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Original Article

Newborn Screening Program: A pilot study in Ahmedabad

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Abstract

Introduction: *Newborn screening (NBS) aims towards early detection of genetic disorders which can be treated to reduce complications and mortality in early childhood.*

From September 2017 through March 2020, 31,665 newborns were screened for seven diseases namely Congenital Hypothyroidism, Congenital Adrenal Hyperplasia, Glucose-6- Phosphate Dehydrogenase (G6PD) deficiency, Sickle Cell Disease, Biotinidase deficiency, Galactosemia and Phenylketonuria at various govt colleges across Ahmedabad over a period of 3 years under the Red Cross Society Pilot Project on Newborn Screening . The incidence and gender wise distribution was analysed while comparing it with the studies from other region. There is paucity of published studies in the newborn population screening from India. The current study can serve as a substantial source of data for the region and the nation.

Methods: *Dried blood spots were taken from all stable newborns on 3rd day of life and processed on the principle of time-resolved Fluoroimmunoassay (Perkin Elmer GSP)*

Name of statistical test: *Chi-Square Test*

Results & Conclusions: *Around 4% of the population turned positive for any one of the diseases under screening. Sickle Cell Disease & Congenital Hypothyroidism were the most common (1.36% each). Biotinidase deficiency was the least common (0.18%).*

Higher incidence of Congenital Hypothyroidism was observed compared to standard literature & other studies. Racial and geographical variations can attribute to the varying prevalence amongst disorders like Sickle Cell Disease & G6PD deficiency. The thresholds implied in screening are also an important determinant.

We recommend further studies and more robust screening of newborns with subsequent accessible confirmatory tests.

Keywords: *Newborn Screening, Congenital Hypothyroidism, Congenital Adrenal Hyperplasia etc.*

Introduction

Newborn Screening is a public health program designed to screen the babies shortly after birth for a list of conditions that are treatable but not clinically evident in the early infancy.

Wilson and Jungner have outlined specific criteria that serve as a template to decide what disorders to include in the screening at a national platform[1]. The following diseases are screened routinely[2,3]:

- Congenital Hypothyroidism (1 in 2000 infants)
- Congenital Adrenal Hyperplasia (1 in 15,000- 1 in 20,000)
- Glucose-6-Phosphate Dehydrogenase enzyme activity
- Sickle Cell Disease (1 in 1,000 - US Data)
- Galactosemia (1 in 60,000 live births)
- Cystic fibrosis (1 in 9,200 in Hispanics to 1 in 15,000 African Americans)
- Phenylketonuria (1 in 14,000 to1 in 20,000).
- Biotinidase deficiency (1 in 60,000)
- Others - Amino acid disorders (Maple syrup urine disease, Homocystinuria) Fatty acid oxidation disorders (Carnitine uptake deficiency) etc.

The role of Newborn Screening in abbreviating the time between detection of an inborn disorder and the onset of clinical (especially irreversible) manifestations is undisputed. For example, early detection of Congenital Hypothyroidism prevents the impairment of neurological development and the consequent deficit of intelligence. Also, lifesaving treatment can be initiated during crisis if diagnosis is available for some potentially fataldisorders like Congenital Adrenal Hyperplasia. Universal newborn screening may also identify mild forms of inherited metabolic conditions, some of which may never cause clinical manifestations in the lifetime of the individual[2].

Undiagnosed and untreated individuals suffering from these disorders, especially those who have incurred permanent damage remain a financial burden on their families and society. Subsequent palliative interventions also amount to ineffective use of national resources and finances.

Results

In the present study, total 31,665 newborns were screened over a period of three years. The year wise break-up is shown in the given Table 1.

There is paucity of published studies in the normal newborn population screening from India[4]. The study published herewith 31,665 newborns screened over a period of 3 years which can serve as a substantial source of data for the region and can be extrapolated for the national database.

Aims and Objectives

1. To study the incidence of various genetic disorders in the population.
2. To study the difference in the incidence of these disorders both gender.
3. Comparative analysis of these conditions in two different study population.

Materials and Methods

- **Study Period**: September 2017 - March 2020.
- **Study Population**: All the stable newborns of post-natal ward delivered in the maternity care centre of the hospitals connected with the different Medical Colleges.
- **Time of sample collection**: Third postnatal day of life.
- **Method: Heel Prick Method** - This comprises drawing capillary blood from the heel, impregnation of drops of blood on to the filter paper, drying of these blood spots and transport of the specimens (CARDS) to the screening laboratory.They are processed in Perkin Elmer GSP which works on the principle of **time resolved fluoroimmunoassay**.
- **Results** are obtained within 7 days of processing. These results have been used in our study with prior permission from the Indian Red Cross Society, Ahmedabad.

Table 1 Total Newborns Screened

YEAR	MALE	FEMALE	TOTAL
2017-2018	889	890	1779
2018-2019	6758	6018	12776
2019-2020	8840	8270	17110
TOTAL	**16487**	**15178**	**31665**

Table 2. Proportion of Positives Among Screened

	SCREENED	POSITIVES	% POSITIVES
MALE	16487	721	**4.37%**
FEMALE	15178	609	**4.01%**

4.37% of male & 4.01% of female babies were screened positive for various disorder in general.

Table 3 Year Wise Break-Up of Disease & Overall Incidence in %

	TEST NAME	2017- 2018	2018-2019	2019-2020	TOTAL (%)
		(n=1779)	(n=12776)	(n=17110)	(n=31665)
1	SICKLE CELL DISEASE	30	187	217	434 (1.36%)
2	GLUCOSE 6 PHOSPHATE DEHYDROGENASE DEFICIENCY	10	90	19	119 (0.37%)
3	THYROID STIMULATING HORMONE	4	256	173	433 (1.36%)
4	BIOTINIDASE DEFICIENCY	4	51	2	57 (0.18%)
5	GALACTOSEMIA	4	30	38	72 (0.22%)
6	PHENYLKETONURIA	2	117	16	135 (0.42%)
7	17-OH PROGESTERONE LEVEL	0	51	29	80 (0.25%)
	TOTAL	54 (3%)	782 (6.1%)	494 (2.8%)	1330 (4.2%)

Overall 4.2% of all babies were screened positive for various disease. Sickle Cell Disease & Congenital Hypothyroidism were the most common amongst all **(1.36% each)**. The least common was Biotinidase deficiency (**0.18%)**.

Table 4 Sex Wise Distribution

	TEST NAME	MALES		FEMALES	
		NUMBER	INCIDENCE IN PERCENTAGE (n=16487)	NUMBER	INCIDENCE IN PERCENTAGE (n=15178)
1	SICKLE CELL DISEASE	215	**1.30%**	219	**1.44%**
2	GLUCOSE 6 PHOSPHATE DEHYDROGENASE DEFICIENCY	100	**0.61%**	19	**0.13%**
3	THYROID STIMULATING HORMONE	218	**1.32%**	215	**1.41%**
4	BIOTINIDASE DEFICIENCY	34	**0.21%**	23	**0.15%**
5	GALACTOSEMIA	39	**0.24%**	33	**0.22%**
6	PHENYLKETONURIA	62	**0.38%**	73	**0.48%**
7	17-OH PROGESTERONE LEVEL	53	**0.32%**	27	**0.18%**
	TOTAL	**721**		**609**	

Fig 1. Percentage of various diseases among positively screened neonates

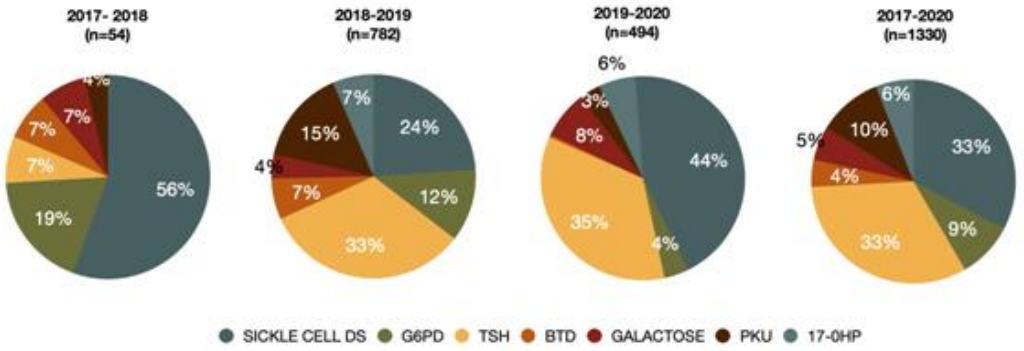
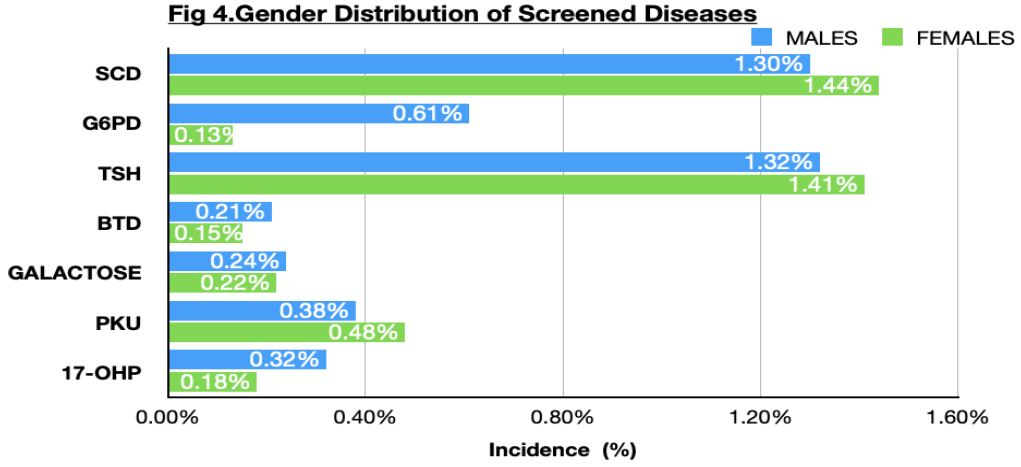


Fig 4.Gender Distribution of Screened Diseases



In the present study we observed that Glucose 6 Phosphate Dehydrogenase deficiency was five times more common in males (0.61% Vs 0.13%). Similarly, Congenital Adrenal Hyperplasia was also more frequent in males. The observed difference for both the disorders is statistically significant as the p value is < 0.05.

Although G6PD deficiency is a X- linked disorder in which only males are affected and females are carrier but according to Lyon's hypothesis, natural denaturation of a normal X chromosome in females can result into disease manifestation in them.

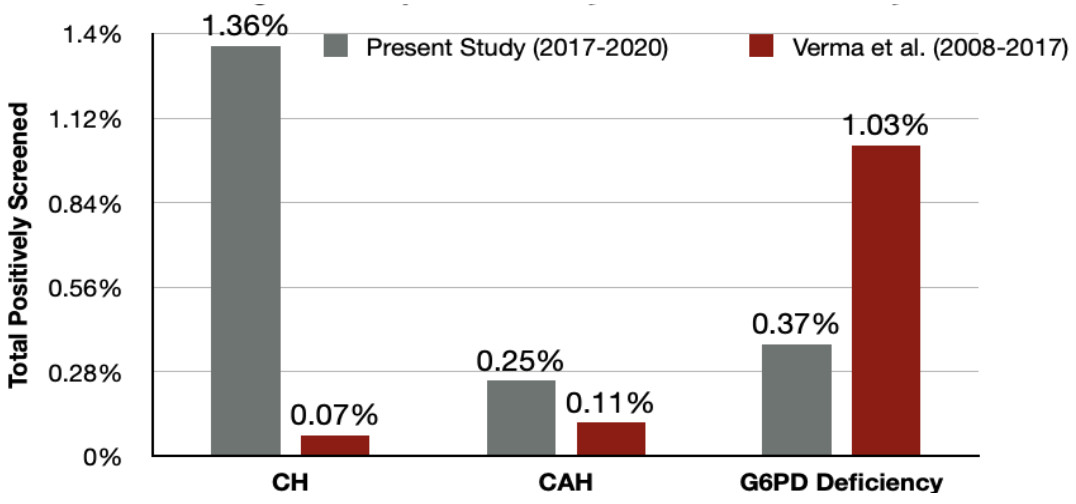
We also observed a relatively higher incidence of Sickle Cell Disease, Congenital Hypothyroidism & Phenylketonuria in females as compared to males. But the observed difference is statistically not significant as the p value was > 0.05 for all three diseases.

Table 5A Comparative analysis with similar study

TOTAL SCREENED	Present Study (2017-2020) (n=31665)	Verma et al. (2008-2017) (n=13376)
MALES	16487 **(52.06%)**	7301 **(54.58%)**
FEMALES	15178 **(47.93%)**	6075 **(45.41%)**

Table 5B. Comparative analysis with similar study

		Present Study (2017-2020) (n=31665)		Verma et al. (2008-2017) (n=13376)	
	DISEASE SCREENED	TOTAL POSITIVES	INCIDENCE IN %	TOTAL POSITIVES	INCIDENCE IN %
1	Congenital Hypothyroidism	433	**1.36%**	9	**0.07%**
2	Congenital Adrenal Hyperplasia	80	**0.25%**	15	**0.11%**
3	G6PD Deficiency	119	**0.37%**	138	**1.03%**
	TOTAL	**632**	**1.99%**	**162**	**1.21%**



As compared to Verma et al study[5], we observed a higher incidence of Congenital Hypothyroidism (1.36% vs 0.07%) & Congenital Adrenal Hyperplasia (0.25% vs 0.11%). In the present study the positively screened samples (for all diseases) were re-evaluated to minimize false positive results.

Similarly, we observed a relatively higher incidence of G6PD deficiency in Verma et al study as compared to present study (1.03% Vs 0.37%) in-spite of the higher cut-off reference value in the latter (Enzyme activity < 5.4IU / gram of Hb against < 2IU / gram of Hb).

This observed difference may be related to variation in the racial &ethnical difference between the sample selected for the study from different geographical area.

Discussions

Over a period of 3 years, we screened 31,665 newborns out of which 4.37% males and 4.01% females turned out positive for various diseases. The marginally high positivity rate in males can be explained by the fact that G6PD deficiency, which is an X-linked disorder, usually manifests in males and disease affection in females (as explained by Lyon's hypothesis) is rare.

In the year 2018-2019, 6.1% newborns were screened positive which were more than twice in comparison to the other two years. We could not find any specific reason for this observation.

Congenital Hypothyroidism and Sickle Cell Disease were the most common disorders each consisting of 1.36%. Biotinidase deficiency was the least common among all (0.18%).

Sickle Cell Disease, Congenital Hypothyroidism and Phenylketonuria were more prevalent in females although it was statistically insignificant. In few studies, ratio of congenital hypothyroidism in Male: Female was ranging from 1: 2 to 3.[8,9,10]

Compared to the study by Verma et al, we observed an overall higher positivity rate for the two diseases - Congenital Hypothyroidism and Congenital Adrenal Hyperplasia. The said difference can be due to the lower reference ranges employed for screening as in Congenital Hypothyroidism (TSH value > 13.54 microU/L against 18 micro U/L) and Congenital Adrenal Hyperplasia (17-OHP value > 43.2 nanomol/L against 90 nano mol/L)[2]. As reported by AAP (American Academy of Pediatrics), the levels of 17-OHP may also remain elevated in the first few days of life in sick & preterm neonates who are otherwise not affected[6]. A repeat screening after few days or a confirmatory test will help eliminate those false positive cases. Timing of the sample needs to be explained to all medical professionals. Methods of 17-OHP assay and the values by different methods should be standardised across the country and we should have nomograms before mass screening is applied[7].

Congenital Hypothyroidism has long been called for universal screening in newborns (as early as 1970s). Various studies from the Asia pacific region have reported the prevalence of around 1:500 to 1:5263 at birth; our study proximate the higher side with 1:623 (corrected birth prevalence after adjusting the TSH cut-offs with the standard)[8,9,10]. Being the most common preventable cause of mental handicap across the world, we strongly recommend a Nationwide Public health program for CH.

Various studies have proven considerable heterogeneity in G6PD deficiency in India owing to the diverse religious and cultural background[11,12]. The prevalence of G6PD deficiency of more than 2.5 times in the study by Verma et al compared to the present study may be related to the variations in the racial & ethnical background between these study samples which belong to different geographical area.

Textbook of Hemato-Oncology by M R Lokeshwar documented the frequency of G6PD deficiency ranging from 0 to 27% from different parts of country in different ethnics.

However, we require further studies from the same geographical area to comment upon.

Health policies in India have typically targeted mortality and infectious morbidities but not disabilities. With advancements in neonatal health facilities and development of newer diagnostic modalities, the call of the hour is to shift the paradigm towards early screening, efficient detection and better management of babies at risk before they develop irreversible damage.

Conflict of Interest: None

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