ORIGINAL ARTICLE

PARENTAL CONSANGUINITY INCREASES THE RISK OF CONGENITAL MALFORMATIONS

Maheen Gul[1], Dil Noor[2], Gulrukh Nazir[3], Ahsan Saidal[2], Haji Bahadar[3]

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Authors' Affiliation
[1]Radiology Technology, Institute of Paramedical Sciences Khyber Medical University, Peshawar
[2]Anesthesia Technology, Institute of Paramedical Sciences Khyber Medical University, Peshawar
[3]Institute of Paramedical Sciences Khyber Medical University, Peshawar

Corresponding Author
Dr. Haji Bahadar
Assistant Professor
Institute of Paramedical Sciences Khyber Medical University Peshawar
Email: bahadarph@kmu.edu.pk

ABSTRACT

Introduction: Congenital malformation is a physical or structural abnormality present either prenatally or after birth. These anomalies are either primary or secondary malformation. Primary malformations adversely affect body functions, however, the secondary malformations are the structural defects which may have less or no effect on body functions. Primary congenital anomalies show marked variations globally with respect to prevalence. The aim of the current study was to further add to the scientific evidences on the pattern and prevalence of congenital anomalies in cousins and non-cousins' marriages in Khyber Pakhtunkhwa.

Material and Methods: Data of 200 patients (divided into two groups) was collected by convenience sampling through cross-sectional survey. Group-I consisted of 100 gravidas who were diagnosed with anomalous foetus either hydrocephalous, anencephaly or cleft lip/palate and Group-II comprised of infants with inborn heart defects were selected.

Results: The study shows 68% consanguineous and 32% non-consanguineous marriages. Hydrocephalous shows the highest rate of incidence (55%) followed by anencephaly (40%) cleft lip/palate (5%), Ventricular Septal Defect (43%), Atrial Septal Defect (29%), Patent Ductus Arteriosus (16%) and Tetralogy of Fallot (12%). The relative risk of hydrocephalus and anencephaly in consanguineous and non-consanguineous marriage was 0.98 while the relative risk of Ventricular Septal Defect and Patent Ductus Arteriosus was 1.1. Rate of miscarriages was comparatively high in cousin marriages. Frequency of CM was higher in multigravida compared to primigravida. Detection rate of hydrocephalus was highest in second trimester, cleft lip/palate in third trimester and anencephaly in first trimester.

Conclusion: Parental consanguinity is one of the major risk factors for structural, neurological and cardiac anomalies.

Key Words: consanguineous, congenital malformations, non-consanguineous marriage

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INTRODUCTION

Congenital malformation (CM) is a structural abnormality present either prenatally or after birth. CM may be primary or secondary malformation. Primary malformations may alter body functions, while secondary malformations are structural defects which may have less or no effect on body functions.[1] Primary CM shows marked variations in the entire world with the prevalence varying from less than 1% to 8%, causing 20% to 30% of perinatal mortality.[2] Beside other risk factors i.e patient's age, radiation exposure and socioeconomic status, 'consanguineous marriages' are considered as a high-risk for congenital anomalies.[1] Consanguineous marriages or endogamy is the unification of husband and wife who are second cousins or closer relatives. Endogamy has been carried out since the existence of human beings. Currently, about 20% of the population live in societies where consanguineous marriages are common.

As per available literature, there is a noticeable geographical and ethnic discrepancy in the distribution, frequency and incidence of different birth defects.[3] The prevalence of CM in muslim world is reported as 10-45%, while in other countries, it has been reported as 43%, 26-34%, 3% and 2-3% in Taiwan, UK, Denmark and the USA, respectively. High ratio of CM is recorded in Muslim countries which may be due to the increased trend of consanguineous marriages.[4] Regarding the patterns of CM, previous studies locally and internationally have revealed various patterns. It has been reported that children born to consanguineous family often affects urogenital, musculoskeletal and cardiovascular systems.[5]

In the context of Pakistan, very few studies have been conducted regarding the pattern of various anomalies in cousin marriages. Studies conducted in the neonatal unit of Kharian Combined Military Hospital and Khyber Teaching Hospital reported high incidence of various pattern of anomalies in CNS (58%) followed by musculoskeletal defects (25%) and genitourinary system.[6] The introduction of Foetal Ultrasound Scanning has greatly increased the chances of earlier detection which has further reduced the rate of newborn

mortality and morbidity. It allows the families and healthcare staff to take decisions on pregnancy management and helps in planning for the complications in childbirth and detecting possible risks of future gravidity.

Approximately, 53% of CM can be diagnosed at 14th week of pregnancy. However, different congenital anomalies are detected by detailed anomaly scan between 18-22-week gestation. With the introduction of prenatal echo to fetal ultrasound scanning in-utero has lead to detection of heart defects with high sensitivity and specificity.[2] National Health Services (NHS) Fetal Anomaly Screening Programme (FASP) has selected two chromosomal anomalies and nine structural malformations i.e skeletal dysplasia anencephaly, cardiac anomalies, spina bifida, exomphalos, cleft lip/palate, gastro schiosis, bilateral renal agenesis and diaphragmatic hernia for which every gravida should be screened.[7] As per available literature, the patterns of CM remained under-studied in Khyber Pakhtunkhwa. Our study aimed to further add to the scientific evidence on the pattern and prevalence of CM in consanguineous and non-consanguineous marriages in Khyber Pakhtunkhwa.

MATERIAL AND METHODS

It was a descriptive cross-sectional design which involved a non-probability convenient sampling technique, with the sample size of 200 participants. It was approved by the ethical review committee of the institute. Study protocol and the use of data for research were fully explained to the Medical Superintendent and head of a Radiology Department. The study included separate performa for ultrasound and echocardiography data collection. Gravida name, age, geographical location, chronic disease if any, type of marriage, history of miscarriage, type of gravidity, history of congenital malformation in previous alive children, trimester, gestational age, type of congenital malformation present i.e. hydrocephalous, anencephaly or cleft lip/palate were included in ultrasound data collection proforma while echo proforma included patient's name, age, geographical location, type of parental marriage, type of Coronary Heart Diseases (CHD) presents i.e. ventricular septal defect (VSD), Atrial Septal Defect (ASD), Patent Ductus Arteriosus (PDA) or Tetralogy Of Fallot (TOF). This study was conducted at Lady Reading Hospital (LRH) Radiology, Cardiology and Gynaecology Department Peshawar. Data of all patients undergoing obstetrics scans and echocardiography for congenital malformations were collected and recorded. The study was conducted from March 2019 to June 2019. A sample of 200 patients was selected for the study. A Sample size of 200 was calculated by the Cochran formula. SPSS version 22 was used for data analysis.

RESULTS

Our study analysed 200 cases, 100 each of ultrasound and echocardiography.

Ultrasound result: Gravidas **w**ho were advised ultrasound scan during the routine antenatal check-up and diagnosed with hydrocephalus, anencephaly or cleft lip/palate were selected for this study. Among 100 patients, the mean age recorded was 26 years and standard deviation was 5.6. The Minimum and maximum ages recorded were 17 years and 43 years, respectively. The highest number of cases recorded were from Peshawar and Swat. The study included 68% consanguineous and 32% non-consanguineous types of marriages. Among the types of gravidity, the incidence of multigravida was highest compared to primigravida i.e. 67% and 33% respectively. The types of CM selected for our study were hydrocephalous, anencephaly and cleft lip/palate. Hydrocephalous showed the highest rate of incidence i.e. 55% followed by anencephaly (40%) and then cleft lip/palate (5%). The rate of CM was highest in consanguineous marriages. Furthermore, the incidence rate of hydrocephalous, anencephaly and cleft lip/palate in consanguineous marriages was 39%, 26% and 3% respectively while in non-consanguineous marriages the incidence rate was 16%, 14% and 2%, respectively. The relative risk of hydrocephalus and anencephaly in consanguineous and non-consanguineous marriage was 0.98.

A correlation study between types of marriages and history of miscarriages showed that rate of miscarriages was high in consanguineous marriages compared to non-consanguineous marriages that was 8%. As shown in Figure I. Correlation between types of CM and type of gravidity showed that rate of CM was highest in multigravida compared to primigravida (Figure II). Correlation between types of CM and trimester showed that detection rate of hydrocephalus was highest in the second trimester and that of cleft lip/palate was highest in the third trimester (Figure III). Whereas the detection rate of anencephaly was highest in the first trimester. Correlation between type of marriage and history of CM in alive children was recorded in gravida with consanguineous marriage.

Echocardiography Results: Infants who were advised echocardiography for confirmation of CHD i.e. VSD, ASD, PDA and TOF were observed. Out of 100 patients, the mean age recorded was 4 months and standard deviation was 2.9. The minimum and maximum ages of patients were 1 month and 11 months, respectively. Among the recorded infants, male were 62 and female were 38, out of which 61% belonged to consanguineous parents while 39% belonged to non-consanguineous. The incidence rate of CM selected for our study was VSD (43%), ASD (29%), PDA (16%) and TOF (12%). The Relative risk of VSD and PDA was 1.1. Correlation between types of marriage and CM showed that rate of CM is highest in consanguineous compared to non-consanguineous marriages. Correlation between gender and types of CM showed comparatively highest rate of CM in male infants as in female infants.

DISCUSSION

In our study, the prevalence rate of selective anomalies was recorded in consanguineous and non-consanguineous families. Population was divided into two groups. Group, I included gravida who were diagnosed with an anomalous fetus either hydrocephalous, anencephaly or cleft lip/palate on ultrasound scans during the routine antenatal check-up. Group II included those patients (infants) who were advised echocardiography for confirmation of CHD. According to the results of groups I and II, the

prevalence of CM was highest in consanguineous marriages compared to non-consanguineous marriages. These results are in accordance with studies previously conducted to describe the correlation between CM and consanguinity.[8]

According to our study, high incidence rates of hydrocephalus was recorded in consanguineous families followed by anencephaly, cleft lip/palate, VSD, ASD, PDA and TOF. Hydrocephalus, anencephaly and cleft lip/palate were common in consanguineous marriages. However, a study conducted in Japan showed no effects of consanguinity on hydrocephalus and controversial results on the association between consanguinity and cleft lip/palate were observed in studies carried out in other developing countries.[9,10,11] Positive relation between VSD, ASD and consanguinity was recorded in studies conducted in Lebanon and Saudi Arabia however, these studies revealed negative relation between TOF, PDA and consanguinity.[12,13] The History of miscarriages in gravida with consanguineous marriage was highest compared to those with non-consanguineous marriages. Our findings are supported by the study conducted in Khyber Teaching Hospital Peshawar.[14] No significant distinction was noticed in consanguineous and non-consanguineous marriages regarding the history of miscarriages.[15]

Among 100 gravida, 67 were multigravida and 33 primigravida. The rate of CM was comparatively high in multigravida compared to primigravida which is in accordance to other studies carried out locally.[16] Nevertheless, numerous congenital anomalies have been reported in primigravida.[17] Furthermore, mental retardation in children suffering with CM was recorded around 4% in consanguineous families. These results are supported by a study conducted in neighbouring country where similar percentage was reported.[18] Studies conducted in other parts of Pakistan and India have reported the highest rates of family history of CM. However, no specification of CM in consanguineous marriages was found in above mentioned studies. Pregnancy consists of three trimesters and each trimester is distinct from another regarding organogenesis. In the current study, the highest rate of CM was found in the second trimester. A study conducted in Nigeria also showed that a large number of CM cases were observed during the second trimester. One reason mentioned behind the occurrence of CM in this study was the lack of routine antenatal care.[19]

CONCLUSION

Parental consanguinity one of the major risk factors for structural, neurological and cardiac anomalies.

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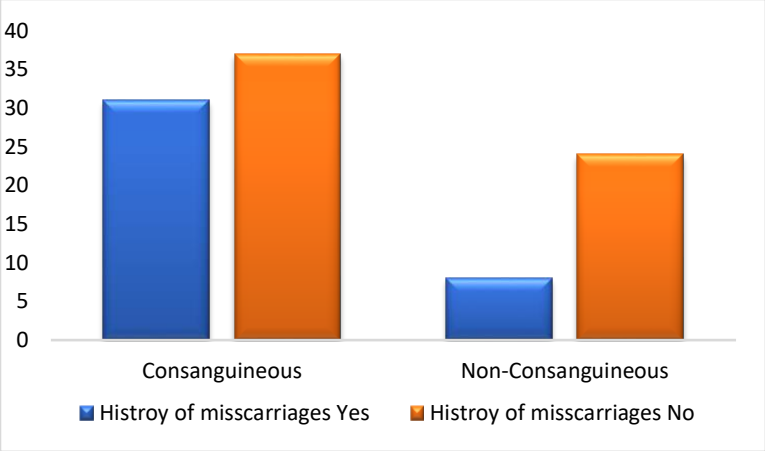

Figure I: Correlation between marriage type and miscarriages history

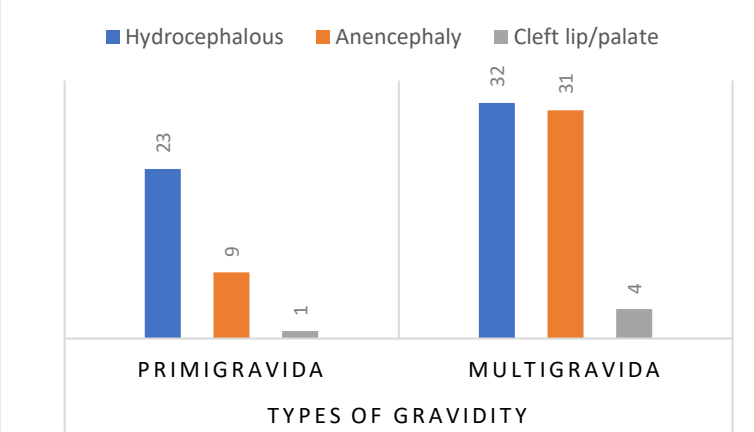

Figure II: Correlation between types of gravidity and types of CM

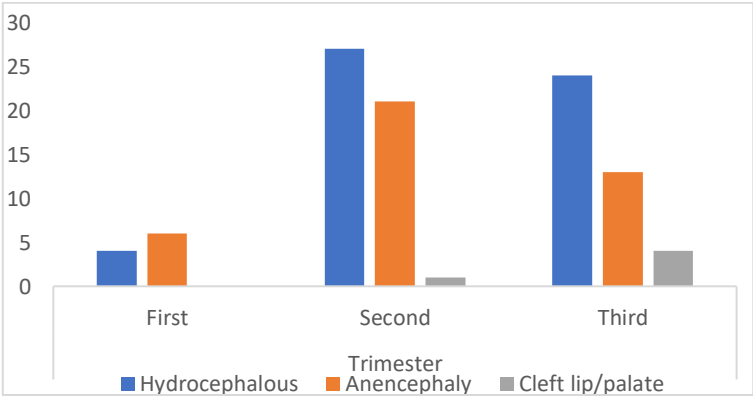

Figure III: Correlation between types of CM and trimester