Risk factors of congenital anomalies in Karbala

Khalid k. alaarji
C.A.B.P., D. CH., M.B.ch.B
Karbala University – College of Medicine

ABSTRACT

BACKGROUND; Congenital anomalies can be defined as structural or functional abnormalities present at birth. They are an important cause of morbidity and mortality in infants. Various risk factors have been identified as contributing factors to these defects. The objectives of the present study are to determine the frequency of different structural congenital anomalies and possible risk factors responsible for these anomalies.

METHODS; This case - control study was carried out in the neonatal intensive care unit of Kerbala teaching hospital for children in Karbala / Iraq. The study was conducted over 18 month's period from January 1, 2014 to May 31, 2015. All babies admitted to neonatal care unit with congenital anomalies during this period were included apart from neonate with suspicion of inborn error of metabolism and those with chromosomal abnormalities because there are no facilities for definite diagnosis of these diseases.

Seventy seven newborns with congenital anomalies included in this study, males 47(61.04%) and females 30 (38.96%) and 100 newborn without congenital anomalies, male 59 (59%) and female 41 (41%), selected randomly as a control.

The statistical method which used to signify the risk factors is relative risk (RR). [RR = 1 no effect, RR > 1 is a risk factor, and RR < 1 is protective]

RESULTS; In present study, the congenital anomalies related to the cardiovascular system (CVS) were the most common 33(42.86%). Males 47(61.04%) were more commonly affected than females 30 (38.96%). Cases of congenital anomaly were found in 60 (77.92%) of multiparas, whereas 17 (22.08%) in primiparas. It has been seen that 45 (58.44%) of the mothers were 20 - 30 years old, 15 (19.48%) of the mothers were between 30 - 40 years old, and 6 (7.79%) of the mothers were over the 40 years old.

In the present study, 54 (70.13%) mothers of babies delivered with congenital anomalies had a history of consanguinity. Also, 6 (7.79%) mothers of babies delivered with congenital anomalies had a history of diabetes mellitus.

CONCLUSION; The congenital anomalies were cardiovascular system (CVS) 33(42.86%), gastrointestinal system 25 (32.47%), and central nervous system 14 (18.18%).
The main risk factors were consanguinity and maternal diabetes.

INTRODUCTION

Congenital anomalies can be defined as structural or functional abnormalities present at birth [1]. These defects are of prenatal origin resulting from defective embryogenesis or intrinsic abnormalities in the process of development. Birth defects can be isolated abnormalities or part of a syndrome and continue to be an important cause of neonatal and infant morbidity and mortality [2]. They are an important cause of morbidity and mortality in infants and the general incidence of congenital anomalies varies considerably in various populations. This accounts for 1.5 to 3% of all births. Almost 20-30% of perinatal deaths in the developed countries are due to congenital anomalies and 50% of the babies with congenital anomalies die in infancy. About 50% of the affected children suffer from severe mental and physical handicaps [3].

Congenital anomalies can effectively be diagnosed on ultrasonography. As 80-90% of the cases of congenital anomalies occur without any risk factor [4], it is mandatory to

have repeated ultrasonographic examination of the whole obstetric population in order to have prenatal diagnosis of structural birth defects. By avoiding many of the known risk factors, the burden of congenital anomalies can be minimized and thereby its social and economic impact on the concerned families and the community can be reduced.

The etiology of congenital malformation is genetic (30-40%) and environmental (5 to 10%). Among the genetic etiology, chromosomal abnormality constitutes 6%, single gene disorders 25% and multifactorial 20- 30%; however, for nearly 50% of congenital anomaly, the cause is yet to be known [5]. Consanguineous marriages have been described as an important factor contributing to increased congenital malformation. Studies have shown a significantly higher incidence of malformations in offspring of consanguineous parents [6].

Various risk factors have been identified as contributing factors to these defects which include genetic factors, maternal age, maternal drug intake (like antiepileptic, ACE inhibitors etc), radiation exposure, maternal illnesses (e.g. diabetes, infection e.g. toxoplasmosis, rubella etc), smoking, folic acid deficiency, and consanguinity[7]. Some of these risk factors can be avoided.

Understanding how these inequalities relating to congenital anomalies arise is key to implementing effective public health interventions to reduce socioeconomic inequalities in infant and neonatal mortality. Socioeconomic inequalities in congenital anomalies have been shown to exist in the rates of stillbirth and perinatal, neonatal, and infant mortality. [8]

The objectives of the present study are to determine the frequency of different structural congenital anomalies and possible risk factors responsible for these anomalies.

PATIENTS AND METHODS

This case - control study was carried out in the neonatal intensive care unit of Kerbala teaching hospital for children in Kerbala / Iraq. This hospital serves both urban and rural area. The study was conducted over 18 month's period from January 1, 2014 to May 31, 2015. All babies admitted to neonatal intensive care unit with congenital anomalies during this period were included apart from neonate with suspicion of inborn error of metabolism and those with chromosomal abnormalities because there is no facility for definite diagnosis of these diseases. The newborns were examined and assessed systematically for the presence of congenital anomalies. Diagnosis of congenital anomalies was based on clinical evaluation of newborn babies by the pediatrician and other appropriate investigations such as radiography, ultrasonography, and echocardiography etc.

Seventy seven newborns with congenital anomalies included in this study, males 47(61.04%) and females 30 (38.96%) and 100 newborn without congenital anomalies, male 59 (59%) and female 41 (41%), selected randomly as a control.

A marriage has been considered consanguineous, when it occurred between a male and a female who are blood-related, e.g., between 1st cousins etc. and two categories of marriages were included consanguineous relation- ship i.e., 1st cousin, 2nd cousin and non-consanguineous relation- ship

After admission, verbal consent was obtained from all the women included in the study to answer a questionnaire list.

The types of congenital anomalies were classified using International Classification of Disease (ICD) 10. Congenital anomalies were divided according to the system involved [cardiovascular system (CVS), central nervous system (CNS), gastro- intestinal (GIT), genitor- urinary system (GUS), musculoskeletal (MS), and skin].

The fetus was diagnosed as having either isolated (only one system involved) or complex anomaly (two or more system involved). Detailed history was obtained especially regarding the risk factors including age of mother, maternal diabetes,

periconceptional use of folic acid, prior history of miscarriage, still birth, prematurity, parity, consanguinity, pervious history of congenital abnormalit, socioeconomic status, family history of congenital abnormality, and gender.

The statistical method which used to signify the risk factors is relative risk (RR). [RR = 1 no effect, RR > 1 is a risk factor, and RR < 1 is protective]

RESULTS

In present study, the congenital anomalies related to the cardiovascular system (CVS) were the most common 33(42.86%). CVS anomalies included acyanotic 24(31.17%) and cyanotic 9(11.69%) congenital heart disease.

The gastrointestinal system anomalies were 25 (32.47%), in which the cleft lip and palate 6 (7.79%) and duodenal atresia 4 (5.19%).

While the central nervous system anomalies were 14 (18.18%), in which meningomyelocele 6 (7.79%) and hydrocephalus 4 (5.19%) as shown in table 1.

Table (1): Frequency and percentage of congenital anomalies.

Type of congenital anomalies	No	%	Type of congenital anomalies	No	%
Congenital heart disease	**33**	42.86	**Genitourinary system**	12	15.58
Acyanotic	24	31.17	Hydronephrosis	4	5.19
Cyanotic	9	11.69	Congenital hydrocele	3	3.89
Gastrointestinal system	**25**	32.47	Hypospedius & epispedius	2	2.59
cleft lip and palate	6	7.79	Ambigous genitelia	1	1.3
Duodenal atresia	4	5.19	Bladder extrophy	1	1.3
Omphalocele	3	3.89	Vaginal atresia	1	1.3
Hirschsprung's disease	3	3.89	**Musculoskeletal system**	11	14.29
Oesophageal atresia	2	2.59	Polydactaly	3	3.89
Volvulus and midgut rotation	1	1.3	Club foot	2	2.59
Gastroschisis	1	1.3	Development dysplsia of hip	2	2.59
Juojenal atresia	1	1.3	Osteogenesis imperfecta	1	1.3
Imperforate anus	1	1.3	Phocomelia	1	1.3
Intestinal webs	1	1.3	Absence depressor anguli oris	1	1.3
Hypertrophic pyloric stenosis	1	1.3	Sacrococcygal teratoma	1	1.3
Meckle diverticulm	1	1.3	**Respiratory system**	3	3.89
Central nervous system	**14**	18.18	Choanal atresia	1	1.3
Meningomyelocele	6	7.79	Diaphragmatic hernia	1	1.3
Hydrocephalus	4	5.19	Eventration of diaphragm	1	1.3
Encephalocele	2	2.59	**Skin**	3	3.89
Microcephaly	1	1.3	Hemangioma	2	2.29
Anencephaly	1	1.3	Epidermylosis bullosa	1	1.3

In this study, males 47(61.04%) were more commonly affected than females30 (38.96%).
Regarding the parity of the mothers, cases of congenital anomaly were found in 60 (77.92%) of multiparas, whereas in primiparas, the congenital anomaly were found in only 17 (22.08%).

It has been seen that 45 (58.44%) of the mothers were 20 - 30 years old, 15 (19.48%) of the mothers were between 30 - 40 years old, and 6 (7.79%) of the mothers were over the 40 years old.

In the present study, 54 (70.13%) mothers of babies delivered with congenital anomalies had a history of consanguinity.

Also, 6 (7.79%) mothers of babies delivered with congenital anomalies had a history of diabetes mellitus.

Family history of congenital abnormality was positive in only 5 (6.49%) cases as shown in table 2.

Table (2): Frequency, percentage, and relative risk of risk factors of congenital anomalies.

Variable	Groups	No.	%	Control	%	RR
Age of mother	<20 yr	11	14.29	17	17	**0.84**
	20 – 30 yr	45	58.44	53	53	**1.1**
	30 -40 yr	15	19.48	22	22	**0.89**
	>40 yr	6	7.79	8	8	**0.97**
Residence	Rural	20	25.97	34	34	**0.76**
	Urban	57	74.03	66	66	**1.21**
Prior history of miscarriage, still birth, and prematurity	Present	16	20.78	17	17	**1.22**
	Absent	61	79.22	83	83	**0.95**
Parity	Primiparas	17	22.08	37	37	**0.59**
	Multiparas	60	77.92	63	63	**1.24**
Consanguinity	Present	54	70.13	35	35	**2**
	Absent	23	29.87	65	65	**0.46**
Pervious history of congenital abnormality	Yes	4	5.19	4	4	**1.29**
	No	73	94.81	96	96	**0.98**
Socioeconomic status	Low	32	41.55	39	39	**1.07**
	Middle	34	44.16	44	44	**1.01**
	Good	11	14.29	17	17	**0.84**
Family history of congenital abnormality	Yes	5	6.49	8	8	**0.81**
	No	72	93.5	92	92	**1.02**
Maternal dis.(Diabetes)	Present	6	7.79	4	4	**1.95**
	Absent	71	92.21	96	96	**0.96**
Consumption of folic acid during pregnancy	Yes	66	85.71	87	87	**0.98**
	No	11	14.29	13	13	**1.09**
Gender	Male	47	61.04	59	59	**1.03**
	Female	30	38.96	41	41	**0.95**

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 [9]. Regarding the distribution of congenital anomalies according to system involved, our study showed that cardiovascular system anomalies (42.86%) are the most common congenital anomalies. Our result was similar to a study done in Fallujah, Alaani et al.[10] but our result was disagreed with the work prepared by some studies recorded higher incidence of CNS malformations followed by GIT and musculoskeletal system,[11] .

Even so, congenital heart defects (CHD) may be underestimated in our study because children born with heart defects may not need hospital admission or attend to hospital for echocardiography study as outpatient especially those with isolated and acyanotic CHD. Other possible explanation for the apparent higher percentage of other types of defects may be because they are obvious at birth and are recorded more carefully than congenital heart defects.

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 regard as cause of this dissimilarity. Other explanations are the type of sample and the criteria for diagnosis that is to say differences in study design and methodology.

Concerning risk factors, Consanguineous marriages are reported to play a major role in the occurrence of congenital malformations.[12]. Increased incidence of congenital anomalies in consanguineous couples is due to homozygous expression of recessive genes inherited from common ancestors.[13]. Our work showed that parental consanguinity was highly significant relative risk factor for the malformations. Shama et al., (2006) confirmed that consanguinity was considered as important risk factor; also consanguineous marriages are recognized common practice in Middle East [14].

Maternal age's association with congenital anomalies is considered an important factor. It has been suggested that the increasing age of mothers is associated with an increase in chromosomal meiotic errors and is probably the only non-genetic risk factor for trisomy in human beings [15]. But unfortunately, congenital anomalies with suspicion of chromosomal error are excluded from our study because there is no facility for definite diagnosis of these diseases.

The relationship between maternal age and babies born with congenital malformations, in present study, revealed that a majority of malformed babies were born to mothers aged 20 - 30 years 45 (58.44%). It was in accordance with earlier studies [16]. Our results are similar to a study done in Iran (maternal age 25.69+5.54 years, 8.7% >35 years age)[17]. Suguna Bai *et al*.[18] reported a higher incidence of malformation in the babies born to mothers aged over 35 years, whereas Dutta *et al*.[19] documented statistically insignificant association of increased maternal age and congenital anomalies.

Besides maternal age, multiparity and multigravidas are also associated with an increased prevalence of congenital anomalies [20]. Almost 77.92% of mothers in our study were multigravidas, which is consistent with a study by Qazi [7]. This is in contrast to a study by Perveen that demonstrated more congenital anomalies in primigravida mothers [13].So the incidence of congenital malformation increases as the birth order increases. For this reason, females who are multigravidas need to be examined more carefully since the risk of giving birth to a fetus with congenital malformations is greater.

Family history of congenital anomalies was present in 5 (6.49%) of our cases and was comparable to 8.6 and 17% reported earlier

[21,22], which is an insignificant relative risk factor

The association between maternal glycemic control and the increased risk of major congenital anomalies has been well established [23] . But in our study, there is slight increase of congenital anomalies in diabetic mothers (7.79%) as compared with control group but with a significant relative risk factor, may be due to small group studied and further study needed for the incidence of congenital anomalies in diabetic mothers separately. Also in another study, the incidence of major congenital anomalies in infants of diabetic mothers was done in Egypt [24] on live borns 11% and Hod et al. ranged between 19.4% and 20.5% [25].

More male 47 (61.04%) babies with congenital anomalies than females 30 (38.96%) were noted in the present study with significant relative risk factor. This finding is consistent with that of Shaw et al. who observed an increased risk for most systems even after adjusting for confounders [26]. Male preponderance was similar to the other studies. [19]. It may be because of the fact that the females were afflicted with more lethal congenital malformations and could be incompatible with life.

History of spontaneous abortion or still birth obtained in this study was 20.78% with a significant relative risk factor, might be due to birth defects of a severe degree in the conceptuses which was incompatible with life [29].

Regarding socioeconomic status, most congenital anomalies in our study are prevalent in low 32 (41.55%) and middle 34 (44.16%) socioeconomic status.

The congenital anomalies increased with increasing socioeconomic deprivation [27]. It was observed the risk in the most deprived quintile of the deprivation index was 40% higher than in the most affluent quintile [28].

Among maternal risk factors, folate supplementations occupy a significant position. Neural tube defects, which include spina bifida and encephaloceles, have long been linked to folic acid supplementation [29]. In our study, only 11 (14.29%) mothers did not receive periconceptual folate. This percentage increased especially in mothers of infants with neural tube defects which is a significant relative risk factor.

CONCLUSION

The congenital anomalies were cardiovascular system (CVS) 33(42.86%), gastrointestinal system 25 (32.47%), and central nervous system 14 (18.18%).

The main risk factors were consanguinity and maternal diabetes.

REFERANCES

1. Rizk Francine, Salameh Pascale, Hamade Aline. Congenital anomalies: prevalence and risk factors. Universal J. of public health 2014; 2(2): 58-63
2. Rosano A et al. Infant mortality and congenital anomalies from 1950 to 1994: an international perspective. Journal of epidemiology and community health 2000; 54:660-6.
3. Vincenzo Pinto, Mira Wankelmuth, Vincenzo D'Add- ario. Donald School Textbook of Ultrasound in Obstetrics and Gynecology, Asim Kurjak, Frank A Chervenak, First Ed, Jaypee Brothers, New Delhi, India. 2004; 365.
4. Kurjak A, Kirkinen P, Latin V et al. Diagnosis and assessment of fetal malformations and abnormalities by ultrasound. J perinat Med. 1980; 8: 219-35.
5. Rajangam S et al. Consanguinity and chromosomal abnormality in mental retardation and or multiple congenital anomalies. Journal of the Anatomical Society of India 2007; 56:30-3. Universal Journal of Public Health 2(2): 58-63, 2014 63
6. Kupka K. International classification of diseases: ninth revision. WHO chronicle 1978; 32:219-25.
7. Qazi G. Relationship of selected prenatal factors to preg- nancy outcome and congenital anomalies. J Ayub Med Coll Abbottabad 2010; 22:41-5.
8. Oakley L, Maconochie N, Doyle P, Dattani N, Moser K. Multivariate analysis of infant death in England and Wales in 2005-06, with focus on socio-economic status and deprivation. Health Stat Q2009; 42:22-39..
9. Tayebi N, Yazdani K, Naghshin N. The Prevalence of Congenital Malformations and its

Correlation with Consanguineous. OMJ. 2010; 25: 37-40.
10. 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. 11.Dutta V, Chaturvedi P. Congenital malformations in rural Maharashtra. Indian Pediatr 2000;37:998-1001.
11. Hudgins L, Cassidy SB. Congenital anomalies. In: Martin RJ, Fanaroff AA, Walsh MC, editors.Neonatal-Perinatal Medicine. 8th ed. Philadelphia: Mosby-Elsevier; 2006. pp. 561–81
12. Tayebi N, Yazdani K, Naghshin N. Prevalence of congenital malformations and its correlation with consanguineous marriages. Oman Med J 2010; 25: 37-40.
13. Shama M., Salva N., Nadya A. The Accuracy of Ultrasound in the Diagnosis of Congenital Abnormalities JPMA. 2006; 56.
14. Yoon PW, Freeman SB, Sherman SL, Taft LF, Gu Y, Pettay D, et al. Advanced maternal age and the risk of Down syndrome characterized by the meiotic stage of chromosomal error. a population based study. Am J Hum Genet. 1996 Mar; 58(3):628-3 16. Taksande A, Vilhekar K, Chaturvedi P, Jain M. Congenital malformations at birth in central India, A rural medical college hospital based data. Indian J Hum Genet 2010; 16: 159-63. 17. de Costa CM. Consanguineous marriage and its relevance to obstetric practice. Obstet Gynecol Surv. 2002 Aug; 57(8):530-6. 18. Suguna Bai NS, Mascarene M, Syamalan K, Nair PM. An etiological study of congenital malformation in the newborn. Indian Pediatr. 1982; 19:1003–7.
1. 19. Dutta V, Chaturvedi P. Congenital malformations in rural Maharashtra. Indian Pediatr. 2000; 37:998–1001.
2. 20. Sipilä P, von Wendt L, Hartikainen-Sorri AL. The grand multipara—still an obstetrical challenge? Arch Gynecol Obstet. 1990; 247(4):187-95.
3. 21. Gul F, Jabeen M, Khan AS. Frequency of congenital malformations and associated risk factors at Liaqat Memorial Hospital Kohat. Khyber Med Univ J 2012; 4: 119-24. 22. Sridhar K. A community based survey of visible congenital anomalies in rural Tamil Nadu. Indian J Plast Surg 2009; 42 (suppl); S184-S91.
4. 23. J.E. Becerra, J.K. Muin, J.F. Cordero, J.D. Erickson. Diabetes mellitus during pregnancy and the risks for specific birth defects. A population based case control study. Pediatrics, 85 (1) (1990), pp. 1–9
5. 24. R.M. Shawky, H.H. Elsedfy, S.K. Abolouz, G.Y. Labatia. Prevalence of congenital malformations in a thousand consecutive Egyptian liveborn. Egypt J Med Hum Genet, 2 (1) (2001), pp. 43–53
6. 25. M. Hod, P. Merlob, S. Friedman, Y. Rusecki, A. Schoenfeld, J. Ovadia. Prevalence of congenital anomalies and neonatal complications in the offspring of diabetic mothers in Israel. Isr J Med Sci, 27 (8–10) (1991), pp. 498–502
7. 26. Shaw GM, Carmichael SL, Kaidarova Z, Harris JA: Differential risks to males and females for congenital malformations among 2.5 million California births, 1989–1997. *Birth Defects Res A Clin Mol Teratol* 2003, 67(12):953-958.
8. 27. Sawardekar K. 2005. Profile of major congenital malformations at Nizwa hospital, Oman: 10- year review. J Paediatr Child Health; 41:323-30.
9. 28. Vrijheida, M.; Dolka ,H.; Stoneb, D.; Abramskyc ,L.; Albermand, E.; S Scott,J.E.S.2000. Socioeconomic inequalities in risk of congenital anomaly. Arch Dis Child; 82:349- 352.
10. 29.Berry RJ, Li Z, Erickson JD, Li S, Moore CA, Wang H, Mulinare J, Zhao P, Wong LYC, Gindler J: Prevention of neural-tube defects with folic acid in China.*N Eng J Med* 1999, 341(20):1485-1490.