

Kashinaj

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## What ail genetic lab service and research in India?

Shardul Nautiyal and Rita Dutta

A four-legged boy, born with two sets of penis, four testicles, two anal openings and a huge bulge in the abdomen recently created a furore in Lucknow, with even his parents refusing to take him home, unless he is surgically operated on to look like a normal child. The newborn is kept at Lucknow's King George Medical University, where doctors are debating on the risks involved in such a surgery.

Why such a condition of "parasitic twins" could not be averted? Why was the mother not screened during pregnancy? With 50 million individuals affected with genetic disease, is India equipped with facilities and experts? In several populations, the diseases are also leading to their extinction. One such tribe are the primitive Onges of Andaman and Nicobar Islands, where the number has dwindled from 700 in 1858 to mere 98 this year.

### Facilities

A decade back, to tackle with one in every 50 to 100 babies born with genetic birth defects, there were not more than ten full-fledged genetic labs in the country. Today, the metropolitan cities have genetic testing labs, providing biochemical, cytogenetic and molecular testing.



Genetic Diagnostic Centre, Mumbai offers guidance for setting up of new genetic labs

### Underutilisation of services

The genetic labs may offer advanced tests like FISH, PCR and karotyping, but has the advancement reached the populace? Lack of awareness about such tests and high cost of tests are attributed for the less number.

The low number of tests reflect gross underutilisation of services. Says Dr S S Agarwal, medical geneticist, Central Drug Research Institute (CDRI), Lucknow, "There is a vicious cycle of demand and supply. Lack of awareness, both among the doctors and the public, as well as the cost, results in no demand for genetic tests and no demand leads to no supply."

Echoes Dr Arvind Lal, Dr Lal's Pathlab, New Delhi, "The number of tests conducted to detect Inborn Errors of Metabolism (IEMs) in newborn genetic screening are poor. We receive only around 10 samples a day of the 25 million babies born per year." Since last year, Dr Lal's Pathlabs is offering tandem mass spectrometry which rules out 30 IEMs for newborns. There is resistance from paediatricians towards neonatal screening as they feel the frequency of IEMs is low to warrant routine screening.

### Lack of experts

But even if the number of tests shoot up, there is an acute shortage of experts in the absence of institutes imparting training in genetics. Most geneticists go abroad for training and experience. There have been whispers of misinterpretation of reports because of lack of expertise.

Says Dr P Madon, geneticist, department of Assisted Reproduction and Genetics, Jaslok Hospital, Mumbai, "We have to train people for conducting such tests and interpreting results as DMLT course does not emphasis on genetics." Only Sanjay Gandhi Post Graduate

Institute of medical sciences (SGPGI), Lucknow offers a post graduate DM course in medical genetics. The Department of Biotechnology (DBT) has taken an initiative this year to start five training units in the field of diagnosis of genetic disorders using cytogenetics and molecular genetic methods in the country to train young scientists/ clinicians/technologists.

Not many experts pursue genetics as job openings for a geneticist is not bright in the public sector. Explains Dr Sharad Gogate, a Mumbai-based medical geneticist, "Highly trained geneticists fail in getting jobs in the public sector due to the beauracratic hurdles and reservation policies of the government. The geneticist finds greener pastures abroad or in private sector leading to brain drain."

### **Treatment**

Experts claim that treatment for genetic disorder has been hampered by lack of expertise. According to Dr Anil Jalan, consultant in paediatric metabolic disorder, MGM Hospital, Navi Mumbai, "Where are the experts to treat children with IEMs? As of now, we have a handful of experts."

Echoes Dr Pravin Potdar, microbiologist, Jaslok Hospital, "Genetic disease is not curable, but preventable. Though we have the necessary instrumentation, we still lack in expertise required to treat the disorder." Parents of children with genetic disorder find the imported dietary supplement required for IEM expensive. "With a can costing Rs 25,000, one has to spend Rs 3 lakh and above annually for the diet," says Dr Jalan.

### **Absence of epidemiological study**

Besides less number of tests and lack of experts, there is dearth of data on the prevalence of genetic disorder. Says Dr I C Verma, head, genetics department, Sir Gangaram Hospital, New Delhi, "There is no nation-wide study on the prevalence of genetic disorders. Most of the studies are hospital related which are extrapolated. The ICMR study (reported in August 1 to 15 issue of Express Healthcare Management) on incidence of IEM would be the first of its kind to find the incidence of genetic disorder in newborns."

Lack of data on epidemiology affects choosing the right tests. Explains Dr S Suresh, director, Surendar Genetic Lab, Chennai, "In the absence of data, labs are at their wit's end as to which tests they should conduct, as it's not feasible for a lab to offer tests for over thousand disorders. Ideally, labs should offer tests for disorders which are prevalent in that area, as is practiced in the West."

Recently, the Indian Society of Genetic Screening, comprising over 40 geneticists, has started Birth Defect Registry of India to look into the infrastructure of genetic lab testing in the country, informs Dr Suresh.

### **Accreditation**

Though the National Accreditation Board for Testing and Calibration Laboratories, (NABL) has started accreditation of all laboratories including genetic labs, but not many labs have come forward. Says Dr A Radha Rama Devi, consultant and head, Center for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad, "Many private labs have taken up the diagnostic testing without any proper guidelines resulting in misdiagnosis. In our lab, we exchange samples with other labs to check our quality. For biochemical tests used in the newborn screening, our lab is accredited by Centre for Disease Control (CDC), USA."

Date: Tue, 8 Apr 2008 11:29:03 +0100 (BST)  
From: mercy raman <mercyraman@yahoo.com>  
To: krishnja@barc.gov.in  
Subject: Re:

Dear Krisnaja,  
Thank you for the information. Hope this VRS decision is not due to health reasons. Taking any other Job?

Any way wish you a PEACEFUL TIME.

Mercy J. Raman  
--- krishnja@barc.gov.in wrote:

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>  
> This is just to let you know that I have opted for  
> VRS from 11th April 2008.  
> Superannuation would have been in september 2011.  
>  
> Meanwhile I can be contacted at the address given  
> below.  
>  
> e-mail : krishnajal1@gmail.com  
>  
> Phone (home): 25584318  
>  
> Mobile : 9323738559  
>  
> Residential address:  
>  
> Dr.Mrs.Krishnaja, A. P.  
> 303-304. Dhiraj Tower  
> V.N.Purav Marg  
> Deonar  
> Mumbai. 400088.  
>  
>  
>  
> With Best Regards,  
> Krishnaja.  
>  
> Attached is a copy of our latest paper on adaptive  
> response.  
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> ----- End forwarded message -----  
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Prof. Mercy J. Raman,  
Cytogenetics Laboratory,

<http://bts.barc.gov.in/horde/imp/message.php?index=8607>

4/9/2008

### Issues related to Cancer Genetics

Although important discoveries occurred in cancer cytogenetics area during 1973-1990, the application of these studies to the patients was a gradual process. This was mainly due to the limitations of availability of skilled and experienced cancer cytogeneticists in the country. The molecular genetics technologies like PCR, blotting techniques, DNA sequencing etc became more popular in comparison with cytogenetics in the scientific community because they were user friendly and quick techniques that could easily be adopted by training.

### Research

The scope for research in public hospital is wide with a vast patient base, large number of trained personnel and large student population. However, labs in private sector and biotechnology industry despite their good infrastructure, sophisticated equipment and a steadily increasing population ready to pay for these tests, face lack of research students and trained personnel.

According to Dr Saroj Kotwaliwale, medical geneticist, Genetic Diagnostic Centre, Mumbai, "There is hardly any research facility available in cancer cytogenetics and human cytogenetics as the finances for applied research and basic research is not available."

Amongst the few centres which are conducting research, CDFD, Hyderabad has characterised gene locations in chromosomal translocations and in balanced chromosomal translocations associated with cancer. The research, supported by the Department of Biotechnology (DBT) was carried out in Germany with the Max Plank Institute. Further identification of the gene involved in the physical presentation in the case is being worked out.

"We also screen cervical samples for the presence of Human papilloma virus (HPV) by molecular testing and carry out typing to find out the cancer causing types among women in Andhra Pradesh. This study is useful for implementation of HPV vaccine use," informs Dr Devi.




Other point out that research in medical genetics should be looked from the perspective of total medical genetics and cancer genetics, and not cytogenetics alone. Says Dr Shubha Phadke, additional professor, medical genetics, SGPGI, Lucknow, "The major research aspects of medical genetics in India are delineation of mutations in Indian patients with genetic disorders namely thalassemias, duchenne muscular dystrophy, Wilson disease, fragile X syndrome, etc. This type of research is useful in the establishment of tests for genetic disorders."

According to Dr Kiran Kucheria, professor and head, department of anatomy and genetics, AIIMS, New Delhi, "Other than the research, diagnostic services using molecular cytogenetics is provided at very few centres in India. Over 50 labs providing services in human cytogenetics are conducting short-term research projects also." Experts rue that hardly the results of the research are translated to improve genetic service.

Genetic labs also find the expensive reagents unaffordable for conducting research. "Each probe for molecular cytogenetic studies from Vysis costs USD 300. In the US, cost of an average test is USD 400 to USD 500. The tests for BRCA1 and BRCA2 could cost up to USD 3000," adds Dr Agarwal.

for appropriate tests to suitable facility," adds Dr Gogate.

Regarding the issue of very limited facility of cancer cytogenetics services in our country, Dr P S Amare , head, Cancer Cytogenetics Laboratory, Tata Memorial Hospital, Mumbai, says that translational research programmes are necessary for the diagnostic and prognostic correlation of genetic results, investigation of cytogenetics variants in a group of patients This leads to the establishment and implementation of studies with an approach to precise diagnosis and better management of disease. "Government-funding agencies should prioritise translational research programmes, which will provide a bridge between clinicians and lab scientists and foster a close link between clinic and laboratory. This will be instrumental in facilitating better quality cancer genetics service programmes with implementation of advanced eminent technologies in cancer diagnostics and disease management," adds Dr Amare.

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| Government-funding agencies should prioritise translational research programmes<br><b>Dr P S Amare,</b><br>Cancer Cytogenetics Laboratory, Tata Memorial Hospital | There is hardly any research facility in cancer and human cytogenetics because of lack of funds<br><b>Dr Saroj Kotwaliwale,</b><br>medical geneticist, Genetic Diagnostic Centre | The identification of a large number of single gene disorders will immensely help families with difficult genetic disorders<br><b>Dr Shubha Phadke,</b> addl professor, medical genetics, SGPGI, Lucknow |

### Significance of Human Genome Project

Thanks to the Human Genome Project, now one can make adequate lifestyle and environmental changes at an early age to eliminate the likelihood of disease or taking treatment at an appropriate early stage. Genome research will therefore ensure rapid and more specific diagnostic tests and help in creating drugs in response to individual's genetic inheritance.

According to Dr Manjeet Kaur, head, department of genetics, Dr Lal PathLabs Pvt Ltd, "Drugs based on proteins, enzymes and RNA molecule associated with genes and diseases will be more effective than drug characterised by treating symptoms. Drug dosages based currently on weight and age will be replaced with dosages based on a person's genetics, thus decreasing the likelihood of overdose."

The project has revealed that merely the number of genes present does not determine the complexity of human genome compared to other organisms. The complexity is with respect to gene regulation and the number of different transcripts originating from a single gene. "The genome project has now given rise to the Proteome project in order to understand the functioning of the genes in terms of the batteries of proteins produced. Understanding of the differences in protein expression between a healthy individual to that of the diseased will pave newer ways for screening, diagnosis and therapeutics," informs Dr Devi.

Realising the potential, some biotech companies like Biocon have expressed their desire to conduct research in this area. Biocon chairman Kiran Mazumdar Shaw has reportedly said that the country's unique gene pools are "gold mines".

#### Genetic Lab Facilities at various hospitals in India

- The cancer cytogenetics laboratory at Tata Memorial Hospital is engaged in basic and applied research programmes in hematological malignancies, urological malignancies and childhood malignancies like retinoblastoma and sarcomas. The laboratory has been actively involved in various large scale clinical research trial programmes of targeted drug therapies like Glivec in CML, ATRA in acute promyelocytic leukaemia (APL), NCI multi-centre chemotherapy trial in ALL for molecular assessment of targeted therapies by molecular cytogenetics. The laboratory reports more than 3000 tests annually. CMC, Vellore and Adiyar Cancer Research Center also provides cancer cytogenetics services.
- Genetic Diagnostic Centre, Mumbai established in 1986 is the first laboratory in India to perform amniotic fluid cell cultures for prenatal diagnosis and till today has analysed more than 3000 samples recommended for cytogenetic diagnosis. The Centre provides genetic counselling, cytogenetic test from blood, chorion villous sampling, amniotic fluid cell cultures, Fetal blood sampling, Products of conception, among others. The centre also offers training courses for individuals interested in pursuing cytogenetics as a profession and also provides guidance for setting up of the new laboratory.
- Some of the main subjects of study in medical genetics department of SGPGI, Lucknow are clinical delineation of new multiple malformation syndromes, not yet reported in the medical literature. Other aspects of research are psychosocial aspects of genetic counselling in Indian scenario, genetic variations in different ethnic group in Indian population and cancer genetics.
- Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad is engaged mainly in providing human cytogenetics for a variety of disorders such as chromosomal defects in structure and in number. Human cytogenetic studies are carried out using the applied Imaging System and different banding techniques are applied for the diagnosis. A proposal has been made by CDFD to the Department of Biotechnology (DBT), Govt of India (GOI) for a cytogenetic workstation to study various cancers.

#### Suggestions for improvement

There is a need for a synergy between public and private sector for making genetic facilities a mutually beneficial business proposition. "The services of each sector can be efficiently utilised to convert basic research into clinical tests and service facilities, which will help generate funds for building the infrastructure of labs. Our intellectual property will also be protected this way," avers Dr Gogate.

Indian scientists have awakened to the need to study the country's endogamous gene pool. Due to India's large population, many rare disorders exist in India. These families can contribute to identification of genetic defects of rare genetic disorders. Identification of cases with possible genetic etiology by primary care physicians is essential so that these families can get facilities of special genetic tests, genetic counseling and prenatal diagnosis. Thus the initiative of the Centre for Cellular and Molecular Biology (CCMB) in Hyderabad in studying the origin and disease susceptibility of various caste and tribal populations of India comes as a good tidings.

Experts suggest that the government should reduce custom duty on imported equipment and reagent required for genetic labs. Other demand that there should be more Indian publication on medical genetics in India. "To address the lack of awareness in general population about genetic disorders, their screening and diagnostic tests, there should be awareness campaign. We also require a national directory of genetic centres/labs offering various tests and facilities for ready reference for clinicians so that patients can be guided

The human genome mapping has lead to identification of more than 400 genes for monogenic or single gene disorders. "Identification of causative genes for these disorders have led to the establishment of tests for diagnosis and prenatal diagnosis for prevention of recurrences. This knowledge will be of immense help to the families with difficult genetic disorders," informs Dr Phadke.

The other important aspect of human genome project is in the field of cancers and identification of genetic defects which predispose a person to common diseases like heart attack, high blood pressure, diabetes , psychiatric illnesses ,etc. A lot of research in this field is going on and may lead to newer modalities of treatment of cancers, say experts.

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