The Goa Newborn Screening Program

3 Year Review

2008 – 2011

September 1, 2011

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1. Introduction

June 14, 2011 marked the third anniversary of "Heel to Heal", Goa Government's comprehensive newborn screening program. The program has been successful in identifying "at risk" infants and taking preventive measures and treatments to ensure babies lead healthy lives.

We firmly believe that the program has contributed to lowering the Infant Mortality Rate (IMR) in Goa, which is currently the lowest in the country.

Other states have been studying the Goa Newborn Screening program as a model. Gujarat started a limited pilot program earlier this year on the lines of the Goa program. The Goa program was mentioned at the Asia Pacific Meeting of the International Society of Neonatal Screening (ISNS) held in Bali, Indonesia in September 2010.

The key learnings during the three years of the program are discussed in this document. Notably, this is the first program of its kind in India and it can serve as a model for other states embarking on a newborn screening program.

In this report, we also follow the first months of life of an infant detected with Phenylketonuria (PKU) in GMC in February 2011. The Newborn screening Test identified the disorder when the baby was only a week old and was therefore, unaffected by the disorder. The family of the infant acknowledged that if she was born in a private hospital, the disorder would have been missed, which could have resulted in dire consequences (mental retardation or death) for the baby.

2. "Heel to Heal" Program Data (2008 – 2011)

Table 1: Screening Data

	2008 – 09	2009 – 10	2010 – 11
Newborn Screened	8,859	9,185	9,534
Cumulative	**8,859**	**18,044**	**27,578**

Table 2: Presumptive Positive Data

DISORDERS	PRESUMPTIVE POSITIVE			
Fatty Acid Oxidation Disorders	**2008-09**	**2009-10**	**2010-11**	**Total**
VLCAD	15	14	5	**34**
MADD	7	10	3	**20**
MCAD	0	0	3	**3**
Total	**22**	**24**	**11**	**57**
Amino Acid Disorders	**2008-09**	**2009-10**	**2010-11**	**Total**
TYR	3	0	0	**3**
PKU	0	0	1	**1**
UCD	1	0	0	**1**
MSUD	0	1	1	**2**
HCY	0	1	0	**1**
Total	**4**	**2**	**2**	**8**

Organic Acid Disorders	2008-09	2009-10	2010-11	Total
MMA/PA	3	2	3	**8**
GA1	2	0	0	**2**
HMG/3MCC	0	2	0	**2**
Total	**5**	**2**	**3**	**12**

Enzyme Immuno Assay	2008-09	2009-10	2010-11	Total
CH	3	1	4	**8**
G6PD Deficiency	9	10	14	**33**
CAH	2	0	0	**2**
Total	**14**	**11**	**18**	**43**
Grand Total	**45**	**39**	**34**	**120**

Table 3: Follow Up (FAO)

Fatty Acid Oxidation Disorders	Presumptive Positive	Expired	Survived	Lost
VLCAD	34	10	20	4
MADD	20	3	13	4
MCAD	3	0	3	0
Total	**57**	**13**	**36**	**8**

Table 4: Follow Up (AA)

Amino Acid Disorders	Presumptive Positive	Expired	Survived	Lost
PKU	1	0	1	0
MSUD	2	1	0	1
TYR	3	1	2	0
HCY	1	1	0	0
UCD	1	1	0	0
Total	**8**	**4**	**3**	**1**

Table 5: Follow Up (OA)

Organic Acid Disorders	Presumptive Positive	Expired	Survived	Lost
MMA/PA	8	5	2	1
GA1	2	2	0	0
HMG/3MCC	2	0	2	0
Total	**12**	**7**	**4**	**1**

3. Key Learnings

Over a 3 year period ending June 2011, 27,578 samples were processed from 3 Hospitals and 13 CHC/PHC in Goa. One of the challenges of the program was that it was the first of its kind in India and there were no earlier models available that we could study and follow. However, after facing unanticipated challenges and working through them, we now have a model that can serve as a standard for other similar programs in India.

3a. Fatty Acid Oxidation Disorders
Another challenge was the high number of Fatty Acid Oxidation Disorder cases detected in Goa. Apparently, there were a few false positives. We investigated and listed below are a few possible causes for the false positives.

- Sample was collected less than 24 hours of birth
- Maternal Riboflavin Deficiency
- Sepsis
- Episodic clinical course of Fatty Acid Oxidation Disorders

Discounting the false positive data, we still see a significant number of these cases. As reported in the previous program review, these cases appear predominantly in a few families (identified by common last names). Also, some of these infants have passed away. The preliminary conclusion is that this may be an issue in Goa. These cases are being followed up and, if the child has expired, the parents undergo counseling.

3b. Follow Up and Monitoring
The third challenge of the program is tracking follow up visits of patients. If an abnormal result is detected, the patient is required to make follow up visits. Some of the disorders may be latent without any visible symptoms. As a result, after a few follow up visits, the parents feel that since there are no visible symptoms, the baby is healthy. However, the disorder is still present. Therefore, it is very critical that the follow up visits happen.

Another challenge is that the baby may have been born at GMC and the parents move back to their community which may be under a different Hospital/CHC/PHC. In this case, when they visit the nearest healthcare facility in their community, there is no record of the follow ups. To address this issue, a new follow up form (presented in a different color for easier identification) is included in the files of those infants that need follow up visits. This allows records to be maintained as they move through the different healthcare facilities in the system. Follow up visit guidelines (number and interval of monitoring samples) are established and printed on the back of the form so that the healthcare workers can check compliance. A copy of the follow up form is attached to this report (Appendix 1).

Additionally, follow up information will also be given to DHS twice a month so that infants that have stopped follow up visits can be tracked by the DHS healthcare workers and brought back into the system. To encourage follow up visits, a gift will be given to parents to bring their infants for follow up.

3c. Issues of Early Identification & Intervention
Most metabolic experts in India see cases only after symptoms appear. Their experience is mostly limited to identifying the disorders and then stabilizing the child. With the Goa NBS program, disorders are being identified before any harm is done. Metabolic experts are now faced with a slightly different problem; "*How do you treat an infant and what works best when a disorder is identified in the neonatal stage?"* This is an area of increasing importance. The experts are being forced to address this issue since they will be seeing more and more of these infants as screening becomes common.

The PKU case presented in this report highlights this case. The metabolic expert at KEM in Mumbai mentioned that she had to get more information since this was one of the first cases she encountered where the disorder was identified within the first week of the baby's life.

3d. Training
The initial training done at the start of the program covered all collection centers. The new nurses rotating in to the neonatal wards are trained by the existing nurses. The passing and sharing of

knowledge has been effective and the new nurses learn methods very quickly (occasionally, we see a small spike in the Quantity Not Sufficient (QNS) samples associated with an untrained nurse which returns to background levels very quickly). Training is offered at least once a month in all birthing centers.

3e. QNS (Quantity Not Sufficient)
In the three years since the program started, we have seen a remarkable decrease in QNS in sample collection. Initial high levels were due to the introduction of a new method (Heel Stick) of sample collection. However, QNS has now tapered off with practice. More importantly, when new nurses joined the hospital they picked up the process easily from the previously trained nurses. The need for specific scheduled training was not required.

Even though QNS has decreased to negligible amounts (under 2% of tests), it has not been eliminated completely. After investigation, we have identified multiple factors other than training, such as: too many infants, too little time, distraction, difficulty in collecting samples from certain infants and saturation issues. These are the issues which can be eliminated with a little bit of care but it is paramount that the nurses understand the importance of collecting the sample correctly the first time, every time.

Reducing QNS to zero has many advantages namely reducing costs of collecting a second sample and speeding up test results. We have taken steps to identify QNS as soon as possible so that the second sample can be taken quickly, before the infant leaves the hospital.

3f. Logistics
An analysis of the time taken from collection of the sample from the patient to the delivery report (TAT or Turn Around Time) at the hospital was investigated. This period could range from 3 to 10 days. The longer it took for a report to be delivered, the harder it was to follow up, in case the patient needed to be contacted for repeat testing.

There were no serious issues in the TAT for the 45 disorders being analyzed by Tandem Mass Spectrometry. Positive results were available within 3 days of sample collection and were notified verbally to the doctor to take the necessary steps. In many cases, the repeat sample was collected before the infant was discharged from the hospital.

The Biochemical testing delayed the reporting cycle since it was optimized to run twice a week. Also, the Cystic Fibrosis assay needed overnight incubation, adding to the delay. One of the key measures taken to reduce the TAT was the cut off time for receiving Goa specimens at the Lab in Bangalore. This was changed to after the Goa samples were delivered (regardless of the time). Processing only started once we received the Goa samples.

With the changes, average times have reduced in the three main hospitals (average TAT 4.5 days, reporting time ranges from 3 to 6 days from date of collection including Sundays). The reporting times at CHC/PHC exceed these times, primarily due to the dispatch of the samples after collection to GMC (Asilo or Hospicio). We are working through notification processes that will reduce it and improve TAT.

3g. Challenges to a Successful Program
The primary challenge the program faces is the inability to source diets easily and inexpensively. The Government of India does not allow the import of diets commercially. We (and the Government of Goa) have worked with diet companies and they have had no success navigating the regulatory framework to import the diets. The implications are that stores, pharmacies and hospitals are unable to stock the diets leading to delays in the start of the treatment.

Individual patients can import diets but costs are high since discounts usually given to commercial entities are not available to them. Also, they can only import the diets after the patient has been confirmed to have the disorder which leads to a delay in beginning treatment. This is just not a Goa specific issue but affects all programs in India.

4. Goa Private Program

DHS is working with the IMA, FOGSI (Goa) and IAP Goa to promote newborn screening. While the patients at the government healthcare facilities have derived value from the newborn screening services, the private sector has been slow to embrace it. An awareness program has been run in the past 12 months with trilingual (English, Marathi and Konkani) leaflets being distributed in various newspapers around the state. This program continues to this day. Other marketing activities promoting the benefits of screening will be rolled out from September 2011.

From August 2011, members of the IAP, IMA and FOGSI (Goa) are being targeted with information packages that promote newborn screening. The residents of Goa are offered the same panel as those in the public sector for a price of Rs. 2,500/-. (The MRP of the panel is Rs. 4,250/-)

A copy of the first postcard that was sent out in support of the private program in August 2011 is included in the Appendix.

5. CASE STUDY: The PKU Infant

On February 21, 2011, an apparently healthy full-term baby was born at Goa Medical College, Goa. Within the second day of life, the baby went into shock and had noticeable heart abnormalities. The doctors could not ascertain the cause. On February 26, 2011, a dried blood sample was collected for the newborn screen. On March 1, 2011, the lab in Bangalore detected Phenylketonuria (PKU).

PKU is a rare, inherited metabolic disorder caused by the inability of the body to metabolize an amino acid, phenylalanine. Phenylalanine plays a role in the production of melanin, and infants with the condition often have lighter skin, hair, and eyes than their siblings. PKU, if untreated, can cause mental retardation, seizures, hyperactivity and delayed social skills. It is estimated the worldwide incidence is about 1 in 25,000 births.

Time Line

2011	Feb 21	Infant born at Goa Medical College (GMC)
2011	Feb 26	Dried Blood Spot sample collected as part of routine screening
2011	Mar 01	PKU detected and information communicated to physician at GMC regarding next steps and treatment
2011	Mar 07	2nd sample tested and is positive for PKU
2011	Mar 09	Urine sample collected for confirmatory testing
2011	Mar 10	PKU Diets sent to GMC
2011	Mar 14	PKU confirmed. Infant started on PKU diets (XP-Analog 1)

2011	Apr 01	First monitoring sample is normal
2011	Apr 21	Sample delivered to PerkinElmer Genetics (PEG), USA, for additional testing.
2011	Apr 27	Second monitoring sample is normal. Consultation with Dr. Mamta Muranjan, Metabolic Expert at KEM Hospital in Mumbai. Diet changes suggested and implemented.
2011	May 05	The results from Sandor Proteomics (using GC-MS) revealed an increase in the concentration of plasma phenylalanine as well as increased metabolites of phenylalanine in the urine. The conclusion was this was a case of PKU or hyperphenylalaninemia.
2011	Jun 03	Monitoring sample for phenylalanine concentration is normal.
2011	Jun 17	Infant is responding to treatment with no adverse affects. Monitoring for phenylalanine concentration continues and phenylalanine results are in the normal range.
2011	Jun 29	Monitoring sample is 'High'. Diet had been changed.
2011	Jul 4	Monitoring sample is 'High'. Continuing effects of diet change. New diet replaced by the old diet.
2011	Jul 13	Monitoring sample is 'Normal'.
		Monitoring Continues.

The baby is now 6 months old. She will continue to be monitored to try and achieve as normal a life as possible.

6. Acknowledgements

The Goa Newborn Screening Program requires many constituents working in partnership to make the program a success. We have been able to achieve it due to the contributions of,

Goa Government Healthcare Personnel

- Director of Health Services and Support Staff
- Doctors, Nurses and Staff at Goa Medical College Hospital, District Hospitals, and all Community and Primary Health Centers

Service Provider

- NeoGen Labs

Technology Partners

- Bio Rad
- GE Healthcare (Formerly Whatman)
- PerkinElmer Genetics

This report has been prepared by NeoGen Labs for the Director of Health Services, Goa Government.

Appendix

a. Follow Up Form
b. Sample Postcard
c. Posters for Hospitals
    i. English
    ii. Marathi
    iii. Konkani