Survey on screening for inborn errors of metabolism among medical professionals caring for children in Sri Lanka

***Imalke Kankananarachchi[1], Dimuthu Liyanage[1], Udari Egodage[1], Pabasara Kalansuriya[1], Sujeewa Amarasena[1], Manjula Hettiarachchi[1]**

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Abstract

Introduction: Newborn screening (NBS) is one of the most efficient and effective ways of detecting disorders among neonates who can then be treated and have an improved quality of life. Inborn Errors of Metabolism (IEMs) are a group of rare metabolic diseases that can be diagnosed at birth.

Objectives: To assess the level of knowledge and opinion on IEMs among medical professionals in paediatric and neonatology units in Sri Lanka

Method: An online survey was carried out using an online questionnaire among paediatric / neonatology professionals in Sri Lanka from April to October 2021.

Results: Participants were from the whole of Sri Lanka (n=320), but only 309 were included after excluding incomplete responses. There were 129 consultants, 124 postgraduate trainees, and the remainder were senior house officers. All respondents knew about the existing newborn screening for congenital hypothyroidism in Sri Lanka. The awareness on screening for congenital heart diseases, congenital adrenal hyperplasia glucose-6-phosphate dehydrogenase deficiency and congenital deafness was 94%, 71%, 34% and 33%, respectively. Of the participants 96% had encountered patients with IEM, and they felt that IEM were underdiagnosed in Sri Lanka. Two hundred and fifty (81%) had heard about expanded newborn screening (eNBS), but only 54% rated average knowledge. Whilst 84% participants have justified eNBS, 67% suggested implementing it immediately. Two out of three participants felt that it should be voluntary and government-funded. However, over 58% indicated screening only for at-risk babies.

Conclusions: Of the paediatric / neonatology professionals participating in the survey, 96% had encountered patients with IEMs, and they felt that IEMs were underdiagnosed in Sri Lanka. Whilst 81% had heard about expanded newborn screening, over 58% advocated screening only at-risk babies.

(Key words: Expanded newborn screening, Inborn errors of metabolism, Paediatricians, Knowledge)

Introduction

Inborn errors of metabolism (IEMs) are a group of rare metabolic diseases with heterogeneous clinical presentations and genetic aetiologies[1]. When untreated, they can cause irreversible mental retardation, physical disability, neurological damage and even fatality[2]. Therefore, early detection and accurate diagnosis are essential for rapid and favourable patient outcomes. Although the incidence of each specific metabolic disorder is rare, their collective importance is deemed to be of considerable public health significance[3]. According to recent systematic literature reviews from 1980 to 2017, birth prevalence and case fatality of IEM were estimated to be 50.9 per 100,000 live births globally[4]. It was reported that out of 2,220 neonatal deaths in 2018, approximately 100 were undiagnosed/un-coded in Sri Lanka[5], while having 14 confirmed deaths due to IEDs.

Objectives

The present study was done among paediatric / neonatology professionals in Sri Lanka to assess their knowledge and opinions on IEMs and to assess their requirement to have expanded newborn screening (eNBS) for such disorders.

Method

An online survey was conducted from August to November 2021 using a web-based anonymous self-administered questionnaire among professionals that practise internal medicine as consultant neonatologists/paediatricians, postgraduate trainees in paediatrics, senior house officers and medical officers in paediatric units in government, private sector hospitals and military hospitals. Intern

[1]*Faculty of Medicine, University of Ruhuna, Sri Lanka*
**Correspondence:* imalke462@gmail.com
https//orcid.org/0000-0002-9351-2966

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medical officers working in paediatric setups were excluded. Contacts were made through personal contacts, social media, information available in telephone directories and health websites. Further, their assistance was requested to disseminate this online form among their colleagues. The online questionnaire consisted of 22 questions to assess the existing knowledge and opinion on eNBS in Sri Lanka.

Ethical issues: Approval for the study was obtained from the Ethical Review Committee of the Faculty of Medicine, University of Ruhuna (2021 P.009). Information on the purpose of the survey and anonymity was provided, emphasizing that their participation was completely voluntary.

Statistical analysis: The submission automatically generated Excel worksheets and forwarded such sheets directly to one of the investigators of the team. Raw data were stored without any information on identification. Data were analysed using Microsoft Excel 2016 and Statistical Package for the Social Sciences (SPSS version 23.0).

Results

From a total of 320 responses, 11 were excluded due to incomplete data. Hence, only 309 responses were taken into the analysis. Table 1 shows the basic demographic details of the respondents. Table 2 shows the knowledge of the respondents about the expanded newborn screening (eNBS).

Table 1: ***Basic demographic details of the respondents (n=309)***

Basic demographic details	Number (%)
Affiliation	
Consultant	129 (41.7)
Postgraduate trainee	124 (40.1)
Medical officer	56 (18.2)
Speciality	
General paediatrics	227 (73.4)
Neonatology	31 (10.0)
Other subspecialties	51 (16.5)
Work experience	
2-5 years	85 (27.5)
6-10 years	89 (28.8)
11-20 years	87 (28.1)
>20 years	48 (15.5)
Involved with undergraduate teaching	
Yes	137 (44.3)
No	172 (55.7)
Involved with postgraduate teaching	
Yes	167 (54.0)
No	142 (46.0)

Table 2: ***Knowledge of the respondents about the expanded newborn screening (n=309)***

Question	Number (%)
What conditions are included in the new-born screening programme in Sri Lanka?	
Congenital hypothyroidism	309 (100.0)
Congenital heart disease	289 (93.5)
Congenital deafness	220 (71.2)
Congenital adrenal hyperplasia	101 (32.7)
Have you heard about expanded inborn errors of metabolism screening before?	
Yes	250 (80.9)
No	59 (19.1)
Have you encountered children with inborn errors of metabolism in Sri Lanka?	
Yes	297 (96.1)
No	12 (03.9)
Do you think inborn errors of metabolism (IEM) are underdiagnosed in Sri Lanka?	
Yes	298 (96.5)
No	11 (03.5)
Is more education on expanded new-born screening and IEM required?	
Yes	305 (98.7)
No	04 (01.3)

Four out of five respondents had heard about the term expanded newborns screening programme (eNBS); however, the majority felt that more awareness has to be raised on the eNBS. All the consultants had come across children with IEM in their day-to-day clinical practice and were of the opinion that IEMs were still underdiagnosed. According to this survey, the commonly encountered IEMs in Sri Lanka are glycogen storage disorder, mucopolysaccharidosis and organic acidaemia (Figure 1). Opinions on the eNBS are shown in Table 3.

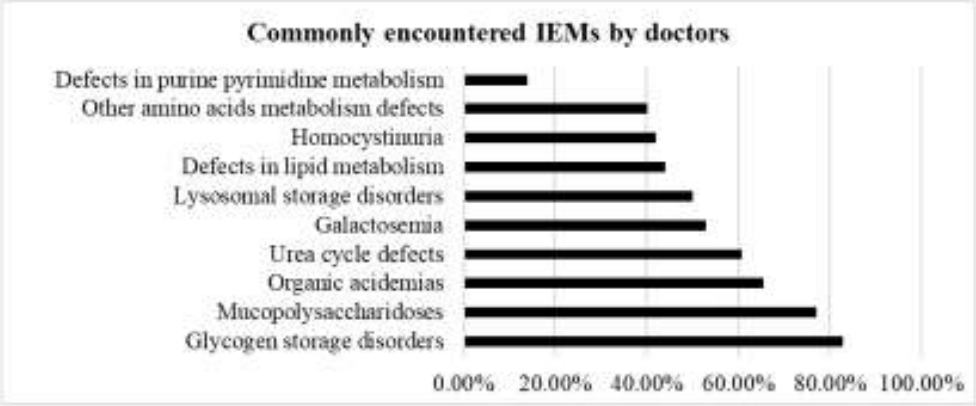

Figure 1: ***Commonly encountered inborn errors of metabolism by doctors***

Table 3: ***Opinion regarding the expanded newborn screening***

Question	Number (%)
Average annual births are around 350,000 in Sri Lanka. In 2018, there were 2220 neonatal deaths of which 100 were undiagnosed. Further, 14 deaths were confirmed as due to metabolic disorders. Do you think these numbers justify population screening?	
Yes	258 (83.5)
No	51 (16.5)
If answer is "Yes" when should expanded newborn screening be implemented in Sri Lanka?	
Immediately	207 (66.9)
3 years later	45 (14.5)
5 years later	06 (01.9)
Should the expanded newborn screening for IEM be voluntary or mandatory?	
Voluntary	197 (63.8)
Mandatory	112 (36.2)
Should the newborn screening for IEM be fully funded by the government?	
Yes	218 (70.6)
No	91 (29.4)
Are you willing to receive IEM screening to improve your patient care?	
Yes	305 (98.7)
No	04 (01.3)
Test results may not be 100% correct with possibilities of false positive and false negative risks. Babies with positive results are required for further investigations. Do you think screening is still worthwhile?	
Yes	299 (96.8)
No	10 (03.2)
What kind of expanded new-born screening you would suggest?	
Screening all newborns	129 (41.7)
Screening newborns with risk factors	180 (58.3)

IEM: inborn errors of metabolism

The majority of respondents thought that the numbers justified population screening for IEM. Furthermore, the majority wanted the eNBS to be implemented immediately. The majority preferred it to be a voluntary assessment.

Furthermore, 58% of respondents suggested screening newborns with risk factors.

Similarly, around 88% (n=271) supported the screening of incurable conditions, whereas the rest

did not support the screening of incurable IEMs. The common reasons against the screening of incurable conditions are given in Figure 2. Economic burden and unnecessary intervention were mentioned as reasons for not screening incurable conditions (Figure 3).

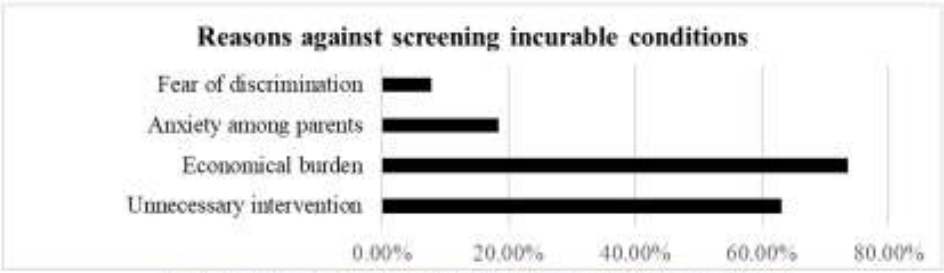

Figure 2: ***Reasons against screening incurable conditions***

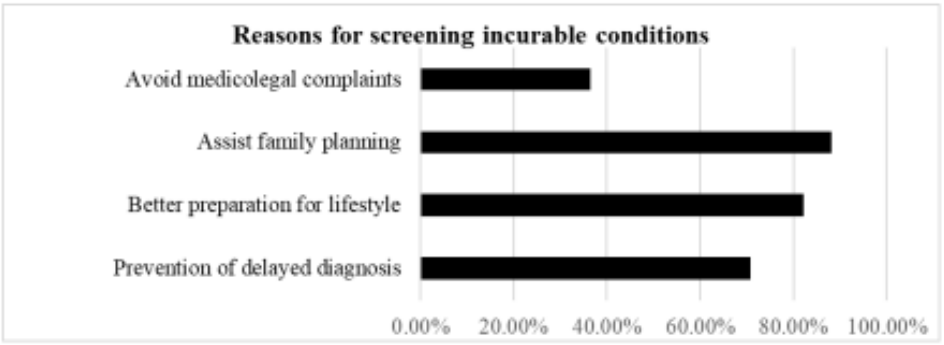

Figure 3: Reasons for screening incurable conditions

Discussion

For the first time in Sri Lanka, this study explored the feasibility assessment of expanding newborn screening opportunities among the main stakeholders in the community. A total of 424 board-certified paediatricians / neonatologists were registered at the Postgraduate Institute of Medicine, Sri Lanka, by 2022[6]. In this study, we were able to obtain the opinions from 30% of them. Most doctors (83%) support this approach of introducing an expanded screening panel. However, in the 1960s, most paediatricians were unwilling to support the initiation of the Guthrie test to identify phenylketonuria (PKU)[7]. Concerns regarding the sensitivity and specificity of the test, doubts about the treatment outcomes and unclear natural history of PKU were the main reasons for the non-acceptance of the Guthrie test[7]. However, with the development of new technologies such as tandem mass spectrometry (MS/MS), which has higher sensitivity, specificity and reliability than traditional assays, the eNBS has become a well-accepted public health intervention by many paediatricians in developed countries. In addition, more than 30 disorders can be diagnosed at birth using a single drop of blood, resulting in higher acceptance for the programme[8]. There is a growing recognition of paediatricians' role in the sustainability of the eNBS programme too[9].

Although several studies have been conducted to assess the attitude of parents toward NBS[10-13], very few studies have been found in the literature on the paediatricians' perspective on eNBS. Bansal S, *et al*[14] surveyed paediatric residents' knowledge, attitudes and practices of NBS in the USA in 2018. Most residents felt that NBS is valuable, and paediatricians play a crucial role in the NBS process. However, only 62% were comfortable with counselling the families with abnormal screening results and 56% were unaware of appropriate follow-up[14]. Moreover, a study by Acharya K, *et al*[15] in 2005 assessed the attitude of 232 paediatricians about screening for cystic fibrosis, Duchenne muscular dystrophy, fragile X, and type 1 diabetes mellitus (T1DM). It was shown that >75% of paediatricians supported screening for the aforementioned conditions except for T1DM[15].

Whereas in the current study, respondents' attitudes towards individual disorders were not considered, the screening for IEMs was taken as a group of diseases. Our data indicate that a majority of respondents were aware of the existing congenital hypothyroidism and congenital heart disease screening offered by the Ministry of Health, Sri Lanka. However, the current study did not assess the knowledge of the follow-up protocol for positive screening. In contrast, the knowledge about the available facilities for screening congenital adrenal hyperplasia and glucose-6-phosphate

dehydrogenase deficiency was substandard. The likely reason would be that the government has not yet included these two conditions in the routine programme. The knowledge gap of eNBS was assessed by Gennaccaro M, *et al*[16] and 14% of paediatricians were unaware of the eNBS, and 42% of them were not comfortable discussing eNBS with families in the USA. In our study, 19% of respondents had not heard about eNBS. Around 96% of respondents in the current study indicated that they had already seen/cared for patients with IEM in Sri Lanka during their career in paediatrics.

Even though reading and reference material are available at their fingertips, the majority of respondents in the current study indicated the need for more education on newborn screening of IEM. Similarly, 54% of paediatricians in the previous study suggested that the knowledge of IEM is inadequate[16]. Knowledge exploration and searching for novel advanced techniques need to be incorporated into the undergraduate as well as postgraduate teaching and learning environment.

Though the majority supported eNBS, 58% of the respondents felt that the programme should screen babies at risk for IEM. Out of 851 at-risk babies, 31.7% were found to have positive screening test results, and 15.6% of babies were confirmed to have IEMs in a multicentre study in India[17]. Based on the majority view, Sri Lanka may consider starting a target group newborn screening as the first step. Similar types of risk group screenings, such as screening for retinopathy of prematurity, are established in Sri Lanka. Babies born <32 weeks, birth weight <1500g and any premature, sick baby are eligible for screening among premature infants[18]. The estimated number of false-positive results per one true positive result varies from 12 to 60 depending on the specificity of the diagnostic panel and the used technology[19]. Therefore, the survey addressed this aspect, and nearly 97% of respondents supported eNBS despite high false-positive rates. Though most respondents claimed that the eNBS should be a voluntary one, it is essential to conduct further studies among parents to assess their opinion.

Conclusions

Of the paediatric / neonatology professionals participating in the current study, 96% had encountered patients with IEMs, and they felt that IEMs were underdiagnosed in Sri Lanka. Whilst 81% had heard about expanded newborn screening, over 58% advocated screening only at-risk babies.

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