

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