ORIGINAL ARTICLE

Association of cousin marriages with congenital malformations

Hina Mehmood, Sobia Shahalam, Shazia Rizwan, Rizwan Waseem, Tayyaba Noor, Ammara Kaleem

Abstract

Introduction: Birth defects are a diverse group of disorders of prenatal origin that can be caused by single gene defects, chromosomal disorders, multifactorial inheritance, environmental teratogens and micronutrient deficiencies. Cousin marriages have been described as an important factor contributing to increased congenital malformations.

Objective: The objective of the study was to determine the association of congenital malformations of the central nervous system, cardiovascular system (VSD, AVSD, Pulmonary stenosis, Pulmonary atresia), cleft lip, cleft palate and polydactyly) with cousin marriages.

Material and Methods: It was a case-control study carried out in Ghurki Trust Teaching Hospital, Lahore from 30th April, 2020 to 30th April, 2021. Total 200 neonates fulfilling the inclusion criteria for cases & controls were included in the study. After taking informed consent from the parents, all anatomical defects (for cases) were recorded on a pre-designed proforma. History of consanguinity and type of consanguinity (first cousins) was taken for both cases and controls and recorded on the proforma. Data was entered and analyzed by using SPSS 20.0 software.

Results: Frequency of consanguinity in parents was recorded which was 73%(n=73) in cases and 38%(n=38) in controls while 27%(n=27) in cases and 62%(n=62) in controls had no consanguinity in parents.

Conclusion: There is an association of consanguinity with congenital malformations.

Received
date: 2nd April, 2022
Accepted
date: 1st Decemer, 2022

Keywords :Consanguinity, congenital malformations, VSD, AVSD, Pulmonary stenosis, Pulmonary atresia), cleft lip, cleft palate, polydactyly

Lahore Medical & Dental College/Ghurki Trust Teaching Hospital, Lahore
H Mehmood
S Shahalam
S Rizwan
R Waseem
T Noor

Children Institute of Health and Sciences University, Lahore
A Kaleem

Correspondence:
Dr. Shazia Rizwan
Lahore Medical & Dental College, Ghurki Trust Teaching Hospital, Lahore
Cell No:+92 000-0000000
email: drshaziarizwan@gmail.com

Introduction:

Congenital anomalies are the leading cause of infant mortality and contribute to long term medical problems.[1] Congenital malformation are present at birth.[2] According to WHO, approximately 240,000 babies die in neonatal period every year due to congenital disorders.[3] The etiology of congenital malformation is genetic (30%-40%) and environmental (5%-10%). Due to genetic factors risk of congenital anomalies is high with cousin marriages. Pakistan is one of those countries who have very high percentage of cousin marriages, nearly 62%, which mainly account for 30 million suffering from inherited disorders.[4] It has been reported in Punjab that congenital anomalies due to consanguinity are in 59% families.[5]

According to the latest WHO data published in April 2011, congenital anomalies deaths in Pakistan reached 26,627 or 2.08% of total deaths.[6] The age adjusted death rate is 10.01 per 100,000 of the population which ranks Pakistan number 14th in the world.[6] The frequency of consanguineous marriages in normal and malformed children was reported to be 31.02% and 55.5% respectively in a study on the prevalence of gross congenital malformations at birth in the neonates in a tertiary care hospital.[7]

It was found that in the Middle East, Pakistan had the most rates of inbreeding marriages

Table 1: Age distribution (n=200)

	Cases (n=100)		Controls (n=100)	
Age (in days)	**No. of patients**	**%**	**No. of patients**	**%**
1-15	66	66	71	*71*
16-28	34	34	29	*29*
Total	100	100	100	*100*
Mean+SD	13.5+6.96		12.82+7.05	

Table 2: Gender distribution of the neonates (n=200)

	Cases (n=100)		Controls (n=100)	
Gender	**No. of patients**	**%**	**No. of patients**	**%**
Male	58	58	61	*61*
Female	42	42	39	*39*
Total	100	100	100	*100*

Table 3: Frequency of consanguinity in parents (n=200)

	Cases (n=100)		Controls (n=100)	
Consanguinity	**No. of patients**	**%**	**No. of patients**	**%**
Yes	73	73	38	*38*
No	27	27	62	*62*
Total	100	100	100	*100*

Odds Ratio= 4.41

Table 4: Stratification for type of consanguinity (n=111)

	Cases (n=73)		Controls (n=38)	
Type to consanguinity	**No. of patients**	**%**	**No. of patients**	**%**
First cousin	47	64.38	23	*60.53*
Second cousin	26	35.62	15	*39.47*
Total	73	100	38	*100*

(60%) followed by Qatar (54%) and Saudi Arabia (51.3%).[7] According to the Pakistan Demographic and Health Survey, more than half of all marriages in Pakistan (61%) are between first and second cousins, 8% of the marriages are between second cousins and 7% between other relations and one third between non-relatives.[8] Sindh has the highest proportion of marriages between first cousins (56%), followed by Punjab(53%), Baluchistan(52%) and NWFP(43%).[8]

On the other hand it also has been observed that the pattern of anomalies witnessed in this cohort and a high occurrence of sporadic cases point to a substantial role of non-genetic etiological factors, which could be minimized by strengthening the health-care system.[9,10]

This study was conducted to determine an association, if any between consanguinity and congenital malformations as the consanguinity ratios are high in Pakistan.

Material and Methods:

It was a case control study carried out in the department of Pediatric medicine, Ghurki Trust Teaching Hospital, Lahore. The duration of study was 12 months. Sample size as 200 containing 100 children with anomalies and 100 without anomalies, estimated by using 1% level of significance, 80% power of test. All babies (28 weeks or above) were included. Children with congenital malformations of the CNS, CVS (VSD, AVSD, pulmonary stenosis and atresia), cleft lip, cleft palate and polydactyly were enrolled. Children with family history of congenital malformations, children born to mothers who had taken teratogenic drugs, substance of abuse, maternal age > 35 years, mothers having TORCH infection, chronic ailments or children with multiple congenital anomalies were excluded. After taking written informed consent from the parents, all anatomical defects (for cases) were recorded on a pre-designed proforma along with particulars of the new born like live born/still born, sex, birth weight, length and head circumference. History of consanguinity and type of consanguinity (first cousins) was taken for both cases and controls and recorded on the proforma. Data was entered and analyzed by using SPSS 20.0 software. The data for age was presented by using mean±S.D for both groups. Gender of the child and consanguinity in parents were presented by using frequency and percentages. Odd's ratio was calculated to determine the association between congenital malformations and consanguinity. An Odd's ratio of >1 was considered significant. Chi-square test was applied to determine the significance between various congenital anomalies and consanguinity. P-value of <0.05 was considered significant.

Results:

A total of 200 subjects (100 cases and 100 controls) fulfilling the inclusion/exclusion criteria

were enrolled to determine the association of consanguinity with congenital malformations of the central nervous system, cardiovascular system (VSD, AVSD, Pulmonary stenosis, Pulmonary atresia), cleft lip, cleft palate and polydactyly. Age distribution of the patients was done which shows that 66%(n=66) in cases and 71%(n=71) in controls were between 1- 15 days and 34%(n=34) in group-A and 29%(n=29) in group-B were between 16-28 days of age, mean+sd was calculated as 13.5+6.96 in cases and 12.82+7.05 in controls. (table No. 1) Gender distribution of the patients is given in table no 2. Frequency of consanguinity in parents was recorded 73%(n=73) in cases and 38%(n=38) in controls while 27%(n=27) in cases and 62%(n=62) in controls had no consanguinity in parents, odds ratio was calculated as 4.41 which is significant. (table no. 3). Stratification for the type of consanguinity shows that out of 73-patients in cases group 64.38% (n=47) were first cousin while remaining 35.62% (n=26) were second cousin while in control group, out of 38 patients, 60.53% (n=23) were first cousin and 39.47% (n=15) were second cousin. (table no. 4)

Discussion:

It is very important to discuss consanguineous marriages in our society as plethora of congenital anomalies are associated with it and although we have the approval in some societies, the infant has to face many a condition, if living, which is not curable.[11] Consanguineous marriage is a type of inter-familial union, defined as the marriage between two blood-related individuals who are second cousins or closer.[12] Congenital malformations are described as major, if associated with medical, developmental or social significance; otherwise they are minor.[13] Major anomalies occur in about 2.5-4% of live births but minor defects are more common in the population.[14] Some major malformations are not compatible with life, others require sophisticated surgical reconstructions as well as expensive rehabilitative therapies for optimal survival. Such multidisciplinary care is often unavailable and unaffordable to affected families, without financial supports. This highlights the need to promote health foundations focusing on prevention and management of birth defects in resource-limited settings to reduce associated mortality and disability-adjusted life years.[14] Pakistan is overly populated country with a lower-middle-income economy. Over 90% of the population are Muslims. Because of a semi-conservative social structure with intense religious sentiments and societal bonding , people prefer cousin marriages. In this study, consanguineous marriages among cases were significantly higher than non-consanguineous marriages. A similar study was conducted in India which showed incidence of congenital anomalies was 1.25%. The commonest congenital anomalies were CNS(37%) followed by musculo-skeletal system(13%) and digestive system(10%).[15] According to study done by Khanal GP et al, in 2019 in Nepal, most commonly involved system was CNS (48%), followed by CVS (11%), musculoskeletal (10%) and digestive system (5%).[16] Study conducted at Hyderabad, Sindh showed that prevalence of congenital birth defects was 11.3%, of these 30% had CNS malformations followed by 30% digestive, 24% musculo-skeletal, 12% genito-urinary and 4% ear malformations.[17] Prevalence of cousin marriages is high in those regions of the world which lack education and awareness. Genetic consultancy may play imperative role in those populations where consanguineous marriages are unavoidable. For early diagnosis and management, pre-natal and post-natal screening programs for genetic diseases would be beneficial in the regions of high consanguinity rates.[18]

Conclusion:

We concluded that there is an association of consanguinity with congenital malformations of the central nervous system, cardiovascular system (VSD, AVSD, Pulmonary stenosis, Pulmonary atresia), cleft lip, cleft palate & polydactyly.

Limitations: There are no national level studies conducted to find prevalence of consanguinity. Therefore, the correlation of observed prevalence in this study to the general population prevalence is not possible.

Conflict of interest: None

Funding source: None

Role and contribution of authors:

Hina Mehmood, Initiator of this study and helped in writing the study protocol and a large part of this manuscript and data collection.

Sobia Shahalam, research coordinator, data collection, writing draft and literature research.

Shazia Rizwan, contributed to intellectual concept of study and research coordinator and data collection.

Rizwan Waseem, review of manuscript, revising, approval of final manuscript.

Tayyaba Noor, supervisor for the protocol and progress of study.

Ammara Kaleem, statistical analysis and validation data curation and correct presentation of the results.

References:

1. Verges F M, Woods S L, Aucott S W, Boss R D, Sulpar L J. Prenatal consultation with a neonatologist for congenital anomalies: Parental Perceptions. Pediatrics. 2009;124:e573-9.
2. Obu H A, Chinawa J M, Uleanya N D, Adimora G N, Obi IE. Congenital malformations among newborns admitted in the neonatal unit of a tertiary hospital in Enugu, South-East Nigeria-a retrospective study. BMC Res Notes.2012;5:177.
3. Congenital disorders [Internet]. World Health Organization. World Health Organization; [cited 2023Apr5]. Available from: https://www.who.int/news-room/fact-sheets/detail/birthdefects#:~:text=An%20estimated%20240%20000%20newborns,1%20month%20and%205%20years.
4. Jabeen, N., & Malik, S. (2014). Consanguinity and its sociodemographic differentials in Bhimber district, Azad Jammu and Kashmir, Pakistan. Journal of health, population, and nutrition, 32(2), 301.
5. Naveed M, Nadeem S, Hassan A, Tanvir I. Association of consanguineous marriages with congenital anomalies. Pakistan BioMedical Journal. 2019;2(1).
6. Sedehi M, Keshtkar A, Golalipour MJ, The knowledge and the attitude of youth couples on/towards consanguineous marriages in the North of Iran. JCDR.2012;6(7):1233-6.Pakistan Demographic & Health Survey 2006-07.
7. Bage NN, Rao S. Is consanguineous marriage responsible for congenital cardiac and extra-cardiac anomalies ?J.Evolution Med.Dent.Sci.2016;5(19):930-932,DOI:10.14260/jemds/2016/216
8. Anwar S, TasleemMourosi J, Arafat Y, Hosen MJ(2020) Genetic and reproductive consequences of consanguineous marriage in Bangladesh . PLoSONE15(11): e0241610.
9. Bhatti NA, Mumtaz S, Malik S. Epidemiological study of congenital and hereditary anomalies in Sialkot District of Pakistan revealed a high incidence of limb and neurological disorders. Asian Biomed. 2019;13(2):49–60. doi:10.1515/abm-2019-0040
10. Bibi A, Naqvi SF, Syed A, Zainab S, Sohail K, Malik S. Burden of congenital and hereditary anomalies in Hazara population of Khyber Pakhtunkhwa, Pakistan. Pakistan Journal of Medical Sciences. 2022;38(5).
11. Bacino C. Birth Defects: Epidemiology, Types and Patterns. UpToDate;2017. Available from: https://www.uptodate.com/contents/birth-defects-epidemiology-types-and-patterns. [Last accessed on 2018 July 02].
12. Sitkin NA, Ozgediz D, Donkor P, Farmer DL. Ccongenital anomalies inlow-middle-income contries: The unborn child of global surgery. World J Surg 2015;39:36-40.
13. Yadav M, Subedi S, Prevalence and Pattern of Birth Defects in a Tertiary Referral Centre ,JoNMC.10:1(2021)20-24.
14. KhanalGP ,Sharma P, Kayastha P, Poudel ., Prevalence and Spectrum of Fetal Congenital Anomalies: A hospital based study from Mid-Western part of Nepal, Nepalese Journal of Radiology. 9:14(2019)2-9.DOI: http://dx.doi.org/10.3126/njr.v9i2.27413
15. Kazi SA,Memon MA, Radhan AH. Frequency of congenital birth defects in newborn babies born at Hyderabad , Sindh. Professional Med J 2020; 27(4):707-710. DOI: 10.29309/TPMJ/2020.27.04.3400
16. Bhinder MA(2017) Consanguineous Marriage: A Peril for Coming Generation. J Genet Disord. Vol.1 No.1:08.