Prevalence and Risk Factors for Congenital Anomalies in Mosul City

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ABSTRACT:

BACKGROUND:

Congenital anomalies define as abnormalities of body structure that originated before birth, about 3% of all children are born with a serious structural defect that interferes with normal body function and can lead to lifelong handicap or even early death. There is a variation in the frequency of congenital anomalies in different populations.

OBJECTIVE:

To determine the prevalence of the easily identifiable congenital anomalies also to estimate the risk factors which may predispose to anomalies and pattern of distribution of congenital anomalies of newborn in Mosul city.

METHODS:

In a cross-sectional study, charts of forty six thousand and seven hundred seventy five deliveries including live births and stillbirths in Al-Batool Teaching Hospital of Obstetrics and Gynecology , during the period from January -2009 to December-2010. The anomalies were then grouped according to the organ, system involvement, gender, maternal age, consanguinity, mortality rate, and mother's natal history.

RESULT:

A total of 323 cases of fetal congenital anomalies were detected, central nervous system were the most common abnormalities while complex congenital malformation was second in rank. The prevalence of anomalies was 0.69%. The majority of fetal malformation was seen in primigravida furthermore the maternal age between20-24years was the largest age group that had congenital anomalies. Mean gestational age at delivery was 36 weeks as well as the mean gestational age at diagnosis of anomaly by ultrasound was 30week. Fetal malformations had predilection to female fetuses, with male to female ratio1:1.09, in addition to 2.167% of ambigunity. Overall perinatal mortality rate was 79.25%.

CONCLUSION:

Congenital anomalies are one of the most important causes of fetal deaths. The present study showed a high incidence of congenital malformations in the young age group and among primi gravida woman. The commonest associated risk factors was consanguineous marriage the frequency of which may be reduced by creating awareness regarding the avoidance of consanguineous marriages . anencephaly was the most prevalent anomaly detected. So proper and timely counseling, regular antenatal care. folate supplementation especially during the most sensitive period of embryogenesis is essential to avoid major congenital malformation for future pregnancy.

KEY WORD : prevalence – risk factor -congenital anomalies .

INTRODUCTION:

A congenital anomaly defined as any abnormality of physical structure found at birth or during the first few weeks of life; or any irreversible condition exiting in a child before birth in which there is sufficient deviation in the usual number, size, shape, location of any part, organ, CELL to warrant its designation as abnormal.[1,2]Because the congenital anomalies are one of the most common causes of disability in developed and developing countries,[3] it began to emerge as one of the major childhood health problems.[4,5]

Structural anomalies are considered to be major when are visible to inspection, the rest of them are considered occult.[6]Since 1960,a general surveillance has been carried out to monitor the appearance of congenital anomalies,[7] these surveys indicated that the worldwide incidence of congenital disorder was 2-3%.The actual

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numbers of these anomalies vary from country to country ; it was reported to be as low as 1.07% in Japan and as high as 4.3% in Taiwan.[8]whereas the birth prevalence of anomalies was 2%in England, 1.49% in South Africa[9]and 3.65% in India.[10]The reason for the regional difference of congenital anomalies might be attributed to the many factors, such as: maternal risk factors, environmental exposures, ecological, economical, ethnic and other factors. [11,12]

In the developed countries congenital malformations are the dominant causes of infant morbidity and mortality.[13] Thus 12.3-32% of neonatal deaths were considered to be secondary to congenital anomalies[4,14]However, treatment and rehabilitation of these morbid children is difficult, and recovery is usually impossible.[15]Although early recognition of anomalies is important for planning care,[1] knowing etiology of congenital anomalies is the base of prevention programs even if these etiology is not completely understood.

The most of congenital anomalies are of multifactorial causation.[6,16] Purely genetic factors (chromosomes, single gene mutations) are believed to account for 15-20% of all congenital anomalies leaving up 80% due to multifactorial inheritance or environmental exposures.[17,18] Risks factors like infectious agents, chemical compounds, radiation, use of medication, maternal metabolic diseases, multiple births, maternal life event stress, prematurity, occupational exposure are associated with higher congenital disorder.[6,19] Furthermore, low schooling and low socioeconomic status in the population are other factors which are highly relevant.[20]An environmental exposure can have a preconceptional mutagenic action or a post-conceptional teratogenic action.[21]Deficiency of folic acid and other nutrients such as vitamin B1 in the periconceptional period are established risk factor for neural tube defects.[22,23] Accurately the danger of anomalies is increasing in old woman pregnancies and in pregnancies which are not monitored.[6] The abnormal intrauterine environment regarding as other cause of impaired fetal development.[24]

Consanguineous marriages regarded as important factor contributing to increased congenital malformations, recessive gene may thus come to light for the first time in an in bred descendant after have been hidden for generations. For this reason, consanguinity influences the incidence of some inherited diseases.[8] Because of high consanguinity rates within the Muslim population, the incidence of congenital abnormalities in Islamic countries is between 10 to 45%.[4]

Although routine screening for fetal abnormalities is very successful, there are limitations to the abilities of both the technique and the operators to detect every anomaly. There are several reasons for this: not all anomalies are evident at 20 weeks, when the routine ultrasound examination for anomalies is performed; there is wide variation in both expertise of staff and quality of equipment; and some fetuses are difficult to scan because of maternal habits, reduction in liquor volume or persistent difficult position. There are very few structural abnormalities for which the detection rate approaches 100%.[25]

This Study was carried out to determine the prevalence of congenital anomalies, estimate the risk factors which may predispose to anomalies and the pattern of distribution of congenital anomalies with a focus on sex ratio of newborn in Mosul city, in the north of Iraq

PATIENTS AND METHODS:

This is a cross sectional study conducted in Al-Batool Teaching Hospital of Obstetrics and Gynecology in Mosul city. This hospital serves both urban and rural area. The study was conducted over 24 months period from 1-1-2009 to 31-12 -2010. The total number of deliveries was 46775, and the total number of congenital abnormalities was 323. The majority of patients had at least one or more ultrasound examinations. All the patients were scanned and diagnosed by specialists in ultrasound. Ultrasound scans were performed by using Philips Envisor Series ultrasound system, manufactured by Philips ultrasound, USA, September 2006, Model number Philips M2540A. Data collection was performed by means of structured form which contained two parts, similar to study of Tootoonchi. [26] In the first part, variables recorded were about maternal characters and included the date of admission, age, parity, history of chronic illness, drug ingestion,

exposure to X-ray, history of congenital anomalies in other offspring, parental consanguinity, type of delivery and were obtained by interviewing with neonates and mother. The second part was about neonate. All newborns with abnormality were either diagnosed prenatally (through obstetric ultrasonography) or diagnosed after delivery. Characters for baby including live, or stillbirth, gestational age, weight, sex, existence of congenital anomaly and type of it, which were collected from medical records. The type of birth defect was classified by

diagnostic standardization of congenital malformation. Major congenital anomalies were divided according to the system involved (cranial, neural tube defect, face and neck, thoracic, cardiac, genitourinary system or skeletal).The fetus was diagnosed as having either isolated anomalies (only one system involved) or complex anomalies (two or more system involved).

Statistical analysis: Package used was SPSS version 17 software, the data of questionnaire were installed in the computer by coding every data of the variable to make it easier to calculate, then interpreting and analyzing the output. statistical analysis was performed like mean and standard deviation ,t-test analysis and chi-square test,. $P<0.05$ was considered to be statistically significant. The prevalence of pattern of congenital anomalies was obtained by descriptive analysis and Fisher‟s exact tests were used in determining the associations between various variable and percentage of congenital anomalies. logistic regression were used for univariate and multivariate analysis respectively.

RESULTS:

During the study period from January 2009 – December 2010, a total number of deliveries 46775 were reported. Out of these, 323 cases of congenital abnormalities were identified and served as the study population. These include live births and still births. The prevalence of major congenital anomalies was 6.9, 5.49, 1.4 per 1000 births for a total birth, a stillbirth , a live birth respectively. Out of 323, pregnant women 82 (25.4%) had fetuses with complex anomalies and 241 patients (74.6%) had fetuses with isolated anomalies**,** as shown in Figure (1)

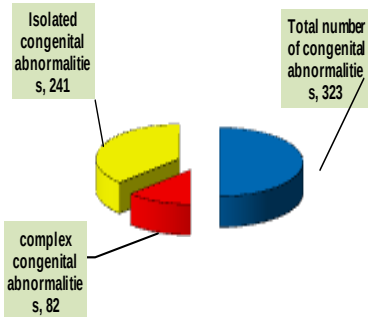


Fig.1: Pie chart - Number of congenital abnormalities out of total 46775 deliveries

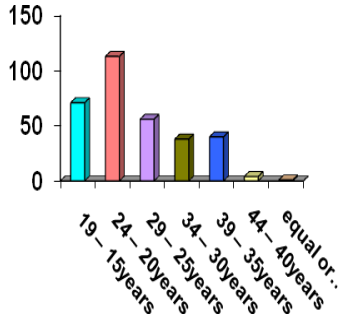
Maternal characteristics by bodily system are shown in Table(1). Parent consanguinity was reported in (21.98%) patients while (1.85%) patients with a history of previously affected children or other family members with similar anomalies. There was a significant increasing percentage of congenital anomalies with consanguinity while there was non-significant decrease of these percentage with median parity and median maternal age. The percentage of congenital anomalies was reflected from family history of other abnormality.

Tab.1: Maternal characteristics by bodily system

system involvement	Number & percentage	median maternal age	median parity	consanguinity(%)	family history(%)
multiple congenital abnormalities	82 (25.38%)	25.6	1.8	19	0
Cranial	51 (15.78%)	24.42	1.45	10	2
neural tube defects	77 (23.84)	23.58	1.34	9	0
Skeletal	20 (6.19%)	24.9	1.65	9	0
congenital heart disease	9 (2.78%)	23.56	1.44	4	1
Gastro - intestinal tract	16 (4.95%)	31	3.06	3	1
abdominal wall	10 (3.09%)	27.8	1.62	4	0
conjoined twin	2 (0.62%)	28	2	0	0
hydrobs fetalis	10 (3.09%)	27.1	3.25	1	1
Renal	10 (3.09%)	26.2	2	6	1
Skin	1 (0.31%)	22	1	0	0
sacrococcygeal teratoma	6 (1.86%)	23.3	1.33	1	0
Down's syndrome	9 (2.78%)	30	3.2	3	0
cleft lip and palate	12 (3.71%)	22	2	2	0
Diaphragmatic hernia	6 (1.85%)	21	3	0	0
cystic hygroma	2 (0.62%)	21	2	0	0
Total	323 (100%)	Mean = 25.08	Mean = 2	71 (21.98%)	6 (1.85 %)
Correlation		-0.006	-0.257	0.876**	0.107(NS)

NS = Not significant using Chi-square test or Fisher Exact test,**=highly significant The regression equation is y = 7.18 - 0.330 x1 + 0.57 x2 + 1.41 x3 - 0.12 x4 R-Sq(adj) = 69.9%

Figure (2) shows a significant difference in percentage of anomalies with maternal age which indicated that the percentage of abnormalities increased significantly at age (20-24) years (34.98%) but there was a non-significant decrease in the remaining groups.

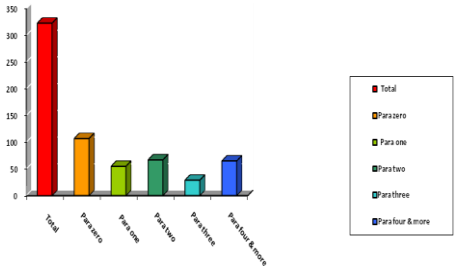


x_c^2 :197,276 , x_t^2 :12.59 have significant difference at p≤0.05 using -Chi-square test or Fisher Exact test

Fig. 2: Distribution of congenital abnormalities according to maternal age

Regarding the number of parity, the percentage of congenital abnormality reached the peak with para zero (33.12%)which was highly significant.

The percentage of anomalies then declined non-significantly with para one (17.03%) , para two (20.75%) and this decline reached the significance with para three (8.98%). As shown in Figure (3)



x_c^2: 48.966 , x_t^2 : 9.49 have significant difference at p≤0.05 using - Chi-square test or Fisher Exact test

Fig. 3: Distribution congenital abnormalities according to parity

Concerning the mean of gestational age at the time of diagnosis by ultrasound was 30.12 weeks, while mean gestational age at delivery was 36weeks. The mortality rate was (100%) in anencephaly, hydrops foetalis, diaphragmatic hernia, cystic hygroma. The perinatal mortality rate was higher with major congenital anomalies and was strongly related to the complexity of the anomalies, while non-significant decrease of congenital anomalies was recorded with gestational age. As shown in Table (2)

Tab. 2: Fetal characteristics by bodily system

system involvement	Number & percentage	Gestational age at diagnosis by U/S (weeks)	Gestational age at delivery (weeks)	Mortality rate & (%)
multiple congenital abnormalities	82 (25.38%)	29	36	80(97.56%)
Cranial	51(15.78%)	31	37	40(78.43%)
neural tube defects	77(23.84)	25	30	65(84.41%)
Skeletal	20(6.19%)	32	36	15(75%)
congenital heart disease	9(2.78%)	28	36	2(22.22%)
Gastro - intestinal tract	16(4.95%)	30	37	12(75%)
abdominal wall	10(3.09%)	32	37	8(80%)
conjoined twin	2(0.62%)	37	38	1(50%)
hydrobs fetalis	10(3.09%)	26	34	10(100%)
Renal	10(3.09%)	28	34	8(80%)
Skin	1(0.31%)	32	35	1(100%)
sacrococcygeal teratoma	6(1.86%)	29	37	4(66.67%)
Down's syndrome	9(2.78%)	30	38	2(22.22%)
cleft lip and palate	12(3.71%)	29	36	0 0
Diaphragmatic hernia	6(1.85%)	32	37	6(100%)
cystic hygroma	2(0.62%)	32	38	2(100%)
Total	323(100%)	Mean = 30.12	Mean = 36	256 Mean % = (79.25 %)
regression Correlations	N	-0.416	- 0.491	0.987

In our results consanguinity (21.98%)and history of toxoplasmosis (4.64%), were reported as a risk factors for congenital anomalies. while history of X-Ray exposure, drugs intake, smoking ,Diabetes, Rh.Incompatibility , virus infection, were not independent risk factors for congenital anomalies .As shown in Table(3)

Tab. 3: Risk factors of congenital anomalies.

Risk factor	Number	(%)
Consanguinity	71	21.98
x-ray exposure	1	0.31
History of taking drugs	0	0
Smoking	5	1.548
Diabetes	8	2.47
Rh incompatability	5	1.548
Reported toxoplasmosis	15	4.64
CMV	9	2.78
Rubela	8	2.47
Herpes virus	8	2.47
Pervious history of congenital abnormality	9	2.78
Family history of congenital abnormality	6	1.86
No risk factor	178	56.7
Total	323	100%

The distribution of congenital anomalies, according to system involved, has been shown in Table 4. Central nervous system, Multiple congenital anomalies, Skeletal system respectively was the most common anomalies fallowed by renal anomalies, congenital heart disease , gastrointestinal tract.

Table 4: Distribution of Congenital abnormalities according to system..

abnormalities	No. of patients	Total No. of patients out of 323
Multiple congenital abnormalities	82 (25.38%)	82 (25.38%)
Central nervous system		128 (39.62 %)
Cranial		
Hydrocephalus	46 (14.24%)	
Microcephaly	5 (1.55 %)	
neural tube defects		
Anencephaly	40 (12.38%)	
Encephalocele	6 (1.85%)	
spina bifida	31 (9.59%)	
Skeletal		20 (6.19%)
osteogenesis imperfecta	2 (0.62 %)	
achondroplasia	16 (4.95 %)	
Amelia	2 (0.62 %)	
Renal		10 (3.1 %)
congenital absence of kidney	2 (0.62 %)	
polycystic kidney	3 (0.93 %)	
congenital hydronephrosis	5 (1.55 %)	
congenital heart disease	9 (2.78 %)	9 (2.78 %)
Gastro - intestinal tract		
Imperforated anus	6 (1.85 %)	16 (4.9 %)
duodenal atresia	1 (0.31 %)	
esophageal atresia	2 (0.62 %)	
Intestinal obstruction	6 (1.85 %)	
abdominal cyst	1 (0.31 %)	
abdominal wall defect		
omphalocele	4 (1.23 %)	10 (3.1 %)
gastroschiasis	4 (1.23 %)	
ectopia vesica	2 (0.62 %)	
Thoracic		
diaphragmatic hernia	6 (1.85 %)	6 (1.86 %)
conjoined twin		2 (0.62 %)
Thoraco-omphalopagus	1 (0.31 %)	
craniopagus and thoraco pagus	1 (0.31 %)	
Face		12 (3.71 %)
cleft lip	5 (1.55)	
cleft lip and palate	7 (2.17%)	
Hydrobs fetalis	10 (3.1 %)	10 (3.1 %)
cystic hygroma	2 (0.62 %)	2 (0.62 %)
Skin	1 (0.31 %)	1 (0.31 %)
Absence of epidermis		
sacrococcygeal teratoma	6 (1.85 %)	6 (1.86 %)
Down's syndrome	9 (2.78 %)	9 (2.78 %)
Total	323 (100%)	323 (100%)

With respect to mode of delivery, 62 patients (19.2%) were delivered by caesarean section and 261 patients (80.8%) by normal vaginal delivery with significant difference (0.05) . As shown in Table (5).

Tab. 5: Mode of delivery.

Abnormality	natural delivery	(%)	caesarean section	(%)
multiple congenital abnormalities	70	85.3	12	14.6
cranial	22	43.13	29	56.8
Neural tube defects	67	87.87	10	12.9
skeletal	19	95	1	5
Genito urinary tract	9	90	1	10
Congenital heart disease	9	100	0	0
GIT	15	93.7	1	6.25
Abdominal wall defect	10	100	0	0
conjoined twin	0	0	2	100
cleft lip and palate	12	100	0	0
hydrobs foetalis	7	70	3	30
diaphragmatic hernia	6	100	0	0
Cystic hygroma	1	50	1	50
Skin	1	100	0	0
saccrococcygeal teratoma	4	66.6	2	33.3
Down's syndrome	9	100	0	0
Total	261	Mean % = 80.8%	62	Mean % = 19.2 %

X^2c:76.872, x^2t:25000 significant difference (0.05)(15)

Tab. 6: Screening tes

Total	Golden Standard Congenital abnormality ultrasound		Screening test
	(-ve) post labor	(+ve) post labor	
223 Total Test Positive (a+b)	0 (b) False +ve	223 (a) True +ve	(+ve) ultrasound
46552 Total Test Negative (c+d)	46452 (d) True –ve	100 (c) Flase –ve	(- ve) ultrasound
46775 Grand Total (a+b+c+d)	46452 Total Disease -ve (b+d)	323 Total Disease +ve (a+c)	Total

The overall sensitivity of ultrasound was (69%), specificity (100%), accuracy (100%), predictive value of (+ve) results (100%), and predictive value of (-ve) results (99.7%). As shown in Table (6).

The new born were 151 (46.75 %) males , 165 (51.083 %) females and (7) (2.17 %) of unrecognized sex . The weight of two hundred two newborns (62,538 %) , was less than (2.5) kg and of 121 (37.461 %) was more than (2.5) kg.

DISCUSSION :

Most children, born with congenital anomalies and survive infancy are affected physically, mentally or socially and can be at increased risk of morbidity due to various health disorders.[4] In this study, the overall prevalence of congenital malformation among the newborn was 0.69% that is near to reports recorded from United Arab Emarat (0.79%) [27] and is lower than that of brazil (1.07%), Gorgan(1.01), Bahrain(2.7%),Tehran(3.5%)[28]and India(3.6%). [29] In our country, Al-Bayati reported that in Al-Basrah city, the prevalence of congenital anomalies was 2.5% and in Fallujah, Alaani et al., found that the congenital malformations were increased to 15%. congenital heart defects have the highest incidence, followed by neural tube defects. [31] These variations between different studies could be explained by the effect of diverse racial, ethnic and social factors in various parts of the world or in different geographical area. Furthermore industrial pollution, environmental, socioeconomic, nutritional status, percent of consanguinity marriage and habits may regarded as cause of these dissimilarity. Other explanations are the type of sample and the criteria for diagnosis that is to say differences in study design and methodology.

Maternal age is an important parameter in the birth of a congenitally malformed fetus. For this reason, females who are older than 35 years of age need to be examined more carefully since the risk of birth of a congenitally malformed fetus is increase. [1,11] In the present study, the median maternal age at diagnosis was 25 years which approximated the ages conducted by other authors as**,** Sallout[32], SING[1] Shama[19]who indicated that the median maternal age was 27.5 and 27.3years respectively[33]. Mohamed *et al*. in 2007, [34] observed direct relation between the maternal age and incidence of congenital anomalies showing low incidence with age <20 years old and high with age between 20-35 years old . Advanced maternal age (> 35 years) reported to be the most frequent risk factor for birth defects in Brazil[20] Isa Abdi-Rad2008 reported that anomalies were common in gestational age between 29-32 weeks. This variation could be due to the effect of the nuclear waste of the war, which occurred in our country in the last 10 years.

Despite the fact that the median parity was two in this study ,the maximum number of congenital anomalies were seen in primigravida107(33.12%) and women with para four or more 65(20.12)respectively. The result was incomparable to observations made by other authors.[35] sallout *et al*.(2010)stated that the median parity of the women was two,Singh[1]recorded increase in frequency of CNS anomalies in primi and fourth gravida mothers. Numerous previous studies have shown conflicting results in relation to parity as a variable. Aguiar *et al*.[36] found a lower risk of neural tube defect in children of multiparous women. The increasing congenital disorder with low parity woman may contributed to consequence of war, a waste product of uranium enrichment that happened in Iraq. An additional observation in this study was that the mean of gestational age at delivery was 36 weeks and at the time of diagnosis of anomaly by ultrasound was 30week. This outcome was similar to the observations of Khaskheli and Michels [37,38] Sallout *et al*. stated that the median gestational age at delivery was 38 weeks [32]Garne *et al*., showed a significant difference in gestational age at birth for cases diagnosed prenatally and postnatally.[39] Congenital anomalies are regarded an important contributor to perinatal mortality. The mean mortality rate with congenital anomaly was (79.25%), and100% of infants born with diaphragmatic hernia, hydrops foetalis and anencephaly did not survive. Singh *et al*. found the same finding of the mortality of malformed foetus72.58%.[40] but the mortality rate recorded by Tomatir was 14.7%.

Concerning Risk factors, Philips – Arnold (2005) stated that there were specific factors lead to increase mother's likelihood of carrying a fetus with congenital abnormalities[41]. Shama *et al*., (2006) confirmed that consanguinity was considered as important risk factor.[19] However, our work showed that parental consanguinity was a significant cause for most of the malformations. Other authors Nath *et al*., [42]Mehrabi *et al*., and

Bromiker[43,44] showed that the consanguinity for malformed patients was high, but there was no significant relationship between malformation and the degree of relation of the parents.[27] In about (60%) of cases, no risk factors were identified. This could be due to structural abnormality that is to say defect or mutation in gene which may be due to the effects of nuclear waste of war. Al- Mendalawi 2008.[45] confirmed that in Baghdad there was 2folds increase in the prevalence of congenital malformation from 10.2/1000 total birth in the pre-war period 1988-1989 to 22.5/1000 total birth in post war period 1999-1997 and the most common anomaly was central nervous system

Regarding type of delivery, a significant difference was observed in the incidence of congenital anomalies among the offspring of women who were delivered with normal vaginal delivery with that how were delivered by caesarean section. The Same reported by Hindryckx *et al*.[46] Who found 68(80%) patient were delivered with vaginal delivery while17(20%) with Caesarean section. The possible explanation for this difference is that vaginal route could traumatize and expose the neural tissue to bacteria normally present in the birth canal.

Regarding the distribution of congenital anomalies according to system involved, central nervous system anomalies (39.63%) are one of the most common anomalies worldwide. Our result was similar to a study done by Shama (2006), which stated that the spectrum of abnormities was as follows: The central nervous system was the highest group (21.2%) , Cardiac anomalies (16.5%), Skeletal system (14.1%), Renal system (11.8%), and our result was disagreed with the work prepared by Shamin which was as follows the respiratory tract (33%), genito urinary system (24.5%), gastrointestinal tract (12.3%), central nervous system (14%), cardiovascular system (7%), skeletal system (3.5%), total (eye, skin) (3.5%)[47] .

In this study, the overall sensitivity of ultrasound was (69%), specificity (100%), accuracy (100%), predictive value of (+ve) results (100%) and predictive value of (-ve) results (99.7%). Others studies have also suggested that a normal high resolution ultrasonographic scanning decreases the risk of missing congenital anomalies. [48]

Although the rate of congenital malformations was higher in female than male newborns with ratio of male to female is(1:1.09) the difference was not statistically significant this result in agreement with the, Singh *et al* . (2006) that establish male:female of 1: 1.13[40] at the same time Sallout *et al* . (2010) said that the male to female was 1: 1.2[5]

CONCLUSION :

Congenital anomalies are one of the most important causes of fetal deaths and hence it becomes mandatory to keep on account of incidence and prevalence of congenital abnormalities in the society. The present study showed a high incidence of congenital malformations in the young age group especial among primi gravida woman. The commonest associated risk factor was consanguineous marriage. Central nervous system malformation was the most prevalent anomaly detected and early prenatal diagnosis is helpful in decreasing perinatal mortality by early termination of pregnancy . This study definitely helps to know the prevalence of congenital anomalies, estimate the risk factors which may predispose to anomalies and the pattern of distribution of congenital anomalies

REFERENCES:

1. SinghA. Ravinder K . and Jammu S. Pattern of Congenital Anomalies in Newborn : A Hospital Based Prospective, Jammu(J&K)-India. 2009;11:34-36.
2. Ali A, Shafikhani Z, Abdulahi M. Congenital malformations among live births at Arvand Hospital Ahwaz , Iran - A Prospective study . *Pak J Med Sci* 2008;24: 33-37.
3. Tomatir A, Demirhan H, Sorkun H., Koksal A., Ozerdem F., Cilengir N. Major congenital anomalies: a five-year retrospective regional study in Turkey. *Genet Mol Res* 2009;8:19-27.
4. Tayebi N, Yazdani K, Naghshin N. The Prevalence of Congenital Malformations and its Correlation with Consanguineous. *OMJ*. 2010; 25: 37-40.
5. Sallout S., Shama ,Stoll B. , Congenital anomalies. In Kliegman R M, Jenson H B, Behrman R E, Stanton B F(eds) Nelson Textbook of pediatrics18th (edn) Philadelphia . WB Saunders , 2008:711-13.
6. Rodica R, Anamaria M, Tudor M, Ştefan I. Congenital Malformation Prevalence in Cluj District between 2003-2007Applied Medical Informatics 2009;25:37-46.

7. Tomatır A, Demirhan H., Sorkun,H. A. Köksal, F. Özerdem, Çilengir N. Major congenital anomalies: a five-year retrospective regional study in Turkey . Genetics and Molecular Research 2009;8: 19-27.

8. Jehangir W, Ali F. , Jahangir T, Sajjad M. Prevalence of Gross Congenital Malformations at Birth in the Neonates in a Tertiary Care Hospital. A.P.M.C 2009;3: 47-50.

9. Biri A, Onan A, Korucuoglu Ü, Tiras B. Birth prevalence and distribution of congenital anomalies in a university hospital. *Perinatol. Dergisi* 2005;13: 86-90.

10. Padma S, Ramakrishna D., Jijiya P ,Ramana P . Pattern Of Distribution Of Congenital Anomalies In Stillborn: A Hospital Based Prospective Study Pathology. 2011;2:604-10.

11. Ingeborg B., epidemiological surveillance of congenital anomalies in europe zdrav vestn 2009; 78:175–79.

12. Morb M. ,Mortal W., Improved national prevalence estimates for 18 selected major birth defects--United States, 1999-2001. JAMA 2006;54:1301-05.

13. Yousfani S., Seema B., Firdous M., Amna M., Imdad A., Farhana S. and Majida K. Perinatal Mortality and Related Obstetric Risk Factors at a Tertiary Care Hospital of Hyderabad JLUMHS . 2008;1: 204-7.

14. *Carla V., Eleonora C., Dandolo G., Giovanni B.* Ultrasound screening in second and third trimester of pregnancy: an update ACTA BIOMED 2007;78: 229-32.

15. Isa Abdi, Masomeh K. , Hamid-Reza F.,The Prevalence at Birth of Overt Congenital Anomalies in Urmia, Northwestern Iran .Archives of Iranian Medicine, 2008;11:148 –51.

16. Sahar M. , Maisa N. , Ahmad R. Approaching a Dysmorphic Newborn Egypt. J. Hum. Genet. 2008;9:121-37.

17. Pamela L. Risk management Congenital abnormalities: failure to detect and treat The Obstetrician & Gynaecologist 2008;10:33–37.

18. Rasmussen S, Erickson J, Reef S, Ross DS: Teratology: from science to birth defects prevention. Birth Defects Res A Clin Mol Teratol 2009, 85:82-92.

19. Shama M., Salva N., Nadya A. The Accuracy of Ultrasound in the Diagnosis of Congenital Abnormalities JPMA. 2006;56.

20. *Silvana G., Maria d.* Congenital malformations in Rio de Janeiro, Brazil: prevalence and associated factors Cad. Saúde Pública, Rio de Janeiro, 2006;22:2423-31.

21. Varela M, Nohr A, Llopis-Gonzalez A, Andersen M, Olsen J. Sociooccupational status and congenital anomalies. *Eur J Public Health* 2009;19:161-67.

22. Botto L, Lisi A, Bower C, Canfield M, Dattani N, de Vigan C, de Walle H, Erickson E, Halliday J, Irgens L, Lowry R, McDonnell R, Poetzsch S, Ritvanen A, Robert-Gnansia E, Siffel C, Stoll C and Mastroiacovo P: "Trends of Selected Malformations in Relation to Folic Acid Recommendations and Fortification: An International Assessment", Birth Defects Research (Part A), 2006;76: 693-705.

23. ching-chun l,jung-der w, gong-yih h, yu-yin c, pau-chung c, Increased Risk of Death with Congenital Anomalies in the Offspring of Male Semiconductor Workers2008;14:112-16.

24. Sreeram V , Guimond C, Criscuoli M, David A , Sarah-M, Irene M, George C Congenital Abnormalities and Multiple Sclerosis. BMC Neurology 2010;10:115-18.

25. Carlos N., Alex S., Olímpio Barbosa de M., Adriana Mota Bione N. Validation of ultrasound diagnosis of fetal anomalies at a specialist center 4 Rev Assoc Med Bras 2009;55:541-46.

26. Tootoonchi P.Easily identification congenital anomalies. prevalence and risk factors .Acta Medica Iranica 2003; 41:15-1.

27. Al Hosani H, Salah M,Abu-Zeid H,Farag HM,Saade D. The National Congenital Anomalies Register in the United Arab Emirates.East Mediterr Health j 2005;11:690-99.

28. Golalipour M.,Ahmadpour-Kacho M.,Vakili and M. Congenital malformations at a referral hospital in Gorgan Islamic Republic of Iran. East Mediterr Health J 2005;11:707-15.

29. Karbasi S., Golestan M., Fallah R., Mirnaseri F., Barkhordari K., and Mahdokht S.Prevalence of Congenital Malformations .*Acta Medica Iranica* 2009;47:149-53.

30. Al-Bayati E.Congenital abnormalities: Risk factors and the role of ultrasound examination in their detection in Basrah msc thesis University of Basrah,Iraq.2005.

31. Alaani S , Savabieasfahani M , Tafash M and ManducaP. Four Polygamous Families with Congenital Birth Defects from Fallujah, Iraq Int. J. Environ. Res. Public Health 2011;8:89-96.

32. Sallout S. ,Al Reham A., Abdelmane A. ,Al Sulemat.. Antenatal diagnosis , prevalence and outcome of majar cogenital anomalies in Saudi Arabia :ahospital- base study. Ann Saudi Med, 2010;28:272-76.

33. Dolk H, Loane M, Abramsky L, de WH, Garne E. Birth prevalence of congenital heart disease. *Epidemiology* 2010;21:275-77.

34. Mohamed A., Mohamed M., Ahmed E.and Wael B.. Dysmorphogenesis, Clinical Study Ass. Univ.,Assiut Med. J2007;30:159- 84.

35. Gupta K, Singh A, Gupta R. Pattern of Congenital Anomalies In Newborn at Birth: A Hospital Based Prospective Study. Scientific paper presented during the Proceedings at 42nd national conference of Indian academy of Pediatrics (Pedicon) at KolKatta, 2005.

36. Aguiar MJB, Campos AS, Aguiar RALP, Lana AMA, Magalhães RL, Babeto LT. Defeitos de fechamento do tubo neural e fatores associados em recémnascidos vivos e natimortos. J Pediatr (Rio J) 2003; 79:129-34.

37. Khaskheli M, Baloch S, Khushk IA, Shah SS. Pattern of fetal deaths at a university hospital of Sindh. *J Ayub Med Coll Abbottabad* 2007;19:32-34.

38. Michels TC, Tiu AY. Second trimester pregnancy loss. *Am Fam Physician* 2007 ;76:1341-1346.

39. Garne, E. M. Loane , Dolk H., Scarano G., *etal* . Prenatal diagnosis of severe structural congenital malformations in Europe Ultrasound Obstet Gynecol. 2005;25: 6–11.

40. Singh S.,. Shergill Gs, Singh A, Chander R . role of ultrasound in detection of antenatal foetal malformations. ind j radiol imag, 2006;16:831-34.

41. Kitwita, P. Arnold,. A retrospective comparison of prenatal diagnosis of congenital heart defects. Doris Duke Medical Student's Journal, 2005;4:69-72.

42. Nath A, Patil C, Naik V. Prevalence of consanguineous marriages in a rural community and its effect on pregnancy outcome. Indian Journal of community Medicine 2004;29:41-43.

43. Mehhrabi A, Zeyghami B. The effect of consanguineous marriage on congenital malformation. Journal of Research in Medical Sciences2005;10:298-301.

44. Bromiker R, Baruch M. Association of parental consanguinity with congenital malformations among Arab newborns in Jerusalem. Clinical Genetics 2004;66:63.

45. Al-Mendalawi M,pattern of neonatal and post neonatal death over a decade(1995-2004)at military hospital in Saudi Arabian. Saudi med j 2008;29:1518-21.

46. Hindryckx .,Karen P. ,Sophie D, Eric L., Francis Z., Dirk V., Anna Thomas D., Has the Prevalence of Congenital Abnormalities after Intracytoplasmic Sperm Injection Increased? The Leuven Data 1994–2000 and a Review of the Literature Gynecol Obstet Invest 2010;70:11–22.

47. Shamim A, Chohan N, Sobia Q.pattern of congenital malformations and their neonatal outcome. Journal of Surgery Pakistan (International)2010;15:34-37.

48. Julian-Reynier C., and *et al.* Impact of prenatal diagnosis by ultrasound on the prevalence of congenital anomalies at birth in Southern France. J. Epidemiol. & Community Health. 2001;48: 290-96.