Indian Journal of Hygiene and Public Health
Publication of All India Institute of Hygiene & Public Health, Kolkata.
ISSN : 2455-1813

Commentary

Public Health Genomics- an Overview

*Dr. Bandana Sen **

1. Introduction:

In recent years, public health genomics has been introduced in the scientific literature as a new endeavour, aiming at the translation of genome-based knowledge and technologies into health interventions and public policies for the benefit of public health[1]. Human Genome Project has raised public expectations that research findings will translate quickly into health benefits; however, the gap between biomedical research and public health application seems still wide. Public health scientists now have the opportunity to help create a broad concept of research translation that integrates genomic information into policies, programs and services benefiting the whole population.

The ambitions of public health genomics as a field can be defined in terms of four movements which describe the activities of its practitioners as distinct from the traditional practices of clinical geneticists. The first of these movements is a shift in focus away from individuals to populations, bringing genetic services to the community as a whole. Then there is a shift from people with symptoms to people without symptoms (the care system). The third one is a shift from reproductive choice as the main focus to options for prevention of disease. The fourth shift is characterised from rare monogenetic disorders to multi-factorial forms of common diseases[2].

Although the first two shifts are clear in defining the agenda of public health genetics, it is the third shift which brings to more revealing and significant questions for this field. Traditionally, reproductive choice has been a major focus of clinical genetic services and public health genetics, likewise, has its roots in population carrier screening programmes offering reproductive choice[3].

2. Possible point of entry in Public Health Genomics in India

In a country like India it is easy to talk about genomic research but translating into reality is

***Director-Professor & Head, Dept. of Statistics**
All India Institute of Hygiene and Health, Kolkata
E mail: vandanadasgupta@gmail.com

not easy. Public health genomics research should include conducting population-based research in genomics in one hand and developing evidence on clinical & public health value of genomic information on the other and finally integrating both into health practice is the ideal goal. Public support for genomic research would lead to new applications and to further understanding of human origins and dispersions. Some research relating to genetic risk factors for complex diseases, is possible to be supported by private funds but it seems that the only genetic service for which a public health role is important is 'new-born screening'[4].

3. Information related to birth defects:

Genetic disorders and birth defects are relatively common in India. This is due to the fact that many communities marry consanguineously. In South India, marriages among Hindus are consanguineous in 20–30% of cases, especially uncle–niece marriages. Muslims marry consanguineously in 20–30% of cases. Thalassemia and sickle-cell disease also have a high frequency in many states[5]. Many infants with birth defects and inborn errors of metabolism now survive due to advancement of treatment. However, due to the large number of births per year, it is estimated that India has the largest number of infants born with birth defects in the world (please see Table 1)

A. Congenital malformations:

In India communicable diseases are on the decline due to better living conditions and health care. On the other hand, the relative increase in the prevalence of non-communicable diseases scares to be a public health issue in this country. One such group of disorders is *congenital malformations*. In a Mumbai hospital that mainly serves the poor, congenital malformations was the third commonest cause (13.2%) of perinatal mortality[6,7,8]. Likewise, in a nationwide study conducted by the National Neonatology Forum in 1995 of 1460 stillbirths and 1400 neonatal deaths, congenital malformations were the second commonest cause (9.9%) of mortality among stillbirths, and the fourth commonest cause (9.6%) of neonatal mortality.

(i) A study funded by the Department of Atomic Energy was carried out in three cities (Baroda, Mumbai and New Delhi) using a uniform performa [9]. The staff members at all centres were trained in dysmorphology. Major malformations recorded from 94610 persons enrolled in the study gave a malformation rate of 2.12% [10]. The systemic distribution of these malformations is depicted in Table 1.

Table 1. Estimated frequency of birth defects and genetic disorders in India

Disorder	Incidence	Births/ year
Congenital malformations	1: 50	678,000
Down syndrome	1: 800	34,000
Metabolic disorders	1:1200	22,477
β thalassemia and sickle-cell disease	1: 2700	16,700
Congenital hypothyroidism	1: 2477	10,900

Duchenne muscular dystrophy	1:5000	2,700
Spinal muscular atrophy	1:10000	2,700

Source: Modified from Verma and Kumar (2012) [11]

(ii) Surveillance study:

It may be mentioned in this connection that two-year birth defects surveillance study was carried out by the Genetic Research Centre, National Institute for Research in Reproductive Health, Parel, Mumbai in collaboration with the Nowrosjee Wadia Maternity Hospital, as a part of Department of Atomic Energy study[12], it was found that, among the 17653 new-borns, 294 (1.6%) had major malformations, 1400 (7.92%) had minor malformations, and 328 (1.8%) were stillbirths. Malformations were highest in the stillbirth group. (Table 2).

Table 2. Rate of selected malformations and total births per annum in India

Malformation	Rate per 10 000	Total/ year
Spina bifida/anencephaly	40.42	109134
Talipes	18.60	5022
Cleft lip and cleft palate /Cleft palate alone	15.42	41634
Hydrocephalous alone	11.20	30240
Hypospadias	5.71	15417
Intestinal and anal atresia	5.08	13716

Table 3, on the other hand, shows the estimated number of infants born annually with various malformations in India deduced from the data of this study.

Table 3. The systemic distribution of malformations in the three-centre study

System	No.	Per 10 000	Total / year
Central nervous system	569	60.18	162486
Musculoskeletal	84	51.12	138024
Gastrointestinal	363	38.37	103599
Genitourinary	204	21.58	58266
Ears	141	14.89	40203
Cardiovascular	120	12.70	34290
Respiratory	65	6.87	18549
Eyes	57	6.03	16281
Miscellaneous	238	25.12	67824
Total	-	-	**493522**

Such studies can be used to assess the requirement for surgical services, as well as to assess the effect of preventive strategies, e.g. for NTDs.

(iii) Neural tube defects (NTD) :

NTDs were the commonest disorders observed in the Department of Atomic Energy study[13, 14]. The prevalence was extremely high in north India (more than 4 per 1000 births), especially in the states of Punjab, Chandigarh, Haryana, New Delhi and Rajasthan, with a decreasing trend in frequency towards the east (Bihar and West Bengal) and south (Tamil Nadu and Kerala. It was suggested that this may be due to consanguinity (Kulkarni, Mathew and Ramachandran, 1987; Kulkarni, Mathew and Reddy, 1989). In cities in India obstetricians do advise their patients to take folic acid periconceptionally. However if pregnancies are unplanned it would be best to fortify food with folic acid and other nutrients[15].

B. Thalassemia

There are several reports on the frequency of β thalassemia trait from different parts of the country, which vary from less than 1% to 17% (Madan et al., 2010). Most of the earlier studies are in small groups of hospital-based patients and/or population groups. It is well known that frequency is higher in some population groups[16]. An important project was carried out under the Prime Minister's Jai Vigyan Thalassemia Control Programme in six cities in India with a high prevalence of haemoglobinopathies: Mumbai (Maharashtra), Vadodora (Gujarat), Dibrugarh (Assam), Kolkata (West Bengal), Ludhiana (Punjab) and Bangalore (Karnataka). Screening was carried out in 29 898 college students and 26 916 pregnant women. The prevalence of β thalassaemia trait was 1.5– 3.4% among college students, and 1.3–4.2% among pregnant women. A high frequency of carriers was observed among certain communities, like Vellalas, Sindhis, Aroras, Lohanas, Mandals, Pillais, Jains, Khatirs and Baidyas[17] .

C. Other genetic disorders

(i) Metabolic disorders: Metabolic studies in New Delhi (AIIMS and Sir Ganga Ram Hospital, Mumbai (KEM Hospital), and Bangalore (National Institute of Mental Health and Neurosciences) demonstrated that mucopolysaccharidoses, lysosomal storage disorders (Gaucher disease, Niemann Pick disease and Pompe disease), Wilson disease, Glycogen Storage Disease and galactosaemia are quite common .

(ii) Down syndrome: Data on the prevalence of malformations in various studies in India were subjected to meta-analysis, which gave a Down syndrome frequency of 1 in 916 (82 cases of Down syndrome in 75 103 births). In the more recent three-centre study that specifically investigated Down syndrome, 1 per 1150 births was affected.

(iii) Fragile X syndrome: Fragile X syndrome is the second commonest cause of mental retardation, and in a study on mentally retarded persons, the prevalence was 2.8%.

D. Disabilities

According to the 2001 Census, 21.9 million people live with disabilities in India, representing 2.13% of the total population. In 2002, the National Sample Survey Organization (NSSO) estimated the number of persons with disabilities to be 18.49 million, or 1.8% of the population[18], an estimate that is widely considered to be more accurate. Distribution by type of disability was: locomotors disability 51%, visual 14%, hearing 15%, speech 10%, and mental 10%. The prevalence is greater among males and in rural areas.

E. Consanguinity

Consanguineous marriages are common among some areas of South India and in all Indian Muslim communities. Consanguineous marriages are more common in rural areas and an increased incidence of autosomal recessive disorders is reported among those who are married consanguineously.

I. Birth defects as per the March of Dimes Report

According to the 'March of Dimes Report', 1722404 infants i.e. 64.3 infants per 1000 live births are born each year with birth defects[19]

4. Response to birth defects

a. Surveillance services:

There is growing interest in starting Birth Defect Registries in India. In Chennai a Birth Defects Registry exists and ICMR has plans to initiate a Birth Defects Registry in North India.

b. Genetic services:

Various genetic services are available in all major towns. There are 54 genetic counselling centres, 40 genetic laboratories, and 20 prenatal diagnostic centres listed on the national web site (http://geneticsindia.org/). The number of laboratories offering various genetic tests is chromosomes, biochemical, and molecular. The referral system for genetic services available in India[20].

c. Screening programmes:

In 2008 the ICMR approved a multi-centric study of new-born screening in five centres in India for two disorders (congenital hypothyroidism and congenital adrenal hyperplasia). This study has now been completed. The State of Goa has a mandatory screening programme for all new-borns, while the states of Tamil Nadu, Chandigarh, Maharashtra and Andhra Pradesh have initiated pilot studies of new-born screening in some districts[21]

d. Prevention programmes:

For NTDs, a prevention programme is a necessity. However, as mentioned in the discussion on micronutrient fortification, only food under the public distribution system is fortified with folic acid. In cities, most obstetricians prescribe folic acid to be taken 3 months before pregnancy and to be continued for 3 months after pregnancy. However, this remains limited to the small number of women who come for pre-pregnancy counselling.

Biochemical screening during the first and second trimester is gaining momentum and a large number of women undergo these tests. Amniocentesis is easily available for women who are detected to be at high risk. Since medical termination of pregnancy is legal in the event of an abnormal foetus, prenatal diagnosis of various genetic disorders is fairly popular.

A welcome trend all over India is the increasing registration of births. For example, in Delhi all 325 000 annual births are registered online. It should be easy to modify the registration form for births to include information regarding the presence of birth defects, and their nature. This would be a good way to begin[22].

5. Limitations of Genomic Studies in India:

Limitations of Genomic Studies are also important to be understood clearly. There are many barriers to effective convergence and approach to prevention and management, especially for complex diseases from a multidisciplinary perspective. Following are some examples.

1) Fear of eugenics

Targeted population may not undoubtedly aware of main objective for using genetic information. It is to be understood that it is not to enhance, change, or remove one's genes, but to promote their optimal expression.

2) The predictive power of genes

Not all genetic variants found to be associated with disease are clinically useful. Genetic tests should be introduced only when the predictive power is established within particular populations, to prevent one case of disease. Cost-benefit analyses and rigorous evaluation of genetic screening programs is essential in such situation.

3) Genetic reductionism

A reductionist approach can be useful for identifying genetic associations with disease and elucidating etiological pathways in a research setting. However, it does not reflect the way genes actually operate in complex biological systems.

4) Non-modifiable risk factors

For some complex diseases, genetic information may be used either pre-symptomatically or after the disease onset, for targeted interventions including diet, medication, and lifestyle modifications.

5) Individuals versus populations

Public health, which seeks to improve the health of populations, has to recognize the importance of the individual. This may be facilitated via informed consent especially for new-born screening.

6) Resource allocation

Imbalance in distribution of public resources in health care has been the issue of every public health professional. A major area of concern is the prioritization of competitive research funding in favour of genetics.

7) Commercial imperative

Commercial laboratories may bypass recommended pre-test counselling when offering "over the counter" genetic testing. It may result into inequalities in access and in addition there are concerns about privacy, safety, and quality as well.

8) Discrimination

Genetically susceptible population subgroups may be identified, marginalized, or discriminated against in various ways – the creation of a "genetic underclass". Family relationships, insurance (life, travel, and health), employment, finance, adoption, migration, and legal settings (paternity testing) are all examples of where genetic discrimination may occur or not.

9) Understanding and education

The complexity of genomics dictates the need for specialized languages and bodies of information. Genetic literacy assumes that the average person can evaluate the credibility of information that has implications for personal and public health, but most do not have this skill. Multidisciplinary education programs for health professionals are needed on the scientific, ethical, legal, and social issues related to public health genomics, as are programs on bioinformatics and statistical genetics, cultural anthropology, and health behaviour.

6. Conclusions:

There has been a significant decline in infant and childhood mortality rates in India in the past two decades. This has primarily been due to extensive and successful use of immunization, control of diarrhoeal disorders, acute respiratory tract infections and improvement in health-care services through a focus on primary health care. The national immunisation policy also has implemented in all corners of India although there is still some lapse in some area.

As a concluding remark, it may be commented that

a. The birth registration form could be modified to collect information on the presence of a malformation at birth.
b. The collection of information on birth defects may be initiated in the neonatal unit in the district level hospital. Plan/ schemes may be set up for a surveillance system for birth defects with some good infrastructure.
c. There is need for further integration of genetic services and education into public health in India. Till date studies show that new-born screening and follow-up are provided safely and effectively.

d. The most important area for strengthening the public health role is in the regulation of genetic tests and other genetic services provided primarily by the private sector. Continued support for basic genetic research is also an integral part.

7. References:

1. Brand A, Brand H. Public health genomics—relevance of genomics for individual health information management, health policy development and effective health services. Ital J Pub Health. 2006;3 (3–4):24–34.

2. Brand A, Schröder P, Brand H, Zimmern R. Getting ready for the future: integration of genomics in public health research, policy and practice in Europe and globally. Community Genet. 2006;9:67–71.

3. Modell B, Kuliev A. The history of community genetics: the contribution of the haemoglobin disorders. Community Genet. 1998;1:3–11.

4. Burke W, Atkins D, Gwinn M, Guttmacher A, Haddow J, Lau J, et al. Genetic test evaluation; information needs of clinicians, policy makers, and the public. Am J Epidemiol. 2002; 156: 311–8.

5. Collins FS, McKusick VA. Implications of the human genome project for medical science. JAMA. 2001; 285: 540–4.

6. Ravikumara M, Bhat BV, Oumachigui A. Perinatal mortality trends in a referral hospital.Indian J Pediatr 1996; 63: 357–361.

7. Bhat BV, Ravikumara M. Perinatal mortality in India — Need for introspection. Indian J Maternal and Child Hlth 1996; 7: 31–33.

8. Ravikumara M, Bhat BV. Early neonatal mortality in an intramural birth cohort at a tertiary care hospital. Indian J Pediatr 1996; 63:785–789

9. Verma IC, Bijarnia S. The burden of genetic disorders in India and a framework for community control. Community Genet. 2002; 5: 192–6.

10. Amar Taksande, Krishna Vilhekar, Pushpa Chaturvedi, and Manish Jain. Congenital malformations at birth in Central India: A rural medical college hospital based data, Indian J Hum Genet. 2010 Sep-Dec; 16(3): 159–163.

11. Verma IC, Kumar D. Epidemiology of genetic diseases in the Indian subcontinent. In: Kumar D, editor. Genomics and health in the 124 developing world. Oxford University Press. 2012. Pp 923-926.

12. Patel ZM, Adhia RA.Birth defects surveillance study.Indian J Pediatr. 2005, Jun;72(6) :489-91.

13. Verma L. R., 1978 a. - Biology of honeybee (Apis mellifera L.) spermatozoa 1. Effect of different diluents on motility and survival. Apidologie, 9, 167-174.

14. Verma L. R., 1978 b. - Biology of honeybee spermatozoa. 2. Effect of washing and of sugars on respiration as measured by the Cartesian diver technique. J. Apic. Res. 14, 113-118.

15. Godbole K, Deshmukh U and Yajnik C (2009) Nutrigenetic determinants of neural tube defects in India Indian Pediatr 46 467-475

16. Verma IC1, Saxena R, Kohli S. Past, present & future scenario of thalassaemic care & control in India Indian J Med Res. 2011 Oct;134:507-21.

17. Mohanty S, Panda MK, Subudhi E, Acharya L, Nayak S (2008). Genetic stability of micropropagated ginger derived from axillary bud through cytophotometric and RAPD analysis. ZNaturforsch. 63c: 747-754.

18. Walia GK. Disability in India. Version 4. South Asia Network for Chronic Diseases.

19. Christianson A, Howson CP, Modell B, editors. March of dimes global report on birth defects: the hidden toll of dying and disabled children. New York: March of Dimes Birth Defects Foundation, White Plains, 2006.

20. Verma ML1, Barrow CJ, Kennedy JF, Puri M , Immobilization of β-d-galactosidase from Kluyveromyces lactis on functionalized silicon dioxide nanoparticles: characterization and lactose hydrolysis. Int J Biol Macromol. 2012 Mar 1;50(2):432-7

21. Kapoor S1, Kabra M. Newborn screening in India: current perspectives. March 2010, Volume 47, Issue 3, 219–224

22. World Health Organization Birth defects in South-East Asia - situation analysis 2013 (Last access on 29.09.2019 from https://apps.who.int/iris/handle/10665/204821).