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Original Research Article

Fetal congenital anomalies among consanguineous and non-consanguineous marriage pregnant women attending in Bangabandhu Sheikh Mujib medical university

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ABSTRACT

Background: Consanguineous marriage has been described as an important factor contributing to increased congenital malformations. Congenital anomalies began to emerge as one of the major childhood health problems and refers to any malformations that occur in a developing fetus. The aim of the study was to assess fetal congenital anomalies among consanguineous and non-consanguineous pregnant marriages.
Methods: An observational study design was adopted. Setting: Data were collected from the fetal medicine unit at Bangabandhu Sheikh Mujib medical university, Dhaka, Bangladesh during the period, from April 2017 to March 2018. Sample: A total sample was 100 pregnant women (Consanguineous and non-consanguineous with fetal congenital anomalies) were recruited according to certain criteria. Two tools were used as materials. Structured interview tool which entailed socio-demographic data; medical history, past obstetrical history, and ultrasonographic fetal assessment record.
Results: More than half of the fetuses in the consanguineous marriage group had multiple affected systems compared to one-quarter of fetuses in the non-consanguineous marriage group (68 and 24% respectively). In this study highly statistically, significant differences were found in central nervous system anomalies, followed by genitourinary, musculoskeletal and nonimmune hydrops fetalis. Prevalence of hydrocephalus was higher in the consanguineous marriage group compared to the non-consanguineous group, while the frequency of hydronephrosis was higher in non-consanguineous marriage group than consanguineous marriage group. Ubiquity of non-immune fetal hydrops was also higher in the non-consanguineous marriage group.
Conclusions: The most affected system of the fetus was CNS, followed by the gastrointestinal, urinary, and Musculoskeletal systems. Consanguineous couples are recommended to have genetic counseling, premarital examination, and screening about hereditary diseases.

Keywords: Congenital anomalies, Non-consanguineous, Consanguineous, Pregnant Women

INTRODUCTION

A congenital anomaly is an abnormality of structure, function, or body metabolism that is present at birth (even if not diagnosed until later in life) which results in physical or mental disability.[1] Congenital anomalies or birth defects are relatively common, offering 3% to 5% of live birth in the united states (us) and 2.1% in Europe congenital anomalies account for 8% of perinatal death and 13% to 16% of neonatal death in India.[2-7] For more than two decades, congenital anomalies have been leading cause of infant mortality in us.[8] The morbidity and disability experienced by surviving children also has a major public health impact.[9] Around 40% to 60% of congenital anomalies are of unknown etiology, 20% attributed to a combination of heredity and other factors 7.5% due to

single gene mutations, 6% is caused by chromosomal abnormalities and another 5% due to maternal illness, such as diabetes or infection or use of anticonvulsant or other drugs.[10-12] In most of the countries to obtain population based data or birth defects registries and surveillance system are commonly used. A prospective study from south India showed that the overall congenital anomalies was 3.7% and it was (3.2%) among live birth and 15.7% among still births. Desai et al have found congenital anomalies to be 3.61% amongst the total 2188 babies in their study in Bombay municipal hospital.[13] Similar finding were observed by signs, Singh et al.[14] Another study done by Asindi et al in Asir central hospital found that for every consecutive year during the study period about are third of the Saudi Infants were admitted into the unit on account of congenital malformation.[15] Parveen et al form Karachi worked on pattern and distribution of congenital anomaly and they found neural tube defects was the commonest anomaly in their settings.[16] Neural tube defects was also reported as most common birth defects in the study done by Gelineau-Van et al as 4-15 per 10,000 live births and study done by Bin-Bacher et al as 1 in 2,000 births.[17,18] Consanguineous marriage has been described as a important factor contributing to increased congenital malformations.[21] Consanguineous marriage is common, where individuals prefer to marry within their clan. Consanguineous unions range from cousin to more distant relatedness and their prevalence by culture consanguinity has been known to increase the chance of the husband and wife carrying an identical gene derived from a common ancestor. Children of such marriage therefore are at greater risk of being homozygous for a harmful gene and consanguinity suffer autosomal recessive genetic disorders.[22] First cousin marriages are the most common reason for couples seeking genetic advice. These are legal in many western countries but may be the subjects of religious or social reactions. In many Asian communities they are actively encouraged. Vain et al demonstrated that consanguinity had no significant effect on fetal losses but that frequency of consanguinity was higher with congenital rates within the Muslim population. The incidence of congenital malformation in Islamic country is between 10 to 45%.[23] Mortality of infants born with congenital anomalies varies with types of anomalies, being highest among those with central nervous system, cardiovascular system respiratory and genetic disorders. Screening of high-risk cases, routine perinatal folic acid supplementation, early prenatal diagnosis and termination of fetus with lethal anomaly before attaining viability will reduce perinatal morbidity and mortality. Advanced diagnostic modalities used for prenatal diagnosis includes high resolution sonography screening for congenital infections, chromosomal study, pre implantation diagnosis of genetic disease. Although efforts are being made to standardize information on congenital anomalies, it is widely recognized that, the reported incidence of congenital anomalies is subject to considerable variation. The factors primarily responsible for variation include the definition of congenital anomalies applied, the method of their ascertainment and length of time the population under observation and ethical and socio-economic characteristics of the population studied. Congenital anomalies contribute a significant proportion of infant mortality as well as morbidity. As a consequence, it is essential to have basic epidemiological information of these anomalies. Congenital anomaly rates can also use for planning health service. This study therefore can serve as a reference point for actual picture congenital anomalies in this tertiary care center and can also provide clue as to the prevalent types and pattern and its association with consanguinity and other factors in our population.

Mortality and morbidity of neonates born with congenital anomalies varies the types of anomalies. Morbidity is highest among those with central nervous system, cardiovascular system and those with genetic disorder. If high risk cases are properly screened and risk factors associated with congenital anomalies are evaluated and known then with proper preconception counseling and with early termination of fetus with lethal anomaly parental morbidity can be reduced. BSMMU serves as a tertiary and reference institution for all other hospitals and clinics in Bangladesh. This hospital has the subspecialties in neonatology, neurology cardiology, and nephrology and pediatrics surgery. There are laboratory facilities for plain and control radiography, ultrasound, echocardiography and chromosomal analysis. So, each case can be investigated as indicated. So, this study has been undertaken which will serve as a reference point for an actual picture of congenital anomalies in this tertiary care center and it will generate data of congenital anomalous fetuses which will help national registry in future.

METHODS

All pregnant women of congenital anomalies diagnosed by ultra-sonogram attending outpatient department (OPD) of obstetric gynecology department of Bangabandhu Sheikh Mujib medical university. From April 2017 to March 2018. A convenience sample of 100 pregnant women with fetal congenital anomaly was selected for the study. Sample was collected from outpatient department (OPD) of obstetric gynecology department of Bangabandhu Sheikh Mujib medical university. All pregnant women with congenital anomalies (diagnosed by ultra-sonogram) visited obstetrics and gynecology department of BSMMU during the study period and those who gave the consent were selected for this study.

Sample selection

Inclusion criteria

All pregnant mothers with congenital anomalous babies were included in the study.

Exclusion criteria

Rh negative hydrops fetus was excluded from the study.

Data collection procedure

Socio-demographic information were taken from the participants in café to face interview by trained research physicians. Participants were divided into two groups. Consanguineous marriage non-consanguineous marriage. Consanguineous marriage was classified into two main levels of relationship: First cousins and closer. These includes double first cousin. In which all grandparents are shared and first cousins in which the couple are parallel or cross cousin of either maternal or paternal decent and distant relative marriage: in which the members of the couple were relatives but not with first degree relations.

Tools

Two tools were used in the study structured interviewing tool and ultrasonographic fetal assessment record.

Structured interviewing tool

It entails four main parts:
Socio-demographic data: It included data related to the pregnant woman's age; residence, educational level, and occupation. It also included data related to the husbands' age, education, occupation and habits (smoker, alcoholic, etc).

Medical history: Included data related to the presence of any medical disorders such as urinary disease, diabetes, heart disease, systemic lupus, hypertension, respiratory disease, phenylketonuria, if any family members have a history of congenital anomalies and epilepsy.

Past obstetric history: It included items such as obstetrical code, complications that occurred with previous pregnancies and deliveries, mode of previous delivery, contraceptive methods, history of infertility, and history of assisted reproduction.

Present obstetric history: It included data related to, gravidity, parity and any complications occurred with current pregnancy, any drugs during the present pregnancy and if yes, at which trimester, exposure to any infection during the present pregnancy and if yes, its type and at time of exposure.

Ultrasonographic fetal assessment record

It includes five items as related to the finding of ultrasonographic fetal examination. The gestational age, gender, and status of pregnancy whether single or multiple, type of congenital anomalies and affected system.

Statistical analysis

All data was analyzed using SPSS program (Version 20.0). Result was expressed in frequencies or percentages. P≤0.05 were considered significant. Statistical test was done.

RESULTS

Table 1 shows no statistically significant difference between both groups in relation to maternal socio demographic characteristics.

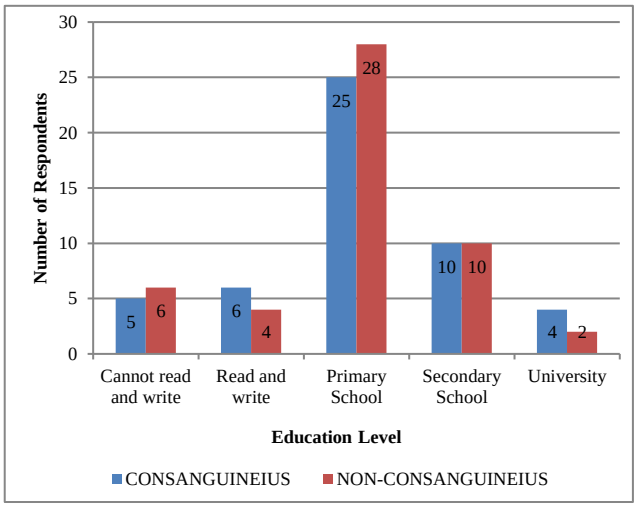

Figure 1: Distribution of the respondents by level of education.

In Table 2, more than half of the fetuses in consanguineous marriage group had multiple affected system, compared to one quarter fetuses in the non-consanguineous marriage group (68% and 24%). Moreover, statistically significant difference was found between both groups in relation to the incidence of congenital anomalies of central nervous system anomalies.

Table 3 Result indicates a statistically significant difference (p<0.05) between consanguineous and non-consanguineous marriage group in relation to incidence of hydrocephalus, anencephalus, polycystic kidney, phocomelia and non-immune fetal hydrops. Prevalence of anencephaly was higher in the consanguineous marriage group compared to the non-consanguineous group, while the prevalence of hydronephrosis was higher in non-consanguineous marriage group than consanguineous marriage group. Prevalence of non-immune fetal hydrops was also higher in non-consanguineous marriage group.

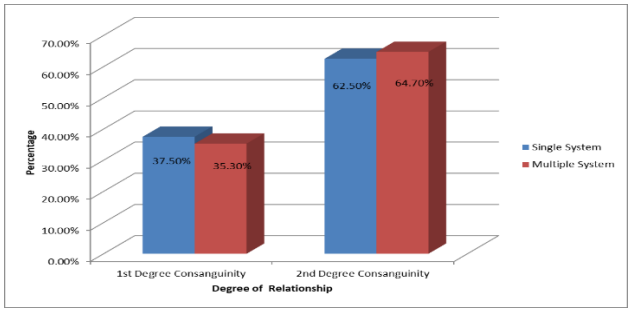

Figure 2: Percentage distribution of fetuses based on number of affected systems in each degree consanguinity.

Table 1: Sociodemographic characteristics of the study participants.

Variables	Consanguineous marriage, n=50		Non-consanguineous marriage, n=50		Tests	
	N	%	N	%	X^2	P value
Maternal education						
Cannot read and write	5	10	6	12	0.090909	0.763
Read and write	6	12	4	8	0.4	0.5271
Primary school	25	50	28	56	0.16981	0.6803
Secondary school	10	20	10	20	0	1
University	4	8	2	4	0.66667	0.4142
Maternal age class (Years)						
20-25	26	52	20	40	0.78261	0.3763
26-30	14	28	16	32	0.13333	0.715
31-35	10	20	14	28	0.66667	0.4142
Maternal occupation						
House wife	48	96	45	90	0.096774	0.7557
working	2	4	5	10	0	1
If working type of work						
Labor	0	0	0	0	1.8	0.1797
Profession	1	2	1	2	0.000	1
Written work	1	2	4	8	1.876	0.1707
Husband education						
Cannot read and write	4	8	3	6	0	1
Read and write	6	12	6	12	0.15789	0.6911
Primary school	30	60	27	54	0.69231	0.4054
Secondary school	5	10	8	16	0.789	0.3748
University	5	10	6	12	0.101	0.7505
Husband occupation						
Worker	40	80	26	52	2.9697	0.08484
Professional	2	4	1	2	0.33333	0.5637
Written work	8	16	13	26	1.1905	0.2752

Table 2: Frequency of congenital anomalies by organ/organ system among the study subjects.

Systems	Consanguineous marriage, n=50		Non-consanguineous marriage, n=50		Tests	
	N	%	N	%	X^2	P value
Single system	16	32	38	76	8.963	0.002755
Multiple system	34	68	12	24	10.522	0.00118
Central nervous system	16	32	14	28	8	0.004678
Genito urinary system	8	16	10	20	3.6	0.05778
Gastrointestinal system	10	20	12	24	0.18182	0.6698
Musculoskeletal system	6	12	5	10	2	0.1573
Non-immune hydrops fetalis	3	6	4	8	2.5714	0.1088

Table 3: Distribution of the fetuses in both groups according to the most common types of fetal congenital anomalies.

Variables	Consanguineous marriage, n=50		Non-consanguineous marriage, n=50		Tests	
	N	%	N	%	X^2	P value
CNS						
Hydrocephalus	4	8	3	6	4.4545	0.03481
Anencephalus	2	4	2	4	4	0.0455
Meningomyelocele	1	2	1	2	1	0.3173
Encephalocele	1	2	1	2	1	0.3173

Continued.

Variables	Consanguineous marriage, n=50		Non-consanguineous marriage, n=50		Tests	
	N	%	N	%	X^2	P value
Urinary						
Hydronephrosis	6	12	8	16		0.1852
Polycystic kidney	1	2	1	2	6	0.01431
Renal agenesis	1	2	1	2	0	1
Gastrointestinal system						
Esophageal atresia	6	12	3	6	1.088	0.2969
Duodenal atresia	2	4	6	12	1	0.3173
Omphalocele	1	2	2	4	2	0.1573
Imperforated anus	1	2	1	2	0.33333	0.5637
Musculoskeletal						
Achondroplasia	4	8	3	6		0.4567
Phocomelia	2	4	2	4	4	0.045
Miscellaneous						
Multiple congenital anomalies	5	10	4	8	0.121	0.7281
Non-immune fetal hydrops	3	6	4	8	5	0.02535
Fetal cardiac	2	4	2	4	0.2	0.6547

Table 4: Distribution of pregnant women in both groups according to their obstetric history.

Variables	Consanguineous marriage, n=50		Non consanguineous marriage, n=50		Tests	
	N	%	N	%	X^2	P value
Primigravida	35	70	30	60	0.38462	0.5351
Gravida (2-4)	12	24	15	30	0.33333	0.5637
Grand multigravida	3	6	5	10	0.5	0.4795

Table 5: Distribution of fetuses in both groups according to their characteristics.

Gender	Consanguineous marriage, n=50		Non-consanguineous marriage, n=50		Tests	
	N	%	N	%	X^2	P value
Male	35	70	36	72	0.014085	0.9055
Female	15	30	14	28	0.034483	0.8527

Table 4 shows that congenital anomalies were more common in primigravida in both the consanguineous and non-consanguineous group.

Table 5 shows that, the most common gender detected with congenital anomalies among consanguineous group was male but no statistically significant difference was found.

DISCUSSION

Study result revealed that more than half of pregnant women in consanguineous group and near half in non-consanguineous groups, age range was (20-25) years with no statistically significant difference. In the same line Anjum et al reported that majority of neonates with congenital anomalies are born to mothers aged 25 to 38 years.[24] Also a study Ismail et al revealed that more than two third of the pregnant women in both age groups, their age range was 22 to 31 years with no statistical significant differences (p=0.11).[25] While the study done by El Koumi, Al Banna and Lebda found that maternal age less than twenty years and more than thirty five years was associated with increased incidence of congenital anomalies although this was not significant.[26] Study revealed that more than half of the pregnant women in both groups were primigravida. Desai et al in their study found that more than one third of their sample was primigravida.[13] Also Parvin et al found that congenital anomalies occurs more in newborns of primigravida.[16] In contrast a study done by Ismail GM reported that more than half of the pregnant women in both groups their gravidity ranged between two and four, the mean gravidity among consanguineous and non-consanguineous group was 3.20±2.70; 3.00±2.17 respectively.[25] In the same line Shawky et al reported that multigravidity was associated increased prevalence of congenital anomalies in their study.[28] Regarding degree of consanguinity among consanguineous marriage group, results of the current study revealed that, near half were first degree consanguinity, about one third were second

degree consanguinity and less than one quarter were third degree consanguinity with a highly statistically significant difference between degree of consanguinity and number of affected system (p= 0.001). This finding is in agreement with the study done in Lebanon on the presence of congenital anomalies in children of consanguineous marriages where a significant association was found between first degree consanguinity and anomalies such as cerebral palsy, cystic fibrosis, physical retardation and congenital blindness by Mckusick et al.[22] Results revealed that, the most common gender detected with congenital anomalies among the consanguineous and non-consanguineous group was male but no statistically significant difference was found. The same results was found by Shawky et al who tried to assess the frequency and nature of congenital malformations among Egyptian infants where males were more affected than females.[28] In addition, the study done by Aryasinghe et al in United Arab Emirates revealed that, male infants showed a frequency of congenital anomalies at 9.3% which is over twice as much seen in female infants, which was 4.3%.[29] On the other hand the study done by El Koumi et al found no significant difference in the frequency.[26] Regarding the occupation, majority of the pregnant women in consanguineous and non-consanguinous marriage groups were housewives, no statistical significant difference was found between the both groups (p>0.05). While high percentage of husbands in consanguineous and non-consanguinous groups were workers. No significant difference was found between both groups. High percentage of pregnant women in the consanguineous and non-consanguineous marriage groups had primary school education. While, low percentage of them went to university (Table 1). As regards to the pregnant women husbands' education, high percentage of husbands in the consanguineous and non-consanguineous marriage groups had primary school education. While, low percentage of them cannot read and write. No statistically significant difference was found. More than half of the fetuses in the consanguineous marriage group had multiple systems affected versus one quater of the fetuses in the non-consanguineous marriage group (68% and 24%). A statistically significant difference was found between both groups (p<0.01). Incongruent with the previous results, Al-Gazali et al who studied the profile of major congenital abnormalities in the United Arab Emirates found that, slightly more than one half of the sample had multiple malformations, and slightly less than one half had a single anomaly.[30] While, Desai et al found that, single anomaly constituted more than two thirds of the cases as compared to less than one third of multiple anomalies.[13] Moreover, in this study highly statistically significant differences were found in central nervous system anomalies (Table 4), followed by genitourinary, musculoskeletal and nonimmune hydrops fetalis. Jehangir et al who studied the prevalence of congenital anomalies reported that, the most common anomalies were central nervous system, cleft lip and cleft palate, musculoskeletal system, and gastrointestinal tract.[31] Another study carried out by Desai et al revealed that, the central nervous system accounted one half of all affected cases, was the most commonly affected system followed by the musculoskeletal system involving one fourth of all congenital anomalies. the study done by Rajech et al to determine the prevalence of various genetic and congenital disorders and their association with parental consanguinity in a selected sample of the Israeli Arab community found the most affected systems were; respiratory diseases (36.9), mental disorders (69.8), physical disorders (35.6), visual disorders (45), hearing disorders (59.7), other hereditary disorders (40).[31,32] More overstudy done by El Koumi et al revealed that, musculoskeletal system was the most commonly affected (23%), followed by the central nervous system (CNS) (20.3%), gastrointestinal system GIT) (16.2%), genitourinary system (13.5%), craniofacial (10.8%), cardiovascular system (CVS) (9.5%), and chromosomal anomalies (6.8%).[26] Almost the same results was found by Mohammed et al in Assiut university hospital, Egypt on neonates with apparent congenital anomalies where the most common congenital anomalies detected were; skeletal system anomalies (37.9%), followed by chromosomal abnormalities (27.2%), circulatory system (CVS) anomalies (22.3%), central nervous system (CNS) anomalies (19.4%), genital organs anomalies (16.5%), gastrointestinal tract (GIT) anomalies (14.6%), eye and ear anomalies (8.7%), and urinary system and others anomalies in 3.9% each.[33] Also, the study done in United Arab Emirates by Aryasinghe et al found the genitourinary malformations formed the bulk of the anomalous population at 40.5%, followed by musculoskeletal anomalies accounting for 28.6% of anomalies.[29] Cardiovascular anomalies were third with 10.7%, miscellaneous anomalies such as cases of tongue-tie and choanal atresia accounted for 7.1% and central nervous system anomalies showed the lowest frequency with only 1.6%. This discrepancy between the present study results and results of other studies may be due to the difference of samples size, geographic location, associated risk factors, availability and variability of diagnostic procedures and equipment, and availability of trained obstetricians.

Limitations

Consanguinity means shared the genetic materials, it has been associated with increased risk pediatric disorders including still birth, dead babies, perinate mortality, congenital birth defects and blood disease. large scale study will be required for genetic association to see family trends genetic association to see family trends in this population. For increased risk of congenital malformation especially neural tube defect. Chromosol analysis and viral infections markers (Torch) were not conducted in this study due to high cost of these test which further add burden to the pt so only symptomatology of viral infection was asked to determine the risk in particular patient.

In this study we also have not compared risk factors in controls so in future we will study to determine the risk of each risk factor with congenital anomalies.

CONCLUSION

In conclusion, consanguinity may play an important role in the high rates of malformation in children and must be taken into account for genetic counseling. For a possible prevention, genetic counseling before marriage must be applied, not only for consanguineous couples but also for any couples that may have a family history of genetic disorders.

Recommendations

Premarital examination and screening about hereditary disease, in the same line, genetic counseling before marriage must be applied, not only for consanguineous couples but also for any couples that may have a family history of genetic disorders. Further studies are recommended to assess consanguineous marriage group with specific affected system. Further studies were recommended to examine impact of consanguineous marriage degree on fetal congenital anomalies. Raising community awareness regarding worse effects of consanguineous marriage through mass media. A qualitative research design to assess the lived experience of families having a child with congenital anomalies.

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