



Determining the Risk Factors of Congenital Anomalies of Newborns in Hamadan Province

Iraj Sedighi¹, Shahla Nouri², Mohammad Kazem Sabzehei^{1,*}, Mahta Sangestani², Younes Mohammadi³, Jalaleddin Amiri¹ and Behjat Qazanfarzadeh¹

¹Department of Pediatric, Faculty of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran

²Family Health Department, Hamadan University Of Medical Sciences, Hamadan, Iran

³Department of Epidemiology, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran

*Corresponding author: Hamadan University of Medical Sciences, Hamadan, Iran. Email: mk_sabzehei@yahoo.com

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Abstract

Background: Congenital anomalies are considered as one of the major causes of neonatal death. The prevalent pattern of congenital anomalies may vary diachronically or geographically. With regard to the pervasiveness of under-five mortality (probability of dying between birth and exactly 5 years old) in Hamadan province in the recent years, the present study intended to determine the risk factors of congenital anomalies of newborns in Hamadan province in 2017.

Methods: The present case-control study was conducted in the hospitals affiliated to Hamadan University of Medical Sciences for 6 months in 2017. The study targeted all the newborns from birth to hospital discharge. The neonatal cases with congenital anomalies were identified through clinical examination. A report sheet was assigned to a healthy newborn, as a control, per each case of congenital anomalies born on the same day and in the same hospital. Once data was collected, they were statistically analyzed by means of SPSS V. 16 software.

Results: According to the current results, the prevalence of congenital anomalies was 0.85% (8.5 per 1,000 live births). Genitourinary (40%), musculoskeletal (25.2%), eye, ear and neck (18.5%), chromosomal (5.9%), respiratory tract (3.7%) and cardiovascular system (2.2%) were the most common congenital anomalies, respectively. Consanguineous marriage, concomitant use of contraceptive methods and male sex were found to be the most important risk factors for congenital anomalies.

Conclusions: The present study aimed at identifying the various types and prevalence of congenital anomalies in Hamadan province. Regular prenatal examination and early diagnosis for prevention, early intervention and scheduled termination of pregnancy are recommended. Besides, public awareness of the disadvantages of consanguineous marriage and other pertaining risk factors affecting the incidence of congenital anomalies is also recommended.

Keywords: Risk Factors, Congenital Anomalies, Newborns

1. Background

Congenital anomalies refer to any anatomic birth malformations that are diagnosable in almost 3% - 5% of newborns (1-4). The etiology of congenital anomalies is multifactorial which remains unrecognized in 40% - 60% of birth defects. The observed risk factors for congenital anomalies consisted of 15% for genetic and chromosomal attributes, 10% for environmental exposures and 20% - 25% for the interplay of genetic and environmental factors (5-9). An annual amount of 30,000 - 40,000 disabled and paralyzed infants are born in Iran; the disability of these infants not only does make them suffer from many physical and psychological disorders throughout their life but also causes their families and the government countless

psychological and economic problems (10-12). Despite etiologic and pathogenic advancements, about 22% cases of neonatal deaths are caused by major congenital anomalies. Such internal malformations as renal, cardiovascular and pulmonary anomalies may not be identified at birth but later in life (13); that is why the prevalence of congenital anomalies reaches 3% - 4% at exactly 1 years old while it equates 5% - 6% at the age of five (14). Congenital anomalies range from mild to severe defects and are classified into single and multiple body involvement. Severe anomalies are easy to diagnose while the mild ones require more accurate clinical examinations. The significance of mild anomalies is due to the fact that they may be a part of a specific syndrome, whose detection facilitates the diagnosis of the syndrome (15-19). Various outbreaks of anomalies

have been proven in different races. Research has shown that nearly 15% of neonatal deaths are attributed to severe anomalies. The prevalence of anomalies in LBW (low birth weight) newborns, preterm infants and both fourth-time mothers and those older than 35 years is respectively 3 times, 4 times and twice as much as the total cases of anomalies at live births. Family medical history, patients' sex and disease severity affect the recurrence of anomalies in subsequent children. The overall prevalence of congenital anomalies has got a descending trend in different countries (20-22).

2. Objectives

The present study intended to determine the risk factors for congenital anomalies of newborns in Hamadan province in order to accentuate the significance of pre- and post-marriage genetic testing so as to prevent births with potential severe malformations through early prenatal diagnosis.

3. Methods

The present case-control study was conducted on the hospitals affiliated with both Hamadan University of Medical Sciences and the Social Security Organization as well as private hospitals in Hamadan for 6 months in 2017. The inclusion criteria targeted all the infants born in the hospitals of Hamadan province whereas exclusion criteria involved Hamadan non-residents and incomplete questionnaires. Case refers to all newborns with congenital anomalies while control denotes infants who were born in the same hospitals and without any clinically observed congenital anomalies. One control was intended per each case with homogeneous neonatal sex, maternal age, and place of residence (city or town). Data collection tool was a standard inventory retrieved from the website (Child Death Care System tab) of Children Department in the Ministry of Health. The questionnaire was composed of 8 sections including demographic information, delivery information, neonatal medical history, and neonatal examination and pertaining anomalies, diagnostic interventions, family medical history, pregnancy history (exposure to risk factors) and maternity lifestyle. The exposure variables used to compare the case and control groups included maternal medications, smoking habit, drug and alcohol abuse, parental consanguineous marriage, history of abortion, history of or exposure to eruptive diseases associated with fever during pregnancy, preterm delivery, maternal underlying diseases, exposure to X-ray or chemicals, surgery during pregnancy, stress, hormonal contraception

and infertility therapies. Sampling was carried out using census method. Neonatal cases with congenital anomalies (minor and major) were identified. The sample size encompassed all births with congenital anomalies during the research time. A report sheet was assigned to a healthy newborn, as a control, per each case of congenital anomalies born on the same day and in the same hospital. Data were collected through neonatal physical examination, interviewing the mothers, reviewing medical dossiers and completing the registration form by the interviewer.

3.1. Statistical Analysis

To analyze data, we used Independent-sample *t*-test and chi-square test to assess the associations. Moreover, to control confounding factor, logistic regression was used. A *P* value less than 0.05 was considered statistically significant. SPSS version 16 was used for analysis.

3.2. Definition of the Key Terms

3.2.1. Congenital Anomalies

Congenital anomalies refer to any anatomic defects at birth, which are diagnosed based on clinical examinations on the delivery day by a pediatrician using fetal or neonatal radiography, ultrasonography and echocardiography which are recorded.

3.2.2. Consanguineous Marriage

Consanguineous marriage is the union between two individuals of the same kinship i.e. the matrimony between either third-degree relatives (coefficient of relationship, $R=12.5\%$) such as cousins or fourth-degree relatives ($R=6.25\%$) such as cousins' children or fifth-degree relatives ($R=3.13$) such as grandchildren of uncles and aunts.

4. Results

About 135 out of 15,901 live births were reported with congenital anomalies, i.e. 0.85% of the total newborns. For the purpose of the present study, 270 subjects were selected and assigned to two groups of case with 135 congenital anomalies and control with 135 healthy infants. There was not any statistically significant difference between the case and control groups in terms of mean neonatal weight, mean parental age, maternal occupation, paternal occupation, place of residence, chronic maternal disease, maternal drug intake, pregnancy problems, radiography during pregnancy, preterm delivery, use of fertility assisted therapy, surgery during pregnancy, stressful pregnancy, exposure to chemicals and family medical history of congenital anomalies ($P > 0.05$). Moreover, there was a significant relationship between congenital anomalies and variables

such as consanguineous marriage, pregnancy despite the use of contraceptive methods, emergency C-section delivery and male-sex ratio ($P < 0.05$). Since both case and control groups were sexually homogeneous, the ratio of male/female sex of all births was compared with the cases of anomalies in order to investigate the relationship between sex ratio and congenital anomalies. The results showed that the sex ratio of male infants was higher than the female ones. There was also a significant relationship between congenital anomalies and such disorders as nutritional and respiratory problems (Table 1).

According to the results of the present study, the most prevalent congenital anomaly belonged to genitourinary system (40%) and the least one was related to cardiovascular system (2.2%). None of newborns had skin anomalies (Table 2).

5. Discussion

Based on the results of the present study, the highest rate of anomalies was respectively observed in Tuyserkan (2.4%), Hamedan (1.3%), and Nahavand (0.4%), while Kaboudarhang (0.2%) and Razan (0.2%) had the least prevalence. However, a part of the observed data on the prevalence of congenital anomalies in Hamedan encompassed the referrals from other towns due to the high frequency of high-risk pregnancy referrals to the provincial capital. The prevalence of congenital anomalies was 0.85% (8.5 per 1,000 live births) in the present study. According to various studies over Iran and other countries, there has been different statistics (1% - 10%) on the prevalence of congenital anomalies. Such cities as Zanjan had the highest prevalence (5.5%) while Arak was least prevalent (0.82%) in Iran. Amongst foreign countries, Uganda was reported to have the highest rate of congenital anomalies (7.6%) in the world (23). The contradictory statistics on the prevalence of congenital anomalies in Iran over other countries may contribute to the genetic, racial, cultural, social and economic differences as well as diverse neonatal assessment methods and distinct types of anomalies. It should be noted, however, that some studies have only targeted observable anomalies. In addition to the distinctive characteristics (live or dead births) of the intended statistical population in each study, the use of different diagnostic methods is conducive to the emergence of different findings.

The most common congenital anomaly was related to the genitourinary system (40%), with hypospadias ranking first, while musculoskeletal system (25.2%) scored second, with clubfoot as highly prevalent amongst the observed anomalies. Khoshhal-Rahdar *et al.* (24) and Alijahan *et al.* (25) found musculoskeletal anomalies as the most common congenital defects. In the Hosseini *et al.* (26) study,

anomalies of eye, ear and face ranked first followed by nervous system disorders. According to Jalali *et al.* (23), the most and the least prevalent congenital anomalies were respectively linked to musculoskeletal and genitourinary abnormalities. The contrasting rate of prevalence reported by various studies may be attributed to the significant role of underlying factors in disease development and the basis for the diagnostic methods of congenital anomalies since most inherited defects are mainly recognized on the basis of clinical examinations. Despite precise initial physical examinations by pediatricians, some congenital anomalies were not initially diagnosed due to their specific nature (unobservable at birth) while other defects required radiography and echocardiography.

Considering the relationship between the occurrence of congenital anomalies and the potential risk factors, the most significant risk factors affecting congenital anomalies were recognized to be consanguineous marriage, concomitant use of contraceptive methods, emergency C-section delivery, and male-sex ratio in the present study. Moreover, congenital anomalies were highly observable in male than female newborns, which was consistent with findings of Mohammadzadeh *et al.* (27), Shokouhi and Mani Kashani (28), and Gosalipour *et al.* (29). The prevalence of anomalies in male newborns may be due to the fact that female births undergo more lethal congenital anomalies and are less likely to survive than the male infants (30).

The present findings showed that the risk of malformed births was 4.5 times higher in parents with consanguineous marriage, with the third-degree marriages (92.5%) ranking first. Alijahan *et al.* (25) and Kushaki and Zeyghami (31) indicated that parental consanguinity significantly surged the risk of abnormal births to respectively 2.3 and 8.7 time more than other factors. The prevalence of consanguineous marriage ranges from 17 to 31 percent in Iran (31), the differing range of which may contribute to its diverse frequency in different districts of Iran.

Moreover, emergency C-section delivery was the most common risk factor for congenital anomalies amongst various types of delivery. Nevertheless, since the presence of a potential congenital abnormality may necessitate an emergency C-section, they present more association than vaginal delivery; this is in line with the findings of Sarkar *et al.* (30).

The significant relationship between hormonal contraceptive methods and the risk of congenital anomalies in the intended newborns highlights the importance of healthy fertility care.

Since such variables as parental age, parental occupation and place of residence (city or town) did not significantly correlated with congenital anomalies, they were not

Table 1. Comparison of Risk Factors for Congenital Anomalies in the Intended Newborns^a

Variable	Case Group	Control Group	P Value
Mean neonatal weight, gr	2800	2900	0.68
Mean maternal age	28.6	28.5	0.89
Mean paternal age	32.1	32.8	0.75
Maternal occupation			0.99
Employed	9 (6.7)	9 (7.4)	
Housewife	126 (93.3)	125 (92.6)	
Paternal occupation			0.09
Employed	28 (20.7)	18 (13.3)	
Self-employed	68 (50.4)	87 (64.4)	
Worker	38 (28.1)	29 (21.5)	
Unemployed	1 (0.7)	1 (0.7)	
Place of residence			0.99
City	84 (62.2)	85 (62.9)	
Town	51 (37.7)	50 (37.1)	
Acute maternal disease			0.18
Yes	10 (7.4)	3 (2.2)	
No	51 (37.7)	132 (97.8)	
Consanguineous marriage	10 (7.4)	6 (4.4)	0.001
3rd-degree	25 (18.5)	3 (2.2)	
4th-degree	1 (0.7)	1 (0.7)	
5th-degree	1 (0.7)	2 (1.4)	
Maternal drug intake			0.3
Yes			
A. Folic acid	112 (83)	116 (85.9)	
B. Other drugs	7 (5.2)	2 (1.5)	
No	16 (11.9)	17 (12.6)	
History of pregnancy problems	6 (4.4)	1 (0.7)	0.12
Oligohydramnios	1 (0.7)	0 (0.0)	
Myoma	2 (1.5)	0 (0.0)	
Intrauterine death	1 (0.7)	0 (0.0)	
Frequent abortion	2 (1.5)	1 (0.7)	
Radiography during pregnancy	1 (0.7)	1 (0.7)	0.99
Preterm delivery	37.9	38.3	0.15
Hormonal contraception	6 (4.4)	0 (0.0)	0.03
Use of contraceptive methods	1 (0.7)	2 (1.4)	0.99
Maternal surgery during pregnancy	2 (1.4)	0 (0.0)	0.06
Stressful pregnancy	4 (3)	0 (0.0)	0.14
Exposure to chemicals	1 (0.7)	6 (4.4)	0.14
Family medical history of congenital anomalies	10 (7.4)	5 (3.7)	0.28
Type of delivery			0.008
Vaginal	54 (40)	59 (43.7)	
Assisted vaginal	1 (0.7)	0 (0)	
Elective C-section	26 (19.3)	43 (31.9)	
Emergency C-section	54 (40)	33 (24.4)	
Neonatal Disorders			
Nutritional problems	20 (14.8)	5 (3.7)	0.002
Respiratory distress	4 (10.4)	1 (0.7)	0.001
Sex^b			0.02
Female	42 (31)	7739 (48.7)	
Male	93 (69)	8162 (51.3)	

^aValues are expressed as No. (%).^bAll births.

Table 2. Prevalence of Anomalies in the Intended Newborns

Anomalies	No. (%)	Type of Anomaly, No. (%)
Genitourinary system	54 (40)	Hypospadias: 20 (14.8); undescended testis: 15 (11.1); hydronephrosis: 7 (5.2); kidney dysgenesis: 5 (3.7); epispadias: 2 (1.5); polycystic kidney: 1 (0.7); renal octopi: 1 (0.7)
Musculoskeletal	34 (25.2)	Clubfoot: 21 (15.6); polydactyly: 5 (3.7); limb shortness: 5 (3.7); syndactyly: 3 (2.2)
Eye, ear and neck	25 (18.5)	Cleft lip: 13 (9.6); cleft palate: 3 (2.2); anophthalmia: 2 (1.5); microphthalmia: 2 (1.5); hypertelorism: 1 (0.7); other: 4 (3)
Chromosomal disorders	8 (5.9)	Down syndrome: 5 (3.7); trisomy 13: 1 (0.7); other: 2 (1.5)
Respiratory tract	5 (3.7)	Diaphragmatic hernia: 2 (1.5); other: 3 (2.2)
Cardiovascular system	3 (2.2)	Transposition of great vessels: 1 (0.7); other: 2 (51.5)
Skin	0 (0)	

recognized as risk factors for anomalies. Parental age, however, was considered as an identified agent for fetal chromosomal disorders; accordingly, most birth cases with Down's syndrome were prenatally aborted through early diagnostic screening during pregnancy and those born with Down's syndrome constitute only a little percentage of abnormal cases. This is why maternal age was not found to be a potential risk factor for congenital anomalies.

According to the findings of the present study, such risk factors as acute maternal disease (7.4% vs. 3.3%), maternal drug intake (5.2% vs. 1.5%), family medical history of congenital anomalies (7.4% vs. 3.7%), history of pregnancy problems (3.4% vs. 0.7%) and stressful pregnancy (3% vs. 0%) were apparently observed while insignificantly different, in abnormal births.

Besides, nutritional problems and respiratory distress were most common in the abnormal group that can be assignable to congenital anomalies.

5.1. Conclusions

The results of the present study identified various types and prevalence of congenital anomalies in Hamedan province. Regular prenatal examination and early diagnosis are recommended for prevention, early intervention and scheduled termination of pregnancy. Besides, public awareness of the disadvantages of consanguineous marriage and other pertaining risk factors affecting the incidence of congenital anomalies is also recommended.

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Footnotes

Authors' Contribution: Conception and design: Iraj Sedighi and Shahla Nouri; analysis and interpretation, and data collection: Mahta Sangestani, Younes Mohamamdi, Jalaleddin Amiri, and Behjat Qazanfarzadeh; writing the article: Iraj Sedighi, Shahla Nouri, and Mohammad Kazem Sabzehei; critical revision of the article: Iraj Sedighi and Shahla Nouri; All authors read and approved the content of the manuscript.

Conflict of Interests: There is not any conflict of interests.

Ethical Approval: The present study was conducted once approved under the reference number 9505192938 by the Ethics Committee of Hamadan University of Medical Sciences. Moreover, all parents consented to complete the questionnaires once they were assured of the confidentiality of the provided information.

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