Newborn Screening in Pakistan – Lessons from a Hospital-based Congenital Hypothyroidism Screening Programme

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Abstract

We are living in a time of unprecedented increase in knowledge and rapidly changing technology. Such biotechnology especially when it involves human subjects raises complex ethical, legal, social and religious issues. The establishment of newborn screening programmes in developing countries poses major challenges as it competes with other health priorities like control of infectious diseases, malnutrition and immunization programmes. Despite this, it is imperative that the importance of newborn screening programmes is recognised by developing countries as it has been proven through decades of experience that it saves thousands of babies from mental retardation, death and other serious complications. Pakistan has an estimated population of 167 million inhabitants, 38.3% of whom are under 15 years of age. Pakistan lacks a national programme for newborn screening. However, as individual practice at the local level, Aga Khan University Hospital (AKUH) and a few other hospitals are doing newborn screening for congenital hypothyroidism. The main hurdle in the implementation of newborn screening in Pakistan is the lack of good infrastructure for health. Eighty percent of deliveries take place at home. Moreover, little resources are available for children identified with a genetic condition due to the non-existence of genetic and metabolic services in Pakistan. In a 20-year audit of congenital hypothyroid screening at AKUH we found 10 babies with congenital hypothyroidism. However due to missing data links spanning several years, we were unable to calculate its true incidence during this period. In order to estimate the incidence of congenital hypothyroidism (CH) we reviewed in detail data over 10 months in 2008, a period where there was better compliance for repeat thyroid stimulating hormone (TSH) testing, and found 2 babies with CH. This gave an estimated incidence of 1 in 1600 live births.

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Introduction

We are living in an era of unprecedented increase in knowledge and rapidly changing technology. This progress in biotechnology raises complex ethical, legal, social and religious issues. Newborn screening for detection of congenital metabolic and endocrine disorders exists as established programmes in most of the developed world but its establishment in developing countries poses major challenges as other health issues like control of infectious diseases, malnutrition and immunization programmes take precedence over it.

Pakistan, a developing country with an estimated population of 167 million inhabitants, 36.3% of whom are under 14 years of age, has as yet no newborn screening programme at the national level. The crude birth rate is 38 to 40 per 1000 and the infant mortality rate is 80 per 1000 livebirths.[1] The healthcare system is mainly hospital-based and primary health care facilities are practically non-existing. Here more than 80% of deliveries occur at home and 80% of these home deliveries are usually attended by unskilled birth attendants.[2]

Pakistan has a very high consanguinity rate of 46% to 61% due to strong cultural preferences.[3] As a result we face a huge burden of inherited diseases, which contribute significantly to the alarmingly high infant mortality rate in Pakistan. Due to the lack of diagnostic facilities and absence of national registries for diseases, prevalence of various inherited diseases are not known. β thalaessemia is probably the most common single gene disorder in our population, as Pakistan is situated in the β thalaessemia belt[4] and 5.4% of Pakistanis are carriers for β thalaessemia.[5] Other inherited diseases more prevalent in the Pakistani community are

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G6PD deficiency and congenital hypothyroidism (CH). Ali et al reported a G6PD deficiency frequency of 1.8% among healthy Pakistani adults.[6]

Although Pakistan lacks a national programme for newborn screening for any inherited disease, at the local level Aga Khan University Hospital (AKUH) and few others are doing newborn screening for CH.

We present our data on CH screening over a period of 20 years. We identified hurdles a newborn screening programme can face in a developing country like Pakistan.

Patient and Methods

CH screening started at AKUH in March 1987. In the first 2 years of screening all newborns delivered at AKUH and 4 other maternity homes working under the banner of AKUH were targeted, which included 5,000 livebirths. In the subsequent years due to logistic reasons CH screening was limited to babies born at AKUH only. We covered a period of over 20 years, from 1989 to October 2008, in which a total of 53,619 babies were screened.

Venous blood samples were collected on either the second or third day of life. Thyroid stimulating hormone (TSH) levels were measured by the chemiluminescence method till 1995; afterwards the method was switched to electro-chemiluminescence. Recall strategy (Fig. 1) was planned if TSH was more than 13 mIU/L.

Results

In the first 2 years of CH screening between 1987 and 1988, 5,000 babies were screened and of these 5 were found to have CH, which was confirmed on the basis of a low T4 and high TSH as has been presented by Lakhani et al.[7]

For our audit we requested for medical records to provide the number of livebirths at AKUH per year for the period mentioned. Although we got the number of births and their medical record numbers, it was not possible to get TSH values of these babies through their medical records, as these files were still not in electronic format. Also since the TSH results usually come back after the babies are discharged the coding was not done in the records even if the values are found to be high.

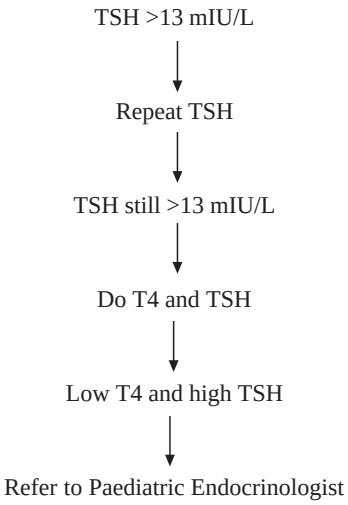

Fig. 1. Recall strategy for elevated TSH.

The next option was to request neonatal TSH data from the laboratory. We faced issues in this step as well**.** For the period between 1989 and 2008, we were unable to retrieve TSH screening results of 11,803 (22.0%) out of 53,619 babies born at AKUH. Thus screening data for only 41,816 (78.0%) babies was available for review. According to our lab reference values babies with TSH more than 13 mIU/L were to be recalled during the first 2 weeks of age for repeat TSH. There was another missing link here as repeat TSH values for the majority of babies were not available. Among the babies whose repeat TSH was more than 13 mIU/L, 10 babies were found to have low T4 and high TSH. None of these babies had radioisotope scanning of the thyroid gland done, thus the etiology of CH could not be ascertained. From January till mid-October 2008, we carefully analysed data for each and every patient. This period has lowest dropout rate with the highest compliance for repeat TSH. In this period we found 2 babies with TSH both in initial and repeat of more than 100 mIU/L. Both babies had low free and total T4 too. Based on just this year's data (10 months), a mathematical estimated incidence of CH would be about 1 in 1600 livebirths (Table 1).

Discussion

It is difficult to calculate the incidence of CH based on our data because in 22.0% of babies first TSH values were not available. Possible reasons for the missing records could be that AKUH medical records were shifted from paper to electronic and during this process some medical records were lost. A second possibility was that some of the babies were discharged before the second day of life when CH screening was supposed to be done.

Most of these discharges were on parental request. Parents were however given a lab request to get TSH screening done as out-patient, after 3 days of age. More than 80% in drop out rate was seen in repeat TSH, as the majority of parents did not come for follow-up TSH when they were recalled. Most of them probably thought that the baby had no problems because there were no symptoms. It is possible that among most of the babies who dropped out, some of them had repeated their TSH at some other laboratory for which data was not available to us. Lack of awareness among parents was another contributing factor for not repeating TSH levels. Also there are many private paediatricians in city and each one not only uses different

Table 1. CH Screening – A 20-year Audit

Year	Total birth	TSH done n (%)	CH cases detected
1989	1414	891 (63%)	1
1990	1669	776 (47%)	3
1991	1667	1400 (84%)	0
1992	1753	1554 (89%)	0
1993	1847	1700 (92%)	1
1994	1977	1701 (86%)	0
1995	2261	1680 (74%)	1
1996	2479	1976 (80%)	0
1997	2731	2114 (77%)	0
1998	2779	2403 (86%)	0
1999	2891	2296 (79%)	0
2000	2967	805 (27%)	1
2001	2909	2373 (82)	0
2002	3010	2434 (81%)	1
2003	3070	2516 (82%)	0
2004	3414	2824 (83%)	0
2005	3689	2753 (75%)	0
2006	3999	3164 (79%)	0
2007	3919	3282 (84%)	0
Jan-Oct 2008	3174	3145 (99%)	2
Total	53,619	41,816 (78.0%)	10

laboratories for testing, but also have different cut off values for raised TSH.

It has been proved through decades of experience that newborn screening saves thousands of babies from death, mental retardation and other serious complications. It is imperative that the importance of newborn screening programmes is recognised by developing countries like Pakistan and serious steps are taken at the national level to ensure successful newborn screening for conditions like CH, because it is easily diagnosed and the treatment is also very cost effective when compared to the cost of care for a mentally retarded child. Public awareness programmes should be conducted to not only educate parents about the consequences of CH but also to stress the need to initiate therapy as early as possible after birth to ensure proper brain development.

In view of the issues/deficiencies that have been identified we propose the following steps to be addressed at both institutional and national levels.

- Designate 1 or 2 physicians, to whom laboratories will report to regarding raised TSH values. These physicians should then design a system where they not only inform the patients in a timely manner, but also track the follow-up visits.
- It is our estimate, that there are many false positives (raised TSH) when we used the cut-off of 13 micro IU/mL. We have reanalysed our data with a cut-off of 20 and 25 micro IU/mL, and found that our estimated recall would be 5% and 2.3% respectively which is significantly lower than the recall rate of 15% if the cut-off for repeat TSH is kept at 13 mIU/L. This is close to what other countries in the region have reported.[8]
- Another strategy/suggestion at the national level would be to apply for a grant, which would provide an incentive to get TSH repeated free of charge. In this way, we would probably have a big enough sample size to calculate the true incidence of CH.

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