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Original Research Article

Basic new born and antenatal screening for aspirational districts: unique methods of management and treatment of inherited disorders

Komal Uppal[1], Chandrika Joshi[1], Sunil Kumar Polipalli[1]*, Somesh Kumar[1], Ankur Jindal[1], Sangeeta Gupta[2], Amar Verma[3], Seema Kapoor[1]

[1]Department of Pediatrics, [2]Department of Gynecology and Obstetrics, Maulana Azad Medical College, Delhi, India
[3]Department of Pediatrics, RIMS, Ranchi, Jharkhand, India

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***Correspondence:**
Dr. Sunil Kumar Polipalli,
E-mail: sunilpkumar18@gmail.com

ABSTRACT

Background: Early screening, diagnosis and management program can contribute in reducing the burden of genetic disorders which can lead to early neonatal death or long-term disability in the vulnerable areas. UMMID (Unique Methods of Management and treatment of Inherited Disorders) and NIDAN (National Inherited Diseases Administration), aimed at developing a community level program for need assessment and to evaluate the feasibility of basic screening for some genetic/endocrine disorders in high-risk population.
Methods: UMMID was carried out at the aspirational district Ranchi, Jharkhand for 3 years (2019-2022) to perform newborn screening (NBS) in <7 days old newborn babies for 5 metabolic disorders and to screen antenatal mothers for prevention of thalassemia and other hemoglobinopathies.
Results: G6PD deficiency being more prevalent in Ranchi district out of five metabolic disorders screened. 13.6% of screen positive cases were confirmed positive for hemoglobinopathies. c.20 A>T is the most common mutation found among carriers.
Conclusions: This initiative underscores the need of such screening programs in aspirational districts to manage and prevent these disorders effectively.

Keywords: Antenatal screening, New born screening, UMMID

INTRODUCTION

Inborn error born metabolic disorders (IEMs) , hemoglobinopathies, congenital birth defects (CBDs) and various other genetic abnormalities are significant contributors to neonatal mortality , morbidity and health burden especially in the backward states of India.[1-3] Despite the public health care services , high prevalence of these disorders in vulnerable areas attributed to factors like consanguinity, high birth rate, poor accessibility to health facilities, high cost, lack of awareness and expertise in genetic disorders, responsible for poor improvement in public health indicators. Genetic disorders like IEMs if not diagnosed at right time can present with serious complications, cause even early death in neonatal life. However, early screening, diagnosis and management program can mitigate these problems, but, such programme or national policy for genetic disorders has not yet been integrated into the health care system. Hence, pilot studies are urgently needed in vulnerable areas to assess the feasibility of a screening program.[4]

We've selected Ranchi in Jharkhand for a district-level program, as Jharkhand, constituting a lot of tribal population, is one of the empowered action group state

and like many other backward states, faces health facility shortages. So, it is very likely that mothers at high risk of having children with genetic disorders and children born with genetic disorders are being missed.

Programs like UMMID (Unique Methods of Management and treatment of Inherited Disorders) and NIDAN (National Inherited Diseases Administration), supported by the DBT (Department of Biotechnology), aimed at developing a community level program for need assessment and to evaluate the feasibility of basic screening for some genetic/endocrine disorders in high risk population to manage and prevent these disorders effectively.

METHODS

UMMID the prospective initiative was carried out at the aspirational district Ranchi, Jharkhand over a period of 3 years (2019-2022) in collaboration with RIMS (Rajinder Institute of Medical Sciences) to perform newborn screening (NBS) in newborn babies at Division of Genetics, Department of Pediatrics, Maulana Azad Medical College and associated Lok Nayak Hospital, New Delhi for 5 metabolic disorders G6PD, CH, Galactosemia (GALT), biotinidase deficiency (BTD) and congenital adrenal hyperplasia (CAH) in neonates by fluorimetric assays, to identify screen positives and perform confirmatory testing within a turnaround time of 14 days and to initiate therapy within 14 days at least for CH and to screen antenatal mothers for prevention of thalassemia and other hemoglobinopathies by High Performance Liquid Chromatography (HPLC).

Screening of all antenatal mothers by red cell indices, sickling test and HB electrophoresis between period from identification of pregnancy to 18 weeks of gestation period and of all women during preconception period attending the health facility was done. Spouses of the pregnant carrier woman was also tested and molecular testing for HBB gene was done for the carrier couple. All the antenatal mothers who underwent screening took antenatal care in the Department of Gynecology and Obstetrics at RIMS. For prenatal testing referrals were done to the department of Gynecology and Obstetrics at Lok Nayak Hospital after appropriate counselling. Awareness and sensitization of the public and students (XI^{th}, XII^{th}, College) was also done by awareness and academic programs about newborn screening and hemoglobinopathy antenatal screening. Informed consent and ethical approval was obtained.

Inclusion criteria

Newborn babies who's <7 days old, pregnant mothers attending the district hospital of the identified district between period from identification of pregnancy to 18 weeks of gestation were included.

Exclusion criteria

Babies who died at the time of birth or who went against medical advice within 24 hrs of life or whose family did not give consent, antenatal mothers who did not give consent were excluded.

Standard operating procedures were carried out to perform screening. Babies having externally visible birth defects (VBDs), congenital heart diseases and other genetic disorders were also identified at the time of screening. All identified babies were managed at Lok Nayak Hospital, New Delhi. Continuous follow up by each district for all newborns is being done as per project protocol.

Sample size

All the babies born at RIMS and all the antenatal mothers who took antenatal care in the department of Gynecology and Obstetrics at RIMS and attending the district hospital of the identified district during the period of study fulfilling the inclusion criteria.

RESULTS

Here, we are providing preliminary results from September 2019- June 2021 for newborn screening for 5 metabolic disorders and antenatal screening. Out of 8547 were live births, 5369 were screened for 5 metabolic disorders. Demographic data of screened babies is shown in Table 1. Prevalence rate of all the five metabolic diseases is shown in Table 2 and the data of antenatal screening for hemoglobinopathies is shown in Figure No.1. Spectrum of mutation for carrier couple is shown in Table 3.

Table 1: Demographic data of screened babies.

Total number of screened babies n=5369	
Gender	**Percentage**
Male	48
Female	52
Birth weight	
< 2.5 kg	22
> 2.5 kg	78
Gestation	
< 34 weeks	5
≥ 34 weeks	95

Table 2 showing 267 babies screen positive out of 5369 babies who were screened for 5 metabolic disorders, 31 confirmed positive and prevalence of 5 metabolic disorders. G6PD deficiency being more prevalent in Ranchi district.

Among 32 couples, 13 couples underwent prenatal invasive testing (46% amniocentesis and 54% chorionic villi sampling), out of which for 4 couples IVS 1:5 (G>C)

homozygous mutation was seen, for one c.20A>T homozygous mutation was identified, 2 showed IVS 1:5 (G>C) heterozygous mutant and 2 showed c.20 A>T heterozygous mutant. All the newborn babies and antenatal couple identified with the disease referred to tertiary health care center for further management according to project protocol after proper genetic counselling and explaining about the consequences of the disease.

Table 2: Showing 267 babies screen positive out of 5369 babies who were screened for 5 metabolic disorders.

Test performed	Initial positive	Confirmed positive	Clinical follow-up	Prevalence (%)
hTSH-for CH	16	2	2	0.023
17OHP for CAH	3	0	0	0
BTD for biotidinasedeficiency	11	5	5	0.058
TGAL for galactosemia	4	0	0	0
G6PD deficiency	233	24	24	0.28

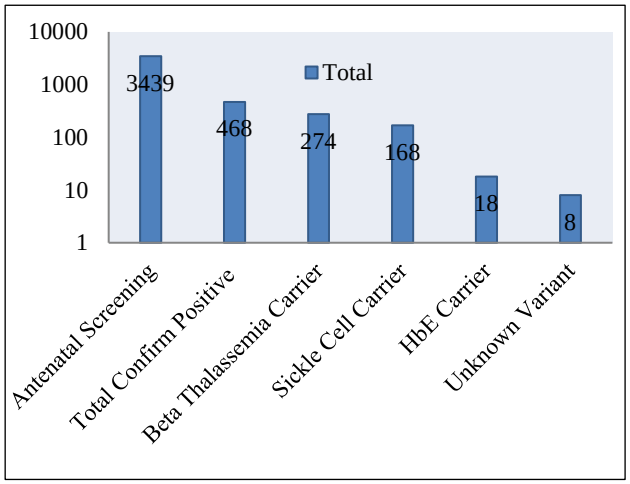

Figure 1: Antenatal screening and confirmed positive cases for hemoglobinopathies.

Table 3: Spectrum of mutation in individuals among couples (n=32).

Mutations	Number of carriers
IVS 1-5 (G-C)	27
Cd. 26 (G>A)	1
c.20 A>T	33
HbE carrier	1
c.79G>A	1
-88 (C-G)	1

DISCUSSION

Previous data has unveiled congenital hypothyroidism being the most prevalent disorder in India yet other disorders also fulfill the criteria for newborn screening (NBS) and cost-benefit analysis, and convincing the need for implementing a NBS programme in India.[5] Our pilot programme reported the prevalence of 0.023% of CH, 0% of CAH, 0.28% of G6PDD, 0.058% of BTD and 0% GALT in the district of Ranchi. Antenatal results showed 13.6% of confirmed positive for hemoglobinopathies out of which 7.96% were carrier for thalassemia, 4.88% were sickle cell disease carrier, 0.5% were Hb E carrier and in 0.23% of cases variants were unknown. Molecular testing in carrier couples showed spectrum of different mutations with c.20 A>T being the most common one.

While different studies showed varied prevalence of metabolic disorders and hemoglobinopathies. Previous literature showed prevalence of 0.029-0.40% for CH, 0.01% - 0.05% for CAH, 0.8-6.3% for G6PDD, 0.001% - 0.0007% for BTD, 0.001-0.003% for GALT in western countries, Indian data regarding GALT prevalence is scanty. Various studies estimated prevalence of hemoglobinopathies 7% -9.75%; beta thalassemia minor 5.08%-40.8%, sickle cell trait 4.03%-27.6%, Hb D Punjab 0.52% and Hb Q India 0.17%, sickle cell anemia 2%, borderline thalassemia trait 29.6%.[6-13]

Ghosh et al reported approximately 90% individuals had one of the 5 common mutations in decreasing order of frequency: IVS 1-5 G>C (1297/2128); codon 26G>A/HbE (451/2128); codon 30G>C (69/2128); codon 15G>A (61/2128); FS41-42–CTTT (48/2128). Undetected mutations amounted to 7.3% (156/2128).[14]

Varied prevalence of these disorders showed that estimating their prevalence is crucial for health service providers and administrators to implement screening programs confidently.[15,16] This variation can be due to different coverage rate of newborns attributing factors like the number of live births, administrative services, financial support, regional influences, and education levels.[16]

In our project, lower prevalence may result from shorter newborn stays with discharge less than 24 hours, NICU admissions, the COVID-19 pandemic, arrival of mothers after the window period of 18 weeks and challenges in recall and directive counseling of spouses of carrier women. Despite the lower prevalence, our project having unique feature of being an outreach program in the

vulnerable region which along with IEMs also got the chance to identify babies with hemoglobinopathies, VBDs, congenital heart disease, and other genetic disorders. Along with feasibility of NBS and antenatal screening demonstration it also raised the need of awareness about these program among the medical practitioners towards their respective responsibilities in offering Newborn screening (NBS) and prenatal screening for hemoglobinopathies for antenatal mothers, parents and families to recognize their responsibility in promoting their child's right to health and by protecting their child from preventable causes of death and disability.[17,18]

Although these screening pilot projects incur costs, yet, various studies suggest that their implementation in India is economically viable and these will improve health quality through early intervention and prevention of these disorders.[19,20] While the World Health Organization's 1998 guidelines don't mandate genetic testing, but, some have made NBS or haemoglobinopathies screening compulsory or voluntary.[21,22] In India, ICMR and The Indian Society for Pediatric and Adolescent Endocrinology recommend NBS for CH and CAH for all newborns, including preterm and low birth weight infants.[8,23] Kerala, Goa, and Chandigarh have implemented NBS programs with government support and India has also launched an antenatal β-thalassaemia carrier screening program during the first antenatal visit.[9] Previous research also shows that screening followed by confirmatory tests can significantly reduce the burden of these disorders in a country like India.[24]

While the Rashtriya Bal Swasthya Karyakram (RBSK) program under the NHM can support the screening for more prevalent disorders through community healthcare workers, yet, the involvement of international agencies, public-private partnerships, Non-Government Organizations (NGOs), and raising awareness and gaining the support of policymakers, clinicians, and the public are essential to promote these screening programs in India.[25]

Limitation of this initiative was small sample size and increasingly better understanding aimed at developing a community level program for need assessment and to evaluate the feasibility of basic screening for some genetic disorders in high risk population effectively more pilot studies with large cohort are required.

CONCLUSION

Incorporating and evaluating more outreach screening programs in aspirational districts, utilizing existing infrastructure and workforce, is necessary to demonstrate the feasibility of effortless initiation of statewide or nationwide screening for prevalent genetic disorders.

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