Review Paper

Genetic Disorders and Consanguinity: Focus on Bangladesh

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Abstract

Genetic disorders are one of the major childhood health problems. Treatment and rehabilitation of children with genetic disorders are costly and complete recovery is usually impossible. Genetic disorders are far more common than is widely appreciated and represent only the tip of the iceberg. Consanguineous marriage increases the risk of mutated autosomal recessive gene expression and consequently increases the risk of inheriting genetic disorders among the offspring. The probability of inheriting genetic disorders depends on the closeness of the relationship between the parents. That's why considerable attention has been attracted towards the consanguineous marriage as a causative factor of the genetic disorders. It was found that the rate of consanguinity is very high among the Muslim countries. Very limited data are available regarding the rate of consanguinity and prevalence of genetic disorders related to consanguinity in Bangladesh. Bangladesh has a lot of achievements in the health sector but still, sufficient initiative have not been taken to control the genetic disorders by informing, motivating and discouraging people in consanguineous marriage. Awareness of the people with premarital and prenatal screening is very important to reduce the incidence of genetic disorders.

Key-words: Consanguinity, Genetic disorders, Bangladesh.

Introduction

Bob Edwards, a world famous embryologist said in 1999, "Giving birth to a disabled child is a sin; no parents should commit this in the present era when prenatal screening for genetic diseases is increasingly available. It is the moral responsibility of the parents too, not to have a child that carries the heavy burden of genetic disease. We are entering a world where we have to consider the quality of our children"[1]. Bob Edward made this comment 18 years back. Bangladesh is a developing country which is growing very fast and achieved most of the Millennium Development Goals especially in the health sector indicators. Though Bangladesh is very much successful in reducing infant and childhood mortality, the genetic disorders are still an unaddressed issue here. Rather, as infant mortality reduces, congenital and genetic disorders emerge as an important cause of early death and chronic disability. So, it is high time for Bangladesh as a developing country to integrate genetic approach into its health care system.

Genetic Disorders

A genetic disorder is a disease that is caused by an abnormality in an individual DNA (Deoxyribonucleic acid). Abnormality can be as small as a single-base mutation in just one gene, or they can involve the entire chromosomes. Human genetic disorders may be classified into three broad categories: Single gene disorders, Chromosomal disorders and Complex Multigenic disorders or Multifactorial disorders.

Single Gene Disorders

Any genetic disorder caused by a change or mutation that occurs in the DNA sequence of a single gene is called single gene disorder. There are more than 6,000 known single-gene disorders, which occur in about 1 out of every 200 births. Mutations involving single gene typically follow one of the three patterns of inheritance: Autosomal dominant disorders, Autosomal Recessive disorders, and X-linked disorders. Autosomal dominant disorders are manifested in the heterozygous state. That is when a child receives one copy mutated gene and one copy normal gene, will be affected with the autosomal dominant disorders. At least one parent of the affected child would be a sufferer of the disease. When an affected person marries an unaffected one, their every child has one chance in two of having the disease. Autosomal recessive disorders make up the largest category of single gene disorders which are manifested in the homozygous state. That is, when a child received two copies of the altered or mutated gene, one copy from each parent will be affected from the autosomal recessive disorders. Parents of the affected individual are the carriers of the altered gene but are not usually affected. Siblings have one chance in four of having the trait (i.e, the recurrence risk is 25% for each birth). If the mutant gene occurs with a low frequency in the population, there is a strong likelihood that the affected individual is the product of a consanguineous marriage. Autosomal recessive disorders are typically not seen in every generation of an affected family. All sex-linked disorders are X-linked, and almost all are recessive.

Chromosomal Disorders

Chromosomal disorders can result from changes in either the number or structure of the chromosomes. Changes in the number of chromosomes happen when there are more or fewer copies of a particular chromosome than usual. Changes in chromosome structure take place when the material in an individual chromosome is disrupted or rearranged in some way.

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Complex Multigenic Disorders or Multifactorial Disorders

They are caused by interactions between multiple variant forms of genes and environmental factors. Since environmental interactions are important in the pathogenesis of these diseases, they are also called multifactorial disorders. In this category are some of the most common diseases that afflict humans, including atherosclerosis, Diabetes mellitus, Hypertension, Autoimmune disease etc[2].

Consanguinity

Consanguinity or Consanguineous marriage may be defined as marriage between blood relatives that indicate the relationships up to second cousin marriage[3], or marriages between individuals sharing at least one common ancestor[4]. In clinical genetics, consanguinity has been defined as a biological relationship between blood relatives up to second cousins or closer, where the inbreeding coefficient (F) is equal to 0.0156 or higher[5].

Global Magnitude of Consanguineous Marriage or Consanguinity

It has been estimated that almost 690 million people in the world are consanguineous[6]. South Asia, Middle East and Northern Africa are regions where the rate of consanguinity is historically and culturally high[4]. One-fifth of the world population lives in regions where the consanguineous marriage is getting preference over the other marriage and at least 8.5% of the children having consanguineous parents[7]. Consanguineous marriage is common in many parts of the world, especially in the Middle-Eastern countries[8,9]. Consanguineous marriage is also common in other Muslim countries and regions like India[10], Pakistan[11] and Uzbekistan[12]. The rate of consanguinity usually varies from one population to another population and it is due to religion, socio-cultural factors, socially accepted norms, race, ethnicity etc. In the Arab countries, the rate of consanguinity has been reported highest in Saudi Arabia[13] where it is 58%but in some parts of the Kingdom it is almost 80%, 59% in Iraq, 49-58% in Jordan, 40-54% in the UAE[14], 29% in Egypt[15], 51.0% in Qatar[16], 40% among the Palestinians, 44% among the Yemenis in Sanaa, 54% in Kuwait[17], 49% to 33% in Tunisia and Morocco[18], 50% in Oman[19]. The prevalence of consanguineous marriage is particularly high among the South Asian population[20]. In Pakistan, the overall rate of consanguineous marriage is 60-70%[21]. In India, it was found about 12%, however, it is much higher among Muslims (22%) than other social groups[10]. Bhagya B et al in 2012 reported that the prevalence of consanguineous marriage in India was 6.53% and it was 13.56% among Muslim, 5.04% among Hindu and 1.08% among Christians[22]. Consanguinity rate was found much higher in rural areas (59.9%) than in urban (17.7%) and semi-urban areas (23.5%)[15].

Present Scenario of Consanguinity and Genetic Disorders in Bangladesh

Bangladesh is one of the most densely populated countries of the world with an estimated population of 152.25 million, the majority (about 88%) are Muslim living in an area of 1,47,570 square kilometers. Bangladesh experienced rapid population growth after the Second World War. The population was 40.21 million in 1951 and has doubled within thirty years, growing to 80.99 million in 1981. The density of population is 1021 per square kilometer which is much higher than the other developed countries. Per capita income is US$ 923 per annum. The literacy rate is 63% for men and 55.4% for women. The average household size is 5.6 people and 16% of households do not own land. Up to 90% of women in Bangladesh marry by 18 years of age and most conceive in their teens. The prevalence of disability per 1000 population by type of disability and sex are as follows[23]:

Table-I: Prevalence of Disability Per 1000 Population by Types of Disability and Sex

Types of disability	Total	Male	Female
Visual Impairment	1.25	1.42	1.08
Hearing Impairment	0.72	0.85	0.58
Speaking Impairment	0.99	1.25	0.73
Physical Retardation	0.11	0.13	0.08
Mentally Handicapped	0.44	0.49	0.38
Memory Impairment	0.10	0.12	0.08

Source: Health and Demographic Survey, 2000, BBS

But it is not known the causes of the above-mentioned disabilities are not known. Very limited data are available regarding the consanguinity and prevalence of genetic disorders related to consanguinity in Bangladesh. Only one study was found in Teknaf region of Bangladesh where it was seen that 17.6% of marriages were consanguineous[24].

The Degree of Closeness among Cousin Marriage

The closer the relationship among the parents the higher will be the incidence of genetic disorders among the children. It was observed that the first cousin marriage was the most consanguinity in parents among the consanguineous marriages[25]. In Jordan, first-cousin marriages constituted 69% among all consanguineous marriages[26], 86% in Egypt[15], 43.6% in Iran[25], 43.42% in India[22] and 26.7% in Qatar[16]. In Qatar, among the first cousin marriage (26.7%), paternal parallel first cousin marriage was 17.6% (most common), double first cousin marriage was 4.3% (second most common) and first cousin once removed was 3.9% and second cousin marriages was 3.0%, while 13.2% of all marriages were between more distant cousins[16]. In another study in Iran, among the first cousin 37.8% were parallel- cousin marriages, 28.9% were cross-cousin and rest 33.2% from distant relative[1]. In India, second cousin marriage was 39.47% and 17.11% were distant relatives[21]. These type of data are not available in Bangladesh.

Reasons for Consanguineous Marriage

The reasons for consanguineous marriage are mainly social and aiming to strengthen the family ties, easily getting a suitable marriage partner, easy adjustment after marriage, economic benefits, keeping property within the family. Consanguineous marriage may

be preferable for the women's status, wife's better relationship with her husband who could support her in time of need. There is a general belief that marrying within the family reduces the possibilities of hidden uncertainties in health and financial issues. It is believed that consanguinity enforces family solidarity, provides excellent opportunities for the transmission of cultural values and cultural continuity[27]. Premarital negotiations regarding financial matters of marriage are more easily conducted and sometimes less costly. Sometimes parents prefer to have their daughter living near them and to enjoy the presence of their grandchildren. Moreover, wealthy landlords sometimes prefer to keep their property within the family[5,28].

Consanguinity and Genetic Disorders

Generally, the offsprings of consanguineous parents have more chance of being homozygous than those of non-consanguineous parents. Recent studies revealed that the average genome-wide homozygosity increases gradually with increasing levels of consanguinity. Consequently, in relation to the general population, consanguineous marriage poses a relatively higher risk of giving birth of a child with genetic damage, owing to the expression of rare recessive mutated genes inherited from common ancestors[4]. Children of consanguineous marriages are at a higher risk of inheriting abnormalities and diseases caused by the expression of altered homozygous recessive genes and consequently become a sufferer of autosomal recessive genetic disorders[29,33-35]. The rate of stillbirths, birth defects, and congenital malformations is significantly higher among the offsprings of first cousin consanguineous parents[30,31]. Close blood relatives have a higher chance of inheriting the same alleles than the less closely related individuals[32].The closer the relationship between parents, the higher is the probability of inheriting identical copies of one or more detrimental recessive genes by their children. For example, first cousins are estimated to share 12.5% (1/8) of their genes. Thus, on average, their progeny will be homozygous at 6.25% (1/16) of gene loci[36]. Consanguinity has also been associated with blood diseases (hemophilia, β-thalassemia)[45], congenital heart disease[46], deafness, cystic fibrosis[47], neonatal diabetes mellitus[48] and chronic renal failure[49]. It is an identified risk factor for many paediatric disorders like stillbirths and perinatal mortality[38,39,40], congenital malformations, birth defects, and mental retardation[41-44]. The insufficient public health measures in preventing congenital and genetic disorders, with inadequate intra-natal and prenatal health care, particularly in the least developed countries might have contributed to the higher rates of genetically determined disorders[37].

In general, consanguinity does not increase the risk for autosomal dominant conditions in offspring when one of the parents is affected, nor for X-linked recessive conditions if neither parent is affected[50]. However, there were no differences in the consanguinity rates in patients with primary infertility and patient with Down syndrome[51] and other chromosomal disorders[52] than that of the general population[38]. The association of consanguineous marriages with late-onset complex diseases such as diabetes, cardiovascular disorders, schizophrenia, and cancer require further studies to precise any existing risk because currently, unambiguous evidence-based conclusions are difficult to establish[35].

Screening and Counseling for Genetic Disorders

Premarital, prenatal and intra-natal screening for identification of career and widespread counseling and motivation for awareness among the general population is the key factor in prevention and control of genetic disorders related to consanguinity. As the consanguineous marriage is preventable by counseling and motivating people, now it is being incorporated into the healthcare system in many countries to bypass the grave consequences of it. In populations with high consanguinity rates and common inherited blood disorders, community programs for premarital screening are in progress to detect carriers of hemoglobinopathies such as thalassaemia and sickle cell anemia as for example in Jordan[26], Saudi Arabia[53], Iran[54], Iraq[55], Bahrain and Turkey[56]. Carrier detection and genetic counseling programs have been very successful in reducing the birth prevalence of inherited disorders in some populations, such as in Iran[57,58]. These programs are most successful when they are sensitive to the cultural backgrounds of populations to which they are applied[59].

Genetic Disorders and Bangladesh

Bangladesh is largely populated Muslim country. Like other Muslim countries, there is a possibility of having a higher rate of consanguinity and genetic disorders in Bangladesh. There is no Genetic health service available at primary and secondary health care level in Bangladesh. Only a very limited service is available at national level which is nearby insufficient. But a number of children are found to be born with genetic disorders. Many of them are from consanguineous parents. A different study revealed that there are higher risks of inheriting genetic and congenital disorders among the children with parental consanguinity. Because of high consanguinity rates within the Muslim population, the incidence of congenital malformation in Islamic countries is between 10 to 45%[60]. In Bangladesh, no such study yet to be found in this field. So, the prevalence of consanguinity and prevalence of genetic disorders of offspring following a consanguineous marriage is unknown in Bangladesh. No statistical data could even be revealed in this regard. But to reduce the incidence of genetic disorders, present situation necessitates the requirements of addressing the issue adequately.

Conclusion

The genetic disorders are incurable disease and the family having a child with a genetic disorder usually suffers throughout their life. So, it is very important to create awareness about the genetic risk of consanguinity at all levels especially among the healthcare personnel and the general population. This fact should also be

brought to the attention of health, social and political authorities. The only measure that can prevent this disorder is a premarital and prenatal screening followed by genetic counseling which are already available in many Muslim countries. Unfortunately, these type of facilities are not available in Bangladesh. Priority should be made to address the problem properly by incorporating and utilizing scientific research in the genetic field.

References

1. Mokhtari, R & Bagga A. Consanguinity, genetic disorders and malformations in the Iranian population. Acta Biologica Szegediensis 2003, 47(1-4):47-50.

2. Kumar V, Abbas AK, Aster JC. Robbins and Cotran pathologic basis of disease. 9th ed, 2015. Philadelphia, PA: Elsevier/Saunders.

3. Bittles AH. The role and Significance of Consanguinity as a demographic variable. Population and development Review 1994; 20:561-84.

4. Halim NB, Bouafif NBA, Romdhane L et al. Consanguinity, endogamy and genetic disorders in Tunisia. Journal of community genetics 2013; 4(2):273-84.

5. Bittles A. Consanguinity and its relevance to clinical genetics. Clin Genet 2001; 60:89–98.

6. Bittles AH, Black ML. Consanguinity, human evolution, and complex diseases. Proceedings of the National Academy of Sciences 2010; 107(suppl 1):1779-86.

7. Modell B and Darr A. Science and society: Genetic Counseling and Customary Consanguineous marriage. Nature Review Genetics 2002; 3:225-9.

8. Gunaid AA, Hummad NA, Tamim KA. Consanguineous marriage in the capital city Sana'a, Yemen. J Biosoc Sci 2004; 36:111-21.

9. Hamamy H and Alwan A. Hereditary disorders in the Eastern Mediterranean Region. Bull World Health Organ 1994, 72:145-54.

10. Bittles AH, Hussain R. An analysis of consanguineous marriage in the Muslim population of India at regional and state levels. Ann Hum Biol 2000, 27:163-71.

11. Butt NH. Childhood Blindness- Aetiological Pattern and Hereditary Factors. Pakistan J Ophthalmol 2002; 18:92-4.

12. Rogers NK, Gilbert CE, Foster A et al. Childhood blindness in Uzbekistan. Eye 1999; 13:65-70.

13. el-Hazimi MA, al-Swailem AR, Warsey AS et al. Consanguinity among the Saudi Arabian population. J Med Genet 1955; 32:623-6.

14. Hafez M, El-Tahan H, Awadalla M et al. Consanguineous mating in the Egyptian population. J Med Genet 1983; 20:58-60.

15. Shawky RM, El-Awady MY, Elsayed SM et al. Consanguineous matings among Egyptian population. Egyptian Journal of Medical Human Genetics 2011; 12(2):157-63.

16. Bener A. Consanguineous marriages and their effect on common diseases in the Qatari population. Genetic Disorders in the Arab World. Qatar 2012; 4:30-9.

17. Tadmouri GO, Nair P, Obeid T et al. Consanguinity and reproductive health among Arabs. Reprod Health 2009; 6:17.

18. Kerkeni E, Monastiri K, Saket B et al. Association among education level, occupation status and consanguinity in Tunisia and Croatia. Croat Med J 2006; 47:656–61.

19. Rajab A, Patton MA. A study of consanguinity in the Sultanate of Oman. Ann Hum Biol 2000; 27:321–6.

20. Chakraborty R and Chakravarti A. Onconsanguineous marriages and the genetic load. Human Genetics 1977; 36:47-54.

21. Liede A, Malik IA, Aziz Z et al. Contribution of BRCA1 and BRCA2 mutations to breast and ovarian cancer in Pakistan. The American Journal of Human Genetics 2002; 71(3):595-606.

22. Bhagya B, Sucharitha S, Avadhani R. Prevalence and Pattern of Consanguineous Marriages among Different Communities in Mangalore. Online J Health Allied Scs 2012; 11(4):7. Available at http://www.ojhas.org/issue44/2012-4-7.html

15. Shawky RM, El-Awady MY, Elsayed SM et al. Consanguineous matings among Egyptian population. Egyptian Journal of Medical Human Genetics 2011; 12(2):157-63.

23. Rahman MN, Rahman A, Kamal GM et al. Statistical pocketbook of Bangladesh-2013. Government of the People's Republic of Bangladesh 2014, Dhaka.

24. Mobarak AM, Kuhn R and Peters C. Consanguinity and other Marriage Market Effects of a Wealth Shock in Bangladesh. Demography 2013, 50(5):1845-71.

25. Amini SR, Kamali M.Consanguineous marriage among the parents of hearing impaired students in Mashhad. Iranian Rehabilitation Journal 2010; 8(12):36-8.

26. Hamamy AH, Al-Hadidy AM & Ajlouni MM. Consanguinity and genetic disorders. Saudi Medical Journal 2007; 28(7):1015-7.

27. Shamshad S. Prevalence of Consanguinity in Muslim Community-A Review.International Journal of Science and Research (IJSR) 2015, 4(5):2203-7.

28. Hamamy, H & Bittles AH. Genetic clinics in Arab communities: meeting individual, family and community needs. Public Health Genomics 2009; 12(1):30-40.

29. Asha Bai et al. Reproductive wastage and developmental disorders in relation to consanguinity in south India.Tropical Geography and Medicine 1981; 33;275-80.

30. Stoll et al. Parental Consanguinity as a cause of increased incidence of birth defects in a study of 131,760 consecutive births. American Journal of Medical genetics 1994; 49(1):114-7.

31. Kulkarni ML, Kurian M. Consanguinity and its effect on fetal growth and development: A south Indian study. Journal of medical genetics 1990; 27(6):348-52.

32. Gowda RS. Ramachandra NB. Parental Consanguinity increases Congenital heart diseases in south India. Annals of human Biology 2006; 33(5-6):519-24.

33. Bittles AH, Mason WM, Greene J et al. Reproductive behavior and health in consanguineous marriages. Science (Washington) 1991; 252 (5007):789-94.

34. Bittles AH, Black ML. The impact of consanguinity on neonatal and infant health. Early Hum Dev 2010; 86:737–41.

35. Hamamy H, Antonarakis SE, Cavalli-Sforza LL et al. Consanguineous marriages, pearlsand perils: Geneva International Consanguinity Workshop report. Genet Med 2011; 13:841-7.

36. Bennett R, Motulsky A, Bittles A et al. Genetic counseling and screening of consanguineous couples and their offspring: Recommendations of the National Society of Genetic Counselors. J Genet Couns 2002; 11(2):97–119.

37. Al-Gazali L, Hamamy H, Al-Arrayad S. Genetic disorders in the Arab world. Bmj 2006; 333(7573):831-4.

38. Temtamy S, Aglan M. Consanguinity and genetic disorders in Egypt. Middle East Journal of Medical Genetics 2012; 1(1):12-7.

39. Hussain R, Bittles AH, Sullivan S. Consanguinity and early mortality in the Muslim populations of India and Pakistan. Am J Hum Biol 2001; 13:777–87.

40. Stoltenberg C, Magnus P. Consanguinity and recurrence risk of stillbirth and infant death. Am J Public Health 1999; 89:517–23.

41. Khoury SA, Massad DF. Consanguinity, fertility, reproductive wastage, infant mortality and congenital malformations in Jordan. Saudi Med J 2000; 21:150–4.

42. Stoltenberg C, Magnus P. Birth defects and parental consanguinity in Norway. Am J Epidemiol 1997; 145:439–47.

43. Queisser-Luft A, Stolz G, Wiesel A et al. Malformations in newborn: Results based on 30,940 infants and fetuses from the Mainz congenital birth defect monitoring system (1990–1998). Arch Gynecol Obstet 2002; 266:163–7.

44. Durkin M, Khan N, Davidson L et al. Prenatal and postnatal risk factors for mental retardation among children in Bangladesh. Am J Epidemiol 2000; 152:1024–33.

45. Basson P. Genetic disease and culture patterns in Lebanon. J Biosoc Sci 1979; 11:201–7.

46. Becker S, Al Halees Z, Molina C et al. Consanguinity and con-genital heart disease in Saudi Arabia. Am J Med Genet 2001; 99:8–13.

47. Zlotogora J. Genetic disorders among Palestinian Arabs: Effects of consanguinity. Am J Med Genet 1997; 68:472–5.

48. Soliman AT, Elzalabany MM, Bappal B et al. Permanent neo-natal diabetes mellitus: epidemiology, mode of presentation, pathogenesis and growth. Indian J Pediatr 1999; 66:363–73.

49. Hamed R. The spectrum of chronic renal failure among Jorda-nian children. J Nephrol 2002; 15:130–5.

50. Hamamy HA, Masri AT, Al-Hadidy AM et al. Consanguinity and genetic disorders. Profile from Jordan. Saudi Med J 2007; 28:1015–7.

51. Abdel-Meguid AN, Zaki MS, Hammad SA. Premarital genetic investigations: Effect of genetic counselling. East Mediterr Health J 2000; 6:652–60.

52. Temtamy SA. Effects of consanguinity on birth defects in Egyptians: Project funded by National Research Centre. Cairo, Egypt:1998-2001.

53. Memish ZA, Saeedi MY. Six-year outcome of the national premarital screening and genetic counseling program for sickle cell disease and β-thalassemia in Saudi Arabia. Annals of Saudi medicine 2011; 31(3):229.

54. Fallah AA, Jafari T, Fallah A et al. Determination of aflatoxin M1 levels in Iranian white and cream cheese. Food and chemical toxicology 2009; 47(8):1872-5.

55. Al-Allawi NA, Al-Dousky AA. Frequency of haemoglobinopathies at premarital health screening in Dohuk, Iraq: Implications for a regional prevention programme. Eastern Mediterranean Health Journal 2010; 16(4):381.

56. Al Arrayed S. Campaign to control genetic blood diseases in Bahrain. Public Health Genomics 2005; 8(1):52-5.

57. Khorasani G, Kosaryan M, Vahidshahi K et al. Results of the national program for prevention of β-thalassemia major in the Iranian Province of Mazandaran.Hemoglobin 2008; 32(3):263-71.

58. Samavat A, Modell B. Iranian national thalassaemia screening programme. Bmj 2004; 329(7475):1134-7.

59. Hamamy H. Consanguineous marriages. Journal of community genetics 2012; 3(3):185-92.

60. Merin S, Lapithis AG, Horovitz, MichaelsonIC. Childhood blindness in Cyprus. Am J Ophthalmol 1972; 74:538-42.