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Original Article

Risk Factors Associated with Non-Cardiac Congenital Anomalies of Fetus Admitted in Chittagong Medical College Hospital

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Key words: *Congenital anomalies, Bangladesh, risk factors.*

Abstract:

Background: *Congenital anomalies make an important contribution to infant mortality and they remain a leading cause of death in many countries of the world. Many babies also died in our country due to congenital anomalies.*

Methods: *This retrospective cross-sectional study was conducted at the Departments of Obstetrics and Gynecology of CMCH between October 2016 to March 2017. Objective of the study was to find out the risk factors of non-cardiac congenital anomaly of fetus. The study population of those women who delivered a baby with different non-cardiac congenital anomalies admitted in Departments of Obstetrics and Gynecology of CMCH.*

Results: *The mean maternal age was found 26.6±5.6 years and the mean paternal age was found 35.8±7.9 years. 28 (28.0%) patients had hydrocephalus, 25 (25.0%) had Anencephaly, 7 (7.0%) had Omphalocele, 7 (7.0%) had Hydrops fetalis, 6 (6.0%) had cleft lip, 6 (6.0%) had cleft palate, 4 (4.0%) had cleft lip and cleft palate. 20 (20.0%) patients had consanguinity, history of high-grade fever with rash in first trimester was 12 (12.0%). 16(16.0%) was diabetes mellitus. Majority (63.0%) patients belonged to gestational age 16-28 weeks. The mean gestational age was found 29.5±7.1 weeks with ranged from 16 to 42 weeks. Majority (89.0%) were singleton pregnancy. 60% reveal congenital anomaly in USG.*

Conclusion: *Risk factors of non-cardiac congenital anomalies were consanguinity, maternal obesity, high grade fever with rash in first trimester due to viral infection, diabetes mellitus (uncontrolled), uncontrolled gestational diabetes mellitus, previous birth defect, inadequate intake of folic acid in first trimester, blood group Rh negative, male baby. Hydrocephalus and anencephaly were the most common congenital anomalies.*

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Introduction:

The incidence of congenital anomalies is increasing nowadays. In order to prevent anomalies, there are several measures which include avoidance of risk factor such as teratogenic exposures and radiation, smoking, drinking alcohol, medical treatment of maternal illnesses, viral infection, lack of nutrient etc. The incidence of significant congenital malformation is about 2-5% at birth, however major fetal abnormalities account for about 20% of perinatal deaths & many survivors are physically & mentally handicapped.[1] Advanced maternal age is a well-established risk factor for fetal chromosomal abnormalities secondary to defects in cell division, however the relationship between advanced maternal age & major congenital anomalies remain unknown.[2]

Around 5% increase in the incidence of ventricular septal defects, atrial septal defects & patent ductus

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arteriosus in off spring has been found to be correlated with advance paternal age. Advance paternal age has also been linked to increased risk of achondroplasia & Apert syndrome. Offspring born to fathers under the age of 20 show increased risk of being affected by patent ductus arteriosus, ventricular septal defects & the tetralogy of Fallot.[2] Cardiac ailments constitute a significant portion of the congenital anomalies. However, non-cardiac congenital anomalies also constitute significant cause of sufferings of the new born babies.

Women may not have adequate knowledge about risk factors which may cause congenital anomalies. They will have interest to know more about prevention of congenital anomalies. If we know the risk factors of congenital anomaly earlier it would be useful for the antenatal mothers to gain knowledge about prevention of fetal congenital anomalies & to reduce neonatal and infant morbidity and mortality. But there is scarcity of study in this context. So, it is a good opportunity to do a study regarding evaluation of risk factors for congenital anomalies among mothers who delivered a baby with congenital anomaly.

Islam et al.[3] find out frequency of various congenital malformations in neonates in a tertiary care hospital in Department of Neonatology, Mymensingh Medical College Hospital, Bangladesh from April 2011 to March 2012. A total 6040 babies were studied in the neonatal period immediately after admission and all cases with congenital anomalies were enrolled. A total of 106 neonates had one or more congenital anomalies accounting to a frequency of 1.75% malformation. The number of congenital anomalies was more in males, where male to female ratio was 1.2:1 and in neonates of young and elderly mothers. The pattern of congenital anomalies related to head and neck, chest and gastrointestinal tract 20.75%, nervous system 19.81%, cardiovascular system 18.87%, musculoskeletal system 12.26%, genitourinary system 11.32%, chromosomal abnormalities 6.6% and others 10.37%.

Fatema et al.[4] did a study to find out proportion, types of congenital anomalies at birth and immediate outcome of anomalous neonates. This cross-sectional study was carried out in the Department of Obstetrics and Gynecology, BSMMU, Dhaka during the period January 2007 to December 2007. During the study period 1630 patients delivered, of which 60 had congenitally malformed babies making the occurrence of 3.68%. Neural tube defect was found to be the commonest (33.33%) type of anomaly.

Methods:

This retrospective cross-sectional study was conducted at Chittagong Medical Collage Hospital, Chittagong (CMCH) between October 2016 and March 2017. 100 Women who delivered babies with different non-cardiac congenital anomalies were selected by purposive sampling. Inclusion criterion was mothers who delivered non-cardiac congenital malformed babies. The exclusion criterion was unwilling to be included and any cardiac anomaly diagnosed at birth.

General objective of the study includes finding out the risk factors for non-cardiac congenital anomaly of the fetus. Specific objectives are to find out the predisposing factors responsible for congenital anomaly, to see the relation of maternal disease, the drug effect of mother, to see the effect of consanguinity and to see the effect of previous history of birth defect on the present anomaly.

Socio-demographic variable taken into consideration include age of mother, age of father, body weight, GDM (uncontrolled), DM (uncontrolled), HTN, Viral diseases, Thyroid dysfunction, Environmental factor, Smoking, socioeconomic status and consanguineous marriage. Patients admitted or visiting OPD and delivered babies with different congenital anomaly was initially recruited as study patients. From all eligible subjects after getting informed written consent clinical history was taken, clinical examination & investigation was done. A structured questionnaire was introduced to find the risk factors related to different congenital anomaly. Statistical analyses were carried out by using the Statistical Package for Social Sciences version 20.0 for Windows.

Results:

Table-I

Maternal & Paternal age of the study population (n=100).

Age range, Mother	Number (percent)	Age range Father	Number (percent)
17-21	21 (21%)	-	-
22-25	23 (23%)	21-25	8 (8%)
26-30	19 (19%)	26-30	18 (18%)
31-35	25 (25%)	31-35	29 (29%)
>35	12 (12%)	>35	45 (45%)

Table-II

Distribution of the mothers by pregnancy status (n=100).

pregnancy status	Number of patients	Percentage
Gravida:		
Primi	48	48 %
Multi	52	52 %
Gestational age (weeks):		
16-28 wks.	63	63 %
29-dˆ37 wks.	23	23 %
38-42 wks. (Terms)	14	14 %
No of Pregnancy:		
Singleton	89	89 %
Twins	11	11 %

Table I shows maternal and paternal age of the study patients, it was observed that 25 (25.0%) patients belonged to maternal age 31-35 years and 12 (12.0%) patients belongs to maternal age more than 35 years. The mean maternal age was found 26.6±5.6 years with ranged from 17-37 years. In paternal age 45(45.0%) patients belonged to age >35 years. The mean paternal age was found 35.8±7.9 years with ranged from 21-49 years.

Table-III

Distribution of the study mothers by investigation (n=100).

Investigation	Number of patients	Percentage
Blood group:		
Rh negative	5	5 %
Rh positive	95	95 %
Thyroid function test		
Thyroid stimulated hormone (>4.4)	12	12 %
Free T_4 (<0.8)	15	15 %
Blood sugar after 75 gm glucose (mmol/L):		
<7.8	87	87 %
≥7.8	13	13 %
Ultrasonogram of pregnancy profile:		
Anomaly present	60	60 %
Anomaly absent	19	19 %
Not done	21	21 %

Table III shows distribution of the study patients by pregnancy status, it was observed almost more than half (52.0%) patients were primi gravida. Majority (63.0%) patients belonged to gestational age 16-28 weeks. The mean gestational age was found 29.5±7.1 weeks with ranged from 16- 42 weeks. Majority (89.0%) were singleton pregnancy.

Table 3.4 shows investigation of the study patients, it was observed that Rh negative (high antibody titer) had found in 5(5.0%) patients. In thyroid function test 15(15.0%) had Free T_4 (<0.8). The mean blood sugar after 75 gm glucose was found 7.2±2.3 mmol/L with ranged from 4.2 to 13 mmol/L. Ultrasonogram of Pregnancy profile reveal that congenital anomaly was present among 60% of patients in this study of group.

Table-IV

Distribution of the study population by termination of pregnancy according to gestational age (n=100).

Gestational age (weeks):		
16-28 wks.	63	63 %
29-≤37 wks.	23	23 %
38-42 wks. (Terms)	14	14 %
Mean±SD	29.5±7.1	
Range (min, max)	16-42	

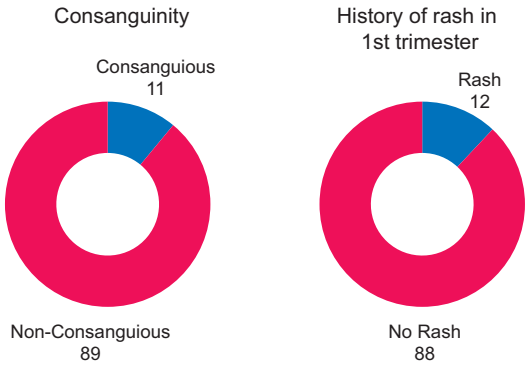
Table IV show distribution of the study patients by termination of pregnancy according to gestational age, it was observed almost more than half about 63% patients was terminated at 16-28 wks. and 23% at 29-d”37 wks.

Table-V

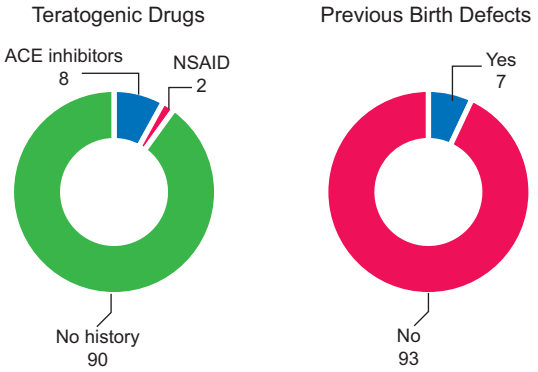
Distribution of the study populations by congenital anomaly (n=100).

Congenital anomaly	Number of	Percent patients
Hydrocephalus	28	28 %
Anencephaly	25	25 %
Omphalocele	7	7 %
Hydrops fetalis	7	7 %
Cleft lip	6	6 %
Cleft palate	6	6 %
Cleft lip and palate	4	4 %
Gastroschisis	3	3 %
Polydactyly	3	3 %
Anorectal malformation (ARM)	3	3 %
Multiple congenital anomaly	2	2 %
Others	6	6 %

Table VI shows congenital anomaly of the study patients, it was observed that 28 patients had hydrocephalus, 25 had Anencephaly, 7 had Omphalocele, 7 had Hydrops fetalis. Others findings are depicted in the above table. It is noteworthy here that not a single patient was detected with cardiac anomalies in this series. This may be either due to low incidence of cardiac anomalies among the patients here or due to failure to detect these by the attending doctors.



Graph 1 A & 1 B. Depicting risk factors consanguinity & history of rash in 1st trimester.



Graph 2 A & 2B. Risk factors: Teratogenic drugs and history of previous birth defects

Graph 1, 2 and Table 3.7 shows risk factors for congenital anomalies in study population, it was observed that 20(20.0%) patients had consanguinity, history of high grade of fever with rash in first trimester had 12(12.0%). In history of medical disease 16(16.0%) had diabetes mellitus and GDM (uncontrolled) and 7(7.0%) patients had previous birth defect.

Table-VI

History of medical disease as risk factors in mothers (n=100).

Diseases	Number	Percent
DM and GDM (uncontrolled)	16	16 %
Bronchial asthma (steroid intake)	10	10 %
HTN (taking ACE inhibitor)	6	6 %
Hypothyroid (untreated)	12	12 %

Table VII shows intake of folic acid of the study patients, it was observed that majority (59.0%) patients did not take folic acid in first trimester. It was observed that majority 21(56.7%) babies belonged to <7 in APGAR score at 1 minute and 20(54%) belonged to <7 in APGAR score at 5 minutes.

Table-VII

Distribution of the mothers by intake of folic acid (n=100)

Intake of folic acid	Number of patients	Percentage
First trimester	41	41 %
Pre-conceptional period	0	0 %
No	59	59 %

Discussion:

This cross-sectional study was carried out with an aim to see the relationship of associated disease with congenital anomaly and analyzed maternal and paternal age variation associated with congenital anomaly. A total of 100 women who delivered a baby with different congenital anomalies admitted in Departments of Obstetrics and Gynecology of Chittagong Medical College Hospital, Chittagong between October 2016 to March 2017 were included in this study. Patients who were unwilling to enroll in this study were excluded from the study. The present study findings were discussed and compared with previously published relevant studies.

Congenital anomaly is an abnormal structural or medical condition that presents at birth.[5] Consanguinity increases the prevalence of rare genetic congenital anomalies and nearly doubles the risk for neonatal and childhood death, intellectual disability and serious birth anomalies in first cousin unions. Some ethnic communities,

e.g. Ashkenazi Jews or Finns, have comparatively high prevalence of rare genetic mutations, leading to a higher risk of congenital anomalies.[6] The rate of anomalies amongst consanguineous couples was found about 11% in this current study./ The rate of parental consanguinity is 11% among the affected babies.

Maternal age is an important parameter in the birth of a congenitally malformed fetus.[7] For this reason, the risk of birth of a congenitally malformed fetus in mothers who are older than 35 years of age needs to be examined more carefully. In this current study, it was observed that about 12% mothers belong to >35 years and 25% mothers belongs to 31-35 years. The mean maternal age was found 26.6±5.6 years with ranged from 17-37 years. In this current series, it was observed that, paternal age 45.0% patients belonged to age >35 years. The mean paternal age was found 35.8±7.9 years with ranged from 21-49 years.

Several studies have shown that folic acid reduces occurrence of some congenital anomalies e.g. neural tube defects, orofacial clefts, limb reduction defects, congenital heart defects, urinary 37 system defects and omphalocele.[8,9] How many of the mothers with babies with neural tube defect in this study were taking folic acid? This study shows only 41% mother had taken folic acid during pregnancy. Similar findings were reported from a study done in Baghdad.[10]

In this current study, it was observed that Rh negative (high antibody titer) had found in 5.0% patients. In thyroid function test 15.0% had Free T_4 (<0.8). The mean blood sugar after 75 gm glucose was found 7.2±2.3 mmol/L with ranged from 4.2 to 13 mmol/L.

In this current study, it was observed that, history of high-grade fever with rash in first trimester had 12(12.0%). In history of taking any teratogenic drugs 10(10.0%) patients received steroid. In history of medical disease 16(16.0%) had diabetes mellitus and GDM (uncontrolled). 7(7.0%) patients had previous birth defect.

In this current study, it was observed that majority 21(56.7%) babies belonged to <7 in APGAR score at 1 minute and 20(54%) belonged to < 7 in APGAR score at 5 minutes. Still birth occurred about 65% babies among the study group. Janev et al.[11] assessed 55.73% of newborns had APGAR score 1-8. In another study, Yang et al.[12] showed the incidence of congenital anomalies according to APGAR score among live births between 0 - 3 was 39.8% and between 4 - 6 was 26.0%, which are comparable with the current study.

Conclusion:

This study was undertaken to find out the risk factors of congenital anomaly of foetus. Majority of the patients with congenital anomalies were in group 31-35 years and above, paternal age >35 years, had secondary level education, house wife, came from low income family, lived in rural area. Hydrocephalus and Anencephaly were more common congenital anomalies. Risk factors of congenital anomalies were consanguinity, maternal obesity, high grade of fever with rash in first trimester due to virus infection, uncontrolled GDM, diabetes mellitus, previous birth defect, inadequate intake of folic acid during pregnancy, blood group Rh negative, male baby. Further studies preferably can be undertaken case control study by including large number of patients.

Conflict of Interest - None.

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