

OCCURRENCE OF CONGENITAL ANOMALIES AND GENETIC DISEASES IN A POPULATION OF GHAZVIN PROVINCE, IRAN: A STUDY OF 33380 CASES

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ABSTRACT

Objectives: The purpose of this study was to determine the incidence of congenital and genetic anomalies in two major referral hospitals and medical Genetic center in a population of Ghazvin Province.

Methodology: A cross sectional study was performed between 2000- 2004 on 33380 children from infancy to age 8 years. The precise and confirmed diagnosis of genetic and congenital anomalies was elaborated by reviewing pedigree of family population screening, genetic records of family data, routine tests such as application of molecular and karyotype and other essential information have been approached.

Results: In total, the more frequent malformation associated congenital anomalies among our patients was inborn error of metabolism (7.18%) followed by disorder of congenital hearth defects (6%).

Conclusion: We suggest a possible role of various factors such as different geographical may influence dissimilarities between present study and other population. Also the necessity of particular attention and emphasize on special screening program that helps to identify early stages of genetic and congenital malformation. These results together provide information to physicians and genetic counselors to realize contribution of congenital abnormalities and setting priorities of screening individual cases

KEY WORDS: Congenital abnormality, Prevalence, Population, Iran distribution, ethnic, different habitual diet and socio - economic differences.

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INTRODUCTION

Genetic and congenital diseases are almost always serious, incurable, a number of these diseases are treatable, and in some cases, their clinical therapeutic intervention and study of

family history and genetic counseling remains of paramount importance.¹

Genetic and congenital abnormalities are more than what is generally appreciated and are the cause of significant morbidity and mortality in pediatrics. With decreasing incidence of fatal infections diseases, congenital anomalies would be one of the main causes of infants mortality in future. Large systematic studies of genetics and congenital abnormalities from Iran are not available. Hence, we investigated large heterogeneous populations of paediatric patients to determine the current prevalence of genetic and congenital anomalies among our populations.

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Table-I: Comparative occurrence of Chromosomal abnormalities.

<i>Diagnosis/Disorder</i>	<i>M</i>	<i>F</i>	<i>Cases</i>	<i>%</i>
Mental Retardation	3	3	6	0.20
Fragile X syndrome	1	-	1	0.02
Down's syndrome	21	14	35	1.00
Wolf Hirschhorn	1	-	1	0.20
Total	26	17	44	1.3

PATIENTS AND METHODS

A retrospective cross sectional study of minor and major anomalies was encountered on 33380 patients with hospital based registry from newborn infant to age 8 years of both sexes, between 2000-2004 in the university center of Genetic division, Ghods major Pediatric hospital. The hospital was chosen as it is a university referral major hospital and provides emergency services to the large district of the province. Demographic information and clinical findings at birth were also collected from Kosar maternal and newborn hospital records and from the parents at the initial evaluation of the patient.

Ghazvin city is located about 100 km away from Capital and surrounded by many factories. Also heterogeneity phenomena is being established here. The precise and confirmed diagnosis of diseases and in proband was supported by reviewing pedigree of family, including genetic records of family data, population screening, the mode of inheritance, assessment of various expertise and special interests of the investigators, routine tests, ELISA, AFP, urinary amino acids were determined by chromatography and various kits, application of karyotype (High Resolution) with banding pattern, routine ultrasonography examination ecocardiography and other essential information have been collected. A classification system was introduced to divide diagnosis into different categories by exhibiting seven tables. The rates of malformation and disease were calculated per 1000 patients.

The sorted patients charts, checklist and data were analyzed by SPSS (version 11.5 Inc. USA) to extract the frequencies, rates and compara-

Table-II: Comparative occurrence of disorder of in born error of etabolism.

<i>Abnormalities</i>	<i>M</i>	<i>F</i>	<i>Cases</i>	<i>%</i>
Hypercalcemia	41	20	61	2.00
Hypocalcemia	38	23	61	2.00
Cholesterolemia	24	3	27	0.90
Galactosemia	2	-	2	0.06
MPS	8	4	12	0.60
Tyrosiemia	1	-	1	0.02
PKU	4	3	7	0.20
Favism(G6PD)	14	10	24	0.70
Hypoureemia	10	7	17	0.50
Acidosis	7	2	9	0.20
Total	149	72	221	7.18

tive occurrence of minor and major anomalies. SPSS 11.5 a leading worldwide provider of predictive analytics software ,delivers more accurate analytical results and enhanced data management which enable users to retrieve and format data faster and easier.

RESULTS

This paper presents, the results, frequency and analysis of congenital malformation and genetic diseases of 33380 children from infancy to age 8 years over a consecutive period of four years. The outcome of clinical and laboratory features observed in our patients are summarized in Tables I-X. As is evident, the prevalence of CA was 2.9% or 29.4/1000 (902 cases) and the prevalence of CA was higher in male (539 cases) than female (363 cases). The more frequent conditions among our patients were noticed for disorders of amino acid metabolism (7.18%) followed by congenital hearth defects (6%). Down's syndrome were found more frequent (1%) among chromosomal defects in Table-I. The prevalence of cholesterolemia was highest among metabolic disorders in (Table-II). Rates of CNS anomalies were estimated to be from 0.12% (Spina bifida) to 1.10% (microcephaly) Table-III. The occurrence of cleft palate (2.5%) was more than cleft lip (1.1%) as demonstrated in Table-IV. The highest rate for anomalies of (Table-V) was that for Hypospadias (1.40%) followed by Cryptorchidism (Table-VI). This study includes 33 patients with

Table-III: Comparative occurrence of Central Nervous System (CNS)

Anomalies	M	F	Cases	%
Meningomyelocele	8	9	17	0.50
Anencephaly	4	3	7	0.20
Omphalocele	13	5	18	0.50
Spinabifida	4	-	4	0.10
Hydrocephaly	13	8	21	0.60
Microcephaly	20	17	37	1.10
Cerebral palsy	8	8	16	0.50
Epilepsy Seizures	5	4	9	0.26
Total	75	54	129	3.76

sensory disorders; they consisted of hereditary deafness (0.70%) and blindness (0.30%). Hirschsprung's diseases exhibit highest rate (1%), esophageal atresia (0.75%), Laryngomalacia (0.23%), Gasteroschisis (0.14%) and anal atresia (0.23%) were the other disorders including thorax and abdominal anomalies in (Table-VII). Among 27 patients which suffered from hematological disorders, occurrence of thalasemia minor (0.40%) and Von Willebrand disease were shown with high and low frequency respectively (Table VIII). Furthermore other disorders, such as congenital hearth defects (6%0), Waardenburg syndrome (0.02%), Tubers Sclerosis (0.05%) and Vater association (0.05%) included 207 patients exhibited in Table-X. The results were double checked with the both hospital registration information related to the study period.

Table-V: Comparative occurrence of external genital anomalies and disorder of gonadals and internal reproductive ducts.

Disorders	M	F	Cases	%
Abnormalities in testis	17	-	17	0.50
Hypospadias	47	-	47	1.40
Cryptorchidism	21	-	21	0.70
Epispadias	2	-	2	0.05
Bladder extrophia	1	-	1	0.02
Renal Urinary tract	4	-	4	0.01
Turner syndrome	-	4	4	0.01
Ambiguous genitalia	6	5	11	0.5
Total	98	9	107	3.3

Table-IV: Comparative occurrence of Cleft lip and Palate

Anomalies	M	F	Cases	%
Cleft Lip	23	14	37	1.1
Cleft palate	45	32	77	2.5
Total	68	46	114	3.4

DISCUSSION

Based on our findings, the prevalence rate of CA was 2.9%. The prevalence rates of present findings on CA are more compatible to studies with four teaching Hospitals in Tehran (2.3%).²

Comparison of international frequency on CA to our results 2.9% (29.4/1000) yielded as follow; in the UAE 10.5/1000),³ in Bahrain 2.7%,⁴ in Lebanon 16.5/1000,⁵ in Turkey 1.1%,⁶ In black South Africa 11.9/1000,⁷ in Russia 1.23%-1.5%,⁸ in China 11.5/1000,⁹ in India 21.1/1000.¹⁰

As in present study, the prevalence rate of mental retardation and chromosomal defects revealed 1.3% per 1000 live births (Table-I). Other study reported from Arak Medical University has shown significant relationship between chromosome aberrations and MR with Down's syndrome.¹¹ Furthermore, in the current situation in India the top three disorders are identifiable syndromes (12%), chromosomal aberration (11.3%) and mental retardation (11%).¹²

The world wide prevalence of Tyrosinemia is approximately 1:100,000.¹³ In our population here (Table-II) the rate (0.02% per 1000) of Tyrosinemia are lower than the rest of the world. The study of hypocalcemia was performed on 153 neonatal and 63 newborn from Shiraz.¹⁴

Some of the rates of anomalies of the central nervous system such as Cerebral Palsy (CP)

Table-VI: Comparative occurrence of sensory disorders

	M	F	Case	%
Hereditary deafness	13	11	24	0.70
Blindness	4	5	9	0.30
Total	17	16	33	1.00

Table-VII: Comparative occurrence of thorax, respiratory and abdominal anomalies

Anomalies	M	F	Cases	%
Esophageal atresia	16	9	25	0.75
Laryngomalacia	5	3	8	0.23
Hirschsprung's disease	17	7	34	1.00
Gastroschisis	3	2	5	0.14
Anal Atresia	6	2	8	0.23
Total	47	23	70	2.35

diagnosed in the present investigation with 0.5% per 1000 (Table-III) is lower than most studied with 2 to 3 per 1000 live birth prevalence.¹⁵ The prevalence of cleft lip and palate in different studies are, in the United States 1 per 700,¹⁶ China 6.11 per 10,000,¹⁷ Korea 1.81 per 1000,¹⁸ Brazil 0.19 per 1000,¹⁹ Ireland 1.14 per 1000,²⁰ 1.03 per 1000²¹ and 0.88 per 1000 in Iran.²² The rate of cleft lip and palate found in our population and other studies appear with approximately similar frequency.

Hearing loss prevalence rates found in various studies range from 1 to 3 cases per 1000 children²³ and in high risk neonates is from 5 to 50 in 1000 live births.²⁴ In the United States 1.4 to 3 per 1000.²⁵ European rates 1.4 to 2.1 per 1000.²⁶ In recent study performed in national congress of genetic disorders at Tehran, 1033 patients with hearing impairment have been reported.²⁷ The data of hearing deafness yielded here (Table-VI) with 24(0.7%) patients. The percentage of hearing impaired found vary

Table-VIII: Comparative occurrence of hematological disorders

	M	F	Case	%
Thalasemia minor	8	6	14	0.40
Thalasemia major	4	2	6	0.20
Hemophilia	6	-	6	0.20
Von-Willebrands disease	1	-	1	0.02
Total	19	8	27	0.82

considerably. As there is no established hearing loss screening program in Iran, the reason for these discrepancies is not completely clear, but may reflect to different unknown etiological factors.

The prevalence of several visual impairment were reported with different range (2.3%-8%) in childhood.²⁸⁻³¹ The different incidence of blindness in this study (0.3%) in Table-VI and other studies may suggest a genetic susceptibility, environment factors or both.

Skeletal and muscle, neuromuscular disorders is the commonest congenital generalized bone malformation at five teaching hospitals in Tehran,¹ India,¹² Bahrain,⁴ black South African,⁷ Denmark.³² The rate of skeletal dysplasia (0.33%) investigated here (Table-IX) were found to be less frequent than generally assumed.

Various studies of Congenital Heart Disease (CHD) in live born infants of 28 centers from different countries yielded 4.05 to 10.2 per 1000³³ which is not similar to present investi-

Table-IX: Comparative occurrence of skeletal and muscle, neuromuscular disorders

	M	F	Case	%
Marfan syndrome	1	-	1	0.02
Osteogenesis Imperfecta	2	-	2	0.05
Achondroplasia	1	-	1	0.02
Spondyloepiphysial dysplasia	-	-	1	0.02
Polydactyly	4	2	6	0.05
Ectrodactyly	1	-	1	0.02
Meckel syndrome	1	-	1	0.02
Pierre Robin syndrome	3	1	4	0.05
Amyotrophic lateral sclerosis	1	1	2	0.05
Duchene muscular dystrophy	6	-	6	0.20
Total	20	5	25	0.5

Table-X: Comparative occurrence of miscellaneous

	M	F	Case	%
Congenital	90	112	202	6.00
Hearth defects				
Waardenburg Syndrome	1	-	1	0.02
Tubersclerosis	2	-	2	0.05
Vater Association	1	1	2	0.050
Total	94	113	207	6.12

gation (6%) (Table-X). Heart failure is a heterogeneous group of disease which includes several discrete syndromes with characteristic clinical and genetic features. However, little is known about the heart disease among our populations.

CONCLUSIONS

The reasons of inconsistency between our results which represents the largest series of genetics and congenital abnormalities ever investigated in Iran and other studies are probably as bellow: Some of the congenital anomalies are not diagnosed at birth and may occur later in the life, therapeutic advances, application of appropriate preconception care, adequate number of geneticists and prenatal diagnosis program. Also this inconsistency might be explained by diagnosis of both minor and major CA in all systems, the large number of cases and the different sex ratio between male and female patients. Moreover the possible role of various factors such as different geographical distribution, ethnic, different habitual diet and socioeconomic differences must not be disregarded.

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