Original Article

Potential Risk Factors for Congenital Malformations in Neonates: A Case Series Study in Two Tertiary Care Hospitals of Lahore City

Najam ud Din, Shahbano Ishfaq, Muhammad Naeem, Malik Shahid Shaukat, Zaheer Iqbal and Zain Safdar

Objective: 1.To Study the potential risk factors for congenital malformations in neonates admitted at two tertiary care hospitals of public sector in Lahore city. 2.To find out the frequency of systems affected in congenital anomalies.

Methods: It was a "case series" study conducted at Children hospital and Services hospital Lahore. All the congenital malformations from 1st April to 30th April, 2013, in neonates admitted in these institutions were included in the study. Mothers of 40 cases of congenital malformations were interviewed after taking verbal consent, using self-administered, pre-tested questionnaire. Data was analyzed by using SPSS version 14.

Results: The frequency of cousin marriages in parents with congenitally malformed children was considerably high i.e. 65%. Majority of mothers i.e. 62.5% were below metric, 87.5% belonged to low income group, 62.5% did not made an increase in diet during pregnancy, 35% suffered from stress during pregnancy and 30% had previous abortion. The number of anomalies of urogenital system and GIT were higher with frequency of 45% and 30% respectively with a cumulative frequency of 75%.

Conclusion: The frequency of congenital malformations was considerably higher among parents with consanguinity, in low income groups, mother's education less than metric and paternal age greater than 30 years. The number of anomalies of urogenital system and GIT were higher in our subjects with frequency of 45% and 30% respectively with a cumulative frequency of 75%.

Keywords: Public hospitals, congenital malformation, congenital anomalies, cousin marriage, stress during pregnancy, diet during pregnancy.

Introduction

Congenital anomaly is a defect at birth and occurs in approximately 5% of babies. Congenital anomalies are categorized in to two groups.[1] First group: Malformations is a primary defect of organ or tissue development in the embryo or fetus. Second group: Deformation is damage caused by external factors influencing previously normal structure. Malformation & deformations occur in a ratio of 3:2.These conditions are important cause in neonatal & prenatal mortality accounting for about 40% of deaths.[2] Congenital malformations affect 2.5% of infants at birth and are responsible for about 15% of perinatal mortality in India.[3,4] In United States in 2013, infant mortality rate was 5.96 infant deaths per 1000 live births and the leading cause of infant death was congenital malformations accounting for 20% of all infant deaths.[5]Birth defects account for 1530% of all pediatric hospitalizations. They exert a proportionately higher health care cost than other hospitalizations and impact a significant burden to families and society.[6] Children with congenital malformations in Egypt, male were more affected than female (1.8:1). According to ICD-10 classification of congenital malformations the system involved in descending order of frequency were nervous system ,chromosomal abnormalities, genital organ anomalies, musculoskeletal system, urinary system, circulatory system, eye ear face and neck anomalies, other congenital malformations, digestive system ,cleft lip and cleft palate anomalies,respiratory System.[7] Congenital Malformations are not rare in Pakistan, studies show that 2.9 to 7% of newborns had various congenital anomalies in Pakistan .[8,9] According to the latest WHO data published in May 2014; congenital anomalies deaths in Pakistan reach 26,353 or 2.34% of total deaths and ranks Pakistan #5 in the world. [10] In many cases, the cause of congenital anomalies is unknown, however, several factors are known to be associated with congenital anomalies including genetic factors i.e. achondroplasia, cystic fibrosis, hemophilia, neural tube defects. Socioeconomic and demographic factors i.e. Low-income may be an indirect determinant of congenital anomalies, with a higher

frequency among resource-constrained families and countries. It is estimated that about 94% of severe congenital anomalies occur in low- and middle-income countries.[11] Factors often associated with lower-income may induce or increase the incidence of abnormal prenatal development. Dietary factors (Folate insufficiency and excessive vitamin A intake) and poorer access to healthcare may also be indirect determinants of congenital anomalies. Advanced maternal age increases the risk of chromosomal abnormalities, including Down syndrome. Environmental factors i.e. Maternal exposure to certain pesticides and other chemicals, as well as certain medications (thalidomide, streptomycin, tetracycline, phenytoin), alcohol, tobacco and radiation during pregnancy, may increase the risk of having a fetus or neonate affected by congenital anomalies. Maternal infections (rubella, cytomegalovirus, toxoplasmosis, syphilis & exposure to Zika virus) may affect the normal development of an embryo or fetus.[11] Recently, it is assumed that the health effects of maternal stress may include increased risk of certain birth defects.[12] A large number of malformations are incompatible with life and they involve one system or multiple systems of the fetus. Congenital malformations cause mental trauma to the parents since it puts the entire life of child with congenital malformations into jeopardy. The congenital malformations are collectively major health problem and leads to lifelong disabilities in children that compromises the quality of life from the very beginning. In Pakistan very few studies have been conducted so far, the data of this study will contribute to explore the risk factors of congenital malformations and some hypothesis can be generated by this descriptive data.

Methods

The Study Design was a "Case Series" conducted at Neonatal Intensive Care Unit, Surgical Neonatal Intensive Care Unit, Cardiac Intensive Care Unit of Children hospital Lahore and pediatrics department of Services hospital, Lahore, after obtaining written permission from higher authorities of these settings. All neonates with congenital malformations admitted in these institutions during 1st April to 30th April, 2013, were included in the study. Mothers of malformed neonates were interviewed after taking informed consent using self-administered, pre-tested questionnaire. Mothers too sick to give interview were excluded from the study. SPSS computer software version 14 was used for entry, compilation, analysis of the data. The outcome variables were listed as frequencies and proportions.

Results

The results shows that out of 40 subjects, 23(57.5%) mothers having anomalies in their babies, were below 30 years of age while 17(42.5%) were 30 years and above. Overwhelming majority i.e. 37(92.5%) mothers were housewives while only 3(7.5%) were workers. Out of 40 mothers, 25(62.5%) were under matriculation while 15(37.5%) were metric and above. Regarding the age of the fathers, 13(32.5%) fathers were 30 years and below while 27(67.5%) were above 30 years. The frequency is considerable high in age above 30year.Regarding the monthly family income, 35(87.5%) families were up to 3000 and 5(12.5%) were above 3000 rupees. The frequency is considerably high in low income group i.e. rupees 3000 and below and constitutes 87.5 %.Regarding the mode of delivery, out of 40 subjects, 30(75%) mothers had SVD while 10(25%) had C-section. As for as the parity is concern, 14(35%) were prime-para and 26(65%) were multiparous. **Table-1** shows that out of 40 subjects, 14(35%) mothers married outside the family while 15(37.5%) married with paternal relatives and 11(27.5%) married with maternal relatives. The frequency is considerably high for cousin marriage i.e. 65%. Out of 40 subjects in our research, 4(10%) of the siblings of the malformed babies were also congenitally malformed. Out of 40, not a single of mother or father suffered from any congenital malformation and not a single mother was drug addict. Out of 40 subjects, 2(5%) of mothers took anti-allergic, 2(5%) took anti-hypertensive, 7(17.5%) took other drugs and 29(72.5%) did not take any drug at all during pregnancy. Out of 40 mothers, 14(35%) suffered from Psychological stress during pregnancy. Out of 40 subjects, 25(62.5%) of mothers didn't make any increase in diet while just 15(37.5%) made an increase in different sort of diets. Out of 40 mothers, 12(30%) had previous abortion while 28(70%) did not have any abortion previously. Only 1(2.5%) of mother had radiation exposure to X-rays, 4(10%) had other types of radiation exposure and 35(87.5%) did not have any kind of radiation exposure. Out of 40, only 1(2.5%) mother gave the history suggestive of rubella infection during pregnancy while remaining mothers i.e. 39(97.5%) did not give any history suggestive of rubella infection during pregnancy.

Table-1: Frequency distribution of potential risk factors for congenital malformations

Risk Factors	Frequency (n=40)	Percentage
Relation with spouse		
Married outside family	14	35.0
Married with paternal relative	15	37.5
Married with maternal relative	11	27.5
Anomaly in siblings		
Yes	04	10.0
No	36	90.0
Congenital anomaly in parents		
Mother No anomaly	40	100.0
Father no anomaly	40	100.0
Mother's illness		
Diabetes	02	5.0
Hypertension	01	2.5
Any other	07	17.5
None	30	75.0
Addiction in mothers		
None	40	100.0
Drugs taken during pregnancy		
Anti-allergic	02	5.0
Anti-Hypertensive	02	5.0
Any Other	07	17.5
None	29	72.5
Psychological stress during pregnancy		
Yes	14	35.0
No	26	65.0
Diet during pregnancy		
No increase in diet	25	62.5
Yes in meat	03	7.5
Yes in fruits and vegetable	10	25.0
Yes in milk	01	2.5
Yes in vitamins and iron supplements	01	2.5
H/O of previous abortion		
Yes	12	30.0
No	28	70.0
Rediation exposure		
X-ray	01	2.5
Any other	04	10.0
History suggestive of Rubella infection		
Yes	01	2.5
No	39	97.5

Table-2: Frequency of Systems affected in congenital anomalies.

Systemic involment of congenital anomalites	Frequency (n=40)	Percentage
Urogenital anomaly	18	45.4
GIT	12	30.0
CVT	03	7.5
CNS	02	5.0
Facial	05	12.5
Total	04	100.0

Table-2 reveals that out of 40 subjects in our research, 18(45%) of the children showed urogenital anomalies, 12(30%) showed GIT anomalies, 3(7.5%) showed CVS anomalies, 2(5%) showed CNS anomalies and 5(12.5%) showed facial anomalies.

Discussion

In our research women less than 30 years of age have highest prevalence of anomalies i.e. 57.55% which is in contrary to research done by Crone and Shaw in California [13] in which it was stated that, the overall prevalence of all congenital anomalies across the age distribution was shown as a J shape, with pregnant women aged 20-29 years having the lowest prevalence, teenage pregnant women having an intermediate prevalence and pregnant women more than 40 years old having the highest prevalence. Findings of another research done by Seda Ates et al with topic of "Pregnancy Outcome of Multiparous Women Aged over 40 years [14] in which it was found that, less than one tenth of the mothers were adolescence and also less than one tenth were old mothers and the infants of the older mothers showed a higher incidence of stillbirth (5.1% versus 0%), admission to the neonatal intensive care unit (5.1% versus 1.03%), and fetal malformation (3.09% versus 0.8%) than younger mother. The reason may be the difference of sample size, place and socioeconomic status of the populations.

Regarding the paternal age, in our research it was found that fathers with age more than 30 years have higher frequency of abnormal babies i.e. 67.5% which goes in accordance with the research conducted at Cairo University, Tehran[15] which showed that overall there were no differences in the prevalence of malformations as a function of paternal age. However, the prevalence of malformations of extremities and syndromes of multiple systems, as well as Down's syndrome, increased with increasing paternal age which is in accordance. In our study population 62.5% women did not make an increase in diet during

pregnancy which is in accordance with research conducted in Haryana on Prevalence of multiple micronutrient deficiencies amongst pregnant women in a rural area of Haryana [16] in which dietary intake data revealed an inadequate nutrient intake. Over 19% Pregnant women were consuming less than 50% of the recommended calories. The consumption of food groups rich in micronutrients (pulses, vegetables, fruits, nuts and oil seeds, animal foods) was infrequent. In our study 65% of all cases with anomalies have parents with consanguinity which indicates a much higher prevalence of congenital malformations in consanguineous marriage which is in accordance with the research conducted in Kashan[15] shows that among the consanguineous group, 7.0% births had congenital anomalies. Congenital malformations in the non-consanguineous group were 2.0%. Therefore congenital malformations were 3.5 times more common in consanguineous versus non-consanguineous marriages. In our studies it is found that only 5% of mothers having babies with congenital malformations used anti-hypertensive drugs which is in contrast with the research conducted in England by Cooper et al [17] on congenital malformations after first trimester exposure to medicines which shows that Infants with only first-trimester exposure to ACE inhibitors had an increased risk of major congenital malformations (risk ratio, 2.71; 95 percent confidence interval, 1.72 to 4.27) as compared with infants who had no exposure to antihypertensive medications. Among infants with exposure to ACE inhibitors in the first trimester alone, the adjusted proportion with any major congenital malformation was 7.1 %. In comparison with children with no fetal exposure to antihypertensive medications, the risk of major congenital malformations in this group was increased by a factor of more than 2 (risk ratio, 2.71; 95 percent confidence interval, 1.72 to 4.27).

Only 2.5% of the subjects of our study population had history suggestive of rubella infection during pregnancy. Literature shows that Congenital Rubella Syndrome (Congenital defects)) can occur in a developing fetus of a pregnant woman who has contracted rubella, usually in the first trimester. If infection occurs 028 days before conception, the infant has a 43% risk of being affected. If the infection occurs 012 weeks after conception, the risk increases to 51%. If the infection occurs 1326 weeks after conception, the risk is 23% of the infant being affected by the disease. If infection occurs 2640 weeks after conception, Infants are not generally affected.[18]

In our research, 18(45%) of the children showed urogenital anomalies, 12(30%) GIT anomalies, 3(7.5%) CVS anomalies, 2(5%) CNS anomalies and 5(12.5%) facial anomalies, however this finding differs from what was observed in a study done in neonatal unit of Combined Military Hospital, Kharian Cantt Pakistan9 ,where it was found that anomalies related to the central nervous system were 46(20.35%), musculoskeletal 42(18.58%), genitourinary 34 (15.04%), cardiovascular system 30 (13.27%), ear, eye, face, neck 27(11.94%), digestive system 19 (8.40%), syndromes and skin 14 (6.19%) each. This difference may be due to many factors like difference in place of study, nature and size of sample and socioeco- nomic status.

Conclusion

The frequency of congenital malformations was considerably higher among parents with consanguinity, in low income group, under matric mothers, multiparity, paternal age greater than 30 years. Moreover, the frequency of congenital malformation was considerably high among mothers who did not make an increase in diet during pregnancy. The number of anomalies of urogenital system and GIT were considerably higher in our subjects with frequency of 45% and 30% respectively with a cumulative frequency of 75%.It is recommended that cousin marriages should be avoided. Balanced diet should be maintained throughout pregnancy including macronutrients as well as micronutrients. Awareness should be created among target groups through media and High school curricula should include a chapter on congenital anomalies emphasizing on primordial prevention of risk factors to reduce the burden of diseases related to such defects.

Department of Community Medicine
SIMS/Service Hospital, Lahore

References

1. Betty R. Denisetran: Maye's Midwifery. 12th edition.1997: 912-914
2. Barker D. Maternal nutrition and cardiovascular disease. Nutr Health 1999;19 (2): p.99
3. Merchant SM. Indian Council of Medical Research. Genetic Research Centre, Bombay. Annual Report 1989: p 27
4. Singh M. Hospital-based data on perinatal and neonatal mortality in India. Indian Pediatr 1986; 23: 579-584.
5. Mathews TJ, Marian F. MacDorman, Marie E. Thoma. National Vital Statistics reports- CDC. Vol 64, No.9, Agust 6,2015.
6. Hobbs CA,Cleves MA,Simmons CJ.Genetic epidemiology and congenital malformations. .Arch Pediatr Adolesc Med 2002;156:315-20.
7. Rabah M S,Doaa I S.Congenetal malformations prevalent among Egyptian children and associated risk factors. The Egyptian journal of medical human genetics 2011; 12:69-78.
8. Khan A, Zuhaid M, Fayaz M, Ali F, Khan A, Ullah R, et al. Frequency of Congenital Anomalies in Newborns and Its Relation to Maternal Health in a Tertiary Care Hospital in Peshawar, Pakistan. Int J Med Students. 2014 Nov;3(1):19-23.
9. Hussain S,Sabir M, Tarar SH,Mushtaq R,Asgar I,Chatta MN.Prevalence and pattern of congenital malformations among neonates in the neonatal unit of a teaching hospital.J Pak Med Assoc 2014 June;64:629.
10. Congenital Anomalies in Pakistan Word life expectancy. [Cited 2016 Dec 31]. Available from Www.worldlifeexpectancy.com/pakistan- congenital-anomalies.
11. WHO fact sheet updated September 2016 .[cited 2016,Dec 31].available from Www.who.int/mediacentre/factsheets/fs370/en/
12. Hendricks CH. Congenital malformations: analysis of the 1953 Ohio records. Obstet Gynecol. 1955; 6:592-598.
13. Crone LA, Shaw GM, Jensvold NG, Harris JA. Birth defects monitoring in California: a resource for epidemiological research. Paediatr Perinat Epidemiol 1991; 5:423-27.
14. Ates S, Betmaz G, Sevket O, Molla T, Dane C, Dan B. Pregnancy Outcome of Multiparous Women Aged over 40 years .Int.J Reprod Med 2013, Online journal [cited 2016 Oct 22]. Available from Https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4388023/
15. Pattern of congenital malformations in consanguineous versus non consanguineous marriages in Kashan, Islamic Republic of Iran. East Mediterrs Health J 2006;13(4):868-75
16. Prevalence of multiple micronutrient deficiencies amongst pregnant women in a rural area of Haryana.Indian J Pediatr 2004;71(11):1007-14.
17. William O, Cooper, Diaz SH, Patrick G, Judith A, Dudley et al. Major Congenital Malformations after First-Trimester Exposure to ACE Inhibitors. N Engl J Med 2006;354:2443-51.
18. Congenital Rubella Syndrome.[cited 2017 , January 4] available from Https://en.wikipedia.org/wiki/Congenital_rubella_syndrome .

Answer Picture Quiz

Granulomatosis with polyangitis (wegener's Granulomatosis)