Research Article

Predominance of fetal malformations among pregnant women: A multi-centric observational study

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Abstract

Objective: To observe the predominance of fetal anomalies in pregnant women in a multi-centric setting.

Methods: This prospective observational study included 20225 pregnant women who came for antenatal care in University Hospital and fetal medicine units from 2016 to 2019. Fetal anatomical scanning was done for all participants.

Results: One hundred eighty-three cases had fetal congenital anomalies, yielding a prevalence of around 0.9%. Third of cases had positive consanguinity, this increased in cases of skeletal and thoracic anomalies. The presence of past history of anomalies was evident in 8.2% mostly with skeletal and heart anomalies. History of drug intake was only verified in 1.6% of cases. Sixty-three women out of 183 (34.4%) were diagnosed to have anomalies in fetal nervous system.

Conclusion: Prenatal diagnosis are recommended for early detection of congenital anomalies and counselling.

Introduction

World Health Organization reported that congenital anomalies can be characterized as malformations in the structure or the function of fetal organs or systems. Fetal malformations can be diagnosed antenatally or later [1].

The incidence of congenital anomalies is 2% - 3% of all deliveries. However, fetal malformations represent 20% - 30% of causes of perinatal deaths [2]. Predominance of fetal malformations differs between countries. In Japan incidence of congenital anomalies is 1.07% while in Taiwan it is 4.3%. It has been registered that United States has prevalence of 2% - 3% of fetal malformations, 2% in England and 1.49% in South Africa [3]. The difference between countries can be attributed to social, economic and racial health impacts. It has been reported that congenital heart and neural tube defects are the most serious malformations [4]. The etiology of congenital malformation is genetic in 30% - 40% and environmental in 4% to 9% of cases. Genetic cause of fetal congenital anomalies represents a great bulk. Six percent of cases are due to

chromosomal aberrations, single gene disturbance and occur in 25% while 20% - 30% of genetic causes are multifactorial. However, in about 50% of fetal malformations, the cause is unknown [5]. Increased age of the mother is correlated to abnormal intrauterine fetal development and chromosomal abnormalities especially Down's syndrome [6]. The main aim of antenatal diagnosis in cases of high maternal age or family history is detection of fetal malformations due to chromosomal aberrations and single gene defects [7]. Since the setting up of the European surveillance of congenital anomalies (EUROCAT) in 1980, many cases with congenital malformations have been detected antenatally [8].

Different arrangements regarding antenatal diagnosis of congenital malformations have been created in many countries. Countries have different cultural, social and religious issues controlling ending of pregnancy. All these factors affect variability of policies in many countries. It has been recommended in the United Kingdom that fetal anomaly scan is offered to pregnant women between 18 weeks+ 0 days and 20 weeks+ 6 days during routine antenatal care

[9]. Thus, our primary outcome is to evaluate the efficacy of implementation of routine diagnostic programs for congenital anomalies and their detection rates.

Patient and methods

This prospective observational study included 20225 pregnant women coming for antenatal care in Beni-Suef University Hospital and multiple fetal medicine units from 2016 to 2019. The study was approved by the ethical committee of faculty of medicine at Beni-Suef University. An informed verbal consent was given by all participants before the study. Inclusion criteria included: congenital anomalies in single fetus. No particular model for age, residence, parity and gravidity was included. Women with medical disorders, smokers or having any infection were excluded.

All participants were subjected to full history taking into consideration to data from EURO-CAT; this includes: Maternal age, history of previous pregnancy (ies) with fetal malformations or aneuploidies and history of peri-conceptional folic acid intake. Other data was included such as: consanguinity, residency (urban, rural or industrial), radiation exposure, drug intake (beyond FDA Class B) and potential teratogen exposure. Fetal evaluation was done by abdominal ultrasonography. Obstetric ultrasound assessed fetal sex, gestational age and fetal anatomy to find out congenital anomalies including types and number. The responsible sonographer recorded all data. A diagnostic ultrasonography system (US-Xario 200, Toshiba America Medical S. Company, California, USA) was used.

Statistical analysis

Analysis of data was done using statistical package for social science, version 16 (SPSS Version 16.0 for Windows, Chicago, Illinois). Mean and SD or median and range were used to express numerical data whichever is appropriate. Frequency or percentage were used for qualitative data. Qualitative variables were compared by chi-square test. p - value less than 0.05 was used when the variables are statistically significant.

Results

Fetal congenital anomalies were detected in one hundred eighty-three (183) women, yielding prevalence of 0.9% in the evaluated participants. Maternal age at time of diagnosis was 29 years; only one case (0.5%) had maternal age above 40 years. 31.1% of cases had positive past history. This increased in cases of skeletal and thoracic anomalies to reach 45% and 55.6% respectively. The presence of past history of anomalies was evident in 8.2% of total studied cases. It was most common for cases of skeletal (27.3%) and heart (16.7%) anomalies. Median gestational age for diagnosis was 24 weeks. History of drug intake was only verified in 1.6% of cases. Peri-conceptional folic acid intake occurred in 60.2% of the

study cases, 75% of cases with spinal anomalies had negative history of folic acid intake, with significant increased risk of cephalic and spinal anomalies. The most frequent anomalies were those affecting the nervous system representing 34.4% of all cases (63 cases), the second common was renal and genital system 45 cases (24.5%) followed by GIT and anterior abdominal wall 37 cases (20.2%), heart 12 cases (6.5%), and then chest 9 cases (4.9%).

Median maternal age for the study cases was 29 years. As for residency, anomalies in general were more common in urban areas, where there was significantly higher incidence of thoracic, GIT, neck, renal, spinal and skeletal anomalies. However, cephalic and cardiac anomalies were significantly more in rural areas (Table 1).

History of consanguinity was found in 31.1% of cases , this ranged widely between different anomalies. As it was found only in 14.3% of neck , 23.8% in cephalic anomalies, 25% of case of spinal anomalies, 35.1% in GIT, 41.7% in cardiac; it reached 45% in skeletal anomalies and 55.6% in thoracic anomalies. As regards distribution between cases; it was mostly related to skeletal anomalies (27.3%), followed by heart anomalies (16.7%) and then cephalic anomalies (9.5%). Absent or inadequate peri-conceptional folic acid intake occurred in 39.8% of cases. Highest rates were among spinal anomalies (75%) and cephalic anomalies (65.9%), followed by chest anomalies (44.4%), cardiac (41.7%) (Table 2).

Median gestational age at diagnosis was 24 weeks. This varied widely between 11-37 weeks. Earliest diagnosis was for neck anomalies (at median of 21 weeks), was around 22 weeks for cardiac and GIT anomalies and was around 24 weeks for cephalic and skeletal anomalies. Rate of neonatal survival at 1 week was also variable. It was best for skeletal anomalies (77.8%) then for renal anomalies (71.4%), 60% for cephalic anomalies, 53.1% for GIT anomalies, 50% for neck anomalies. The lowest survival rates were those of cardiac (37.5%) and thoracic (12.5%) anomalies (Table 3).

Discussion

Prevalence of congenital anomalies was 0.9% in this study. The worldwide rate of congenital malformations ranges between 2% - 3% of all births, and differs between countries according to implementation of powerful routine ultrasound screening programs and detection rates of different anomalies [10]. Our results were a partly comparable with those of Taboo, et al. who evaluated the predominance of congenital anomalies and the associated risk factors in Iraq. They reported 0.7% prevalence of fetal malformations among their studied population [11] and other results in United Arab Emirate were (0.8%) [12]. These results were slightly lower than in brazil (1%) [13]. Also, the incidence of congenital anomalies was 1.3% in Kuwait [14] 1.4% in India [15]. Furthermore, our results agreed with another study where the authors found that the predominance of congenital anomalies was 0.9% [16].

Table 1: Incidence of anomalies in relation to demographic data..

	Head (n = 63)	Neck (n = 7)	Chest (n = 9)	Heart (n = 12)	GIT & abdominal wall (n = 37)	Renal & genital (n = 45)	Spine (n = 8)	Extremities (n = 11)	p - value
Age (years)									
< 20	5 (7.9%)	0	0	2 (16.6%)	0	1 (2.2%)	1 (12.5%)	1 (9.1%)	
20 – 30	43 (68.3%)	3 (42.9%)	5 (55.6%)	6 (50%)	28 (75.7%)	33 (73.3%)	5 (62.5%)	7 (63.6 %)	0.407
> 30	15 (23.8%)	4 (57.1%)	4 (44.4%)	4 (33.4%)	9 (24.3%)	11 (24.5%)	2 (25%)	3 (27.3)	
Mean ± SD	26.6±5.2	28.8±5.1	28.2±3.8	26.5±5.8	27.3±4.3	28.6±4.6	24.3±5.1	24.54.7	
Min. – Max.	17 – 41	22 – 36	21– 32	18-35	21-39	21 – 39	18-31	18-29	0.211
Median	25	30	29	26.5	27	29	23	26.5	
Residency									
Rural	35 (55.6%)	2 (28.6%)	3 (33.3%)	8 (66.7%)	10 (27%)	11 (24.4%)	3 (37.5%)	4 (36.4%)	0.013*
Urban	28 (44.4%)	5 (71.4%)	6 (66.7%)	4 (33.3%)	27 (73%)	34 (75.6%)	5 (62.5%)	7 (63.6%)	

p: *p* value Chi square (2×1 contingency table) *: *p* < 0.05 is significant.

Table 2: Incidence of anomalies in relation to maternal history.

	Head (n = 63)	Neck (n = 7)	Chest (n = 9)	Heart (n = 12)	GIT & abdominal wall (n = 37)	Renal & genital (n = 45)	Spine (n = 8)	Extremities (n = 11)	p - value
Consanguinity									
-ve	48 (76.2%)	6 (85.7%)	4 (44.4%)	7 (58.3%)	24 (64.9%)	34 (75.6%)	6 (75%)	6 (54.5%)	0.327
+ve	15 (23.8%)	1 (14.3%)	5 (55.6%)	5 (41.7%)	13 (35.1%)	11 (24.4%)	2 (25%)	5 (45.5%)	
History of anomalies									
-ve	57 (90.5%)	7 (100%)	9 (100%)	10 (83.3%)	35 (94.6%)	41 (91.1%)	8 (100%)	8 (72.7%)	0.295
+ve	6(9.5%)	0	0	2 (16.7%)	2 (5.4%)	4 (8.9%)	0	3 (27.3%)	
Folic acid intake									
-ve	41 (65.1 %)	1 (14.3%)	4 (44.4%)	5 (41.7%)	12 (32.4%)	13 (28.9%)	6 (75%)	2 (18.2%)	< 0.001**
+ve	22 (34.9%)	6 (85.7%)	5 (55.6%)	7 (58.3%)	25 (67.6%)	32 (71.1%)	2 (25%)	9 (81.8%)	

p: *p* value Chi square (2×1 contingency table) *: *p* < 0.05 is significant; **highly significant < 0.001

Table 3: Relation between gestational age at diagnosis and outcome.

	Head (n = 63)	Neck (n = 7)	Chest (n = 9)	Heart (n = 12)	GIT & abdominal wall (n = 37)	Renal & genital (n = 45)	Spine (n = 8)	Extremities (n = 11)	p - value
Gestational age at diagnosis									
Mean ± SD	26.7 ± 7.8	24.3 ± 3.9	24 ± 7.1	20 ± 2.2	21 ± 3.8	21.3 ± 3.6	22.5 ± 3.7	24.2 ± 6.4	< 0.001**
Min. – Max.	11 – 37	15 – 27	18 – 35	18 – 25	11 – 34	17– 30	19-28	18-30	
Median	28	25.5	19	20	21	21	21	24.5	
Survival at 1 week									
Not completed pregnancy	18 (28.6%)	5 (71.4%)	1 (11.1%)	4 (33.3%)	5 (13.5%)	10 (22.2%)	0	2 (18.2%)	< 0.001**
Completed Pregnancy	45 (71.4%)	2 (28.6%)	8 (88.9%)	8 (66.7%)	32 (86.5%)	35 (77.8%)	8 (100%)	9 (81.8%)	
Died	18 (40%)	1 (50%)	7 (87.5%)	5 (62.5%)	15 (46.9%)	10 (28.6%)	3 (37.5%)	2 (22.2%)	< 0.001**
Survival	27 (60%)	1 (50%)	1 (12.5%)	3 (37.5%)	17 (53.1%)	25 (71.4%)	5 (62.5%)	7 (77.8%)	

*: Statistically significant at *p* < 0.05; **highly significant < 0.001

The present results are lower than those found by a research which was carried out in Zagazig University Hospital in Egypt. The authors in that study evaluated which the prevalence of congenital anomalies during only one year among live born neonates. They concluded that the congenital anomalies among live born neonates were 63 cases among 2517 (2.5%) [17]. The incidence of congenital malformations ranged from 1.2% to 7% as reported by many authors. These ranges may be attributed the type of population evaluated, the duration of evaluation and accuracy of diagnosis of malformations by each sonographer. Thus, assessment including the easily detected anomalies reported higher incidence than those studies evaluating women for only major anomalies. In addition, the research work including women with risk factors correlated to congenital anomalies show high prevalence [18].

Moreover, worldwide differences in prevalence of congenital anomalies may be attributed to ethnic variations that affect mainly genetic causes of fetal malformations. Teratogenicity, environmental factors and family history also play a very important role in these variations among countries [19]. Also, the results vary according to the type and number of participants in each study and duration of assessment [20].

In 2009, the investigators working in EURO-CAT excluded that advanced maternal age itself confers extra risk for congenital anomalies that are not caused by chromosomal aberrations. Maternal age-related risk significantly differed for different structural anomalies. Nervous and digestive system anomalies, maternal intrauterine infection syndromes and tricuspid atresia were found more in young women, while older women were at a greater risk of encephalocele, fetal

alcohol syndrome and esophageal atresia [21]. The current study however, showed no significant difference in maternal age groups between various anomalies. This may be explained by the difference in sample size of studied population. As for the residence, most of the study cases (54.1%) lived in urban areas, while (45.9%) of cases came from rural ones. This difference was statistically significant with the exception for cardiac and cephalic anomalies which were significantly more in rural areas. This may reflect the difference in rate of diagnosing anomalies and access to health services, rather than their actual prevalence. Studies from United States showed increased incidence of major anomalies with lower socioeconomic state which was mostly related to rural areas. While residence-based approach in Canadian study showed no difference in residence as regards incidence of congenital anomalies [22]. Concerning, history of paternal consanguinity, 31.1% of cases had positive history. This increased in cases of skeletal and thoracic anomalies to reach 45% and 55.6% respectively. Studies about genetic causes of fetal malformations and consanguinity in Egypt reported that 33% of women with birth defects showed positive consanguinity [23]. The presence of past history of anomalies was evident in 8.2% of cases. It was most common for cases with skeletal (27.3%) and heart (16.7%) anomalies. This can be related to the mode of inheritance of these conditions. In a Danish study, where authors investigated the risk of recurrence of congenital anomalies; it was highest for cases of neural tube defects (11%) and lowest for heart defects (2%) [24]. History of drug intake was only verified in 1.6 % of cases. However, relation of these exposures to the occurrence of fetal malformations cannot be judged due to multifactorial etiology of these conditions. This coincides with data of Chung W about teratogens and their effects which showed that teratogenic agents cause approximately 7% of all congenital anomalies [25]. Median gestational age for diagnosis was 24 weeks; it's related to the nature of anomaly, and which system affected. Whereas skeletal anomalies were diagnosed at gestational age of 24 weeks, neck anomalies had mean age of diagnosis of 21 gestational weeks. This magnifies the need for a routine application program for early diagnosis of these conditions and hence the referral of complicated ones to higher level of medical care. In England, with routine second trimester scan, mean age of diagnosis of neural anomalies is 21 weeks. While in France it is 19 weeks [26]. In the present study fetal nervous system was the most common to show malformations in 63 women out of 183 participants (34.4%), the second common was renal and genital system 45 cases (24.5%) followed by GIT and anterior abdominal wall 37 cases (20.2%), heart 12 cases (6.5%), and then chest 9 cases (4.9%). These results agreed with those of a study which was conducted in Egypt [27], in which the authors reported that CNS anomalies were the most common (32.1%) then come renal and urinary tract malformations (14%), while cleft lip and/or palate represented 2% in their study. Well organized antenatal visits help accurate prenatal diagnosis of congenital

anomalies early. Fetal medicine requires a multidisciplinary team; obstetrician, pediatrician, geneticist, and pediatric surgeon. Their comprehensive work provides proper counseling to parents of affected fetus. The requirement to follow-up all pregnancies and terminations is necessary to determine the correct ultrasound diagnosis. This study was conducted in a rural setting in our country. Despite some known data in this research work, we believe that it will add to the scientific community and help in prenatal counselling of women especially in countries with low health services.

Ethical approval

The study was approved by the ethical committee of faculty of medicine at Beni-Suef University on the 25th of December 2015. The registration number is 1210-2015.

Consent: All participants gave verbal consent at the start of the study.

Author contributions

Ahmed Khedr Khalifa and Sayed Mohamed Sayed: Protocol development.

Ahmed Khedr, Sayed Mohamed Sayed and Sherwet M. Shawky: Data collection and management

Ahmed Khedr Khalifa, Mohamed A. M. Eweis and Nesreen A. A. Shehata: Data analysis

NAA Shehata and Ahmed Khedr Khalifa: Manuscript writing/editing

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