



## Original Article

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## Maternal Risk Factors Associated with Congenital Abnormalities in Infants Born in Yazd from 2018 to 2021

Sedigheh Ekraminasab<sup>1,2</sup>, Elahe Dadbinpour<sup>3</sup>, Shiva Rafati<sup>3</sup>, Ali Dadbinpour<sup>4,5</sup>,  
Fatemeh Ghasemi<sup>6</sup>, Mahta Mazaheri<sup>1,4\*</sup>

<sup>1</sup> Mother and Newborn Health Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>2</sup> Department of Hematology and Blood Banking, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>3</sup> Department of Medical Ethics and Pediatrics, Faculty of Medicine, Shahed University, Tehran, Iran

<sup>4</sup> Department of Medical Genetics, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>5</sup> Genetic and Environmental Adventures Research Center, School of Abarkouh Paramedicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>6</sup> Department of Midwifery, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

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#### Corresponding author:

Mahta Mazaheri

#### Email:

mazaheri54@yahoo.com

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### ABSTRACT

**Background:** Maternal factors like age, existing medical conditions, and exposure to medications/substances during pregnancy are crucial in the development of congenital anomalies. This study aims to investigate maternal risk factors associated with congenital anomalies in newborns in Yazd from 2018 to 2021.

**Methods:** This particular research entails a cross-sectional descriptive analysis where the data concerning all live births and their respective mothers from the years 2018 to 2021 in the hospitals situated in Yazd were culled from the database of the National Mother and Newborn Health Registration System affiliated with Shahid Sadoughi University of Medical Sciences.

**Results:** Over four years, approximately 122,098 mothers' information was recorded in the mother's information registration system. The outcomes about social factors indicated that 1.3% of mothers with limited educational background and 0.62% of educated mothers had newborns with abnormal conditions. The heightened occurrence of newborns with congenital anomalies among mothers with lower educational attainment in comparison to their educated counterparts was deemed statistically significant ( $P < 0.001$ ). Moreover, mothers under the age of 19 exhibited a 1.2% frequency of abnormalities, a rate significantly surpassing that of other age brackets.

**Conclusion:** The discernment that very young mothers and those with limited education exhibit a higher frequency of abnormalities underscores the necessity for enhanced medical attention and awareness within these specific demographic segments. Nevertheless, further comprehensive inquiries regarding risk factors among mothers and high-risk cohorts are imperative.

## Introduction

Congenital anomalies in newborns present a significant global public health concern. The World Health Organization (WHO) has documented that an estimated 303,000 infants globally succumb to congenital anomalies within the first 30 days of life annually.<sup>1</sup> In Iran, studies have shown that the overall incidence of anomalies is 2.6%,<sup>2</sup> and in Yazd, the prevalence of congenital anomalies is 0.88%.<sup>3</sup> Various studies have explored maternal risk factors associated with the occurrence of congenital anomalies in infants.<sup>4</sup> Environmental influences, such as maternal infections, advanced maternal age, maternal use of certain medications during crucial stages of embryonic development, as well as substances like caffeine, nicotine, and commonly prescribed drugs, along with maternal nutritional and health status, exposure to harmful substances, and maternal alcohol consumption in early pregnancy, are identified as potential contributors to congenital malformations.<sup>5,6</sup> Other research has identified a range of maternal risk factors linked to congenital anomalies, including maternal diabetes, obesity, a history of previous miscarriages, gestational hypertension, upper respiratory infections, and exposure to anti-inflammatory agents.<sup>7-10</sup> These factors have been associated with anomalies in various body systems, such as the genito-urinary system, cardiovascular system, kidneys, urinary tract, central nervous system, and musculoskeletal system.<sup>7-9</sup> Major anomalies in neonates refer to abnormalities that significantly impact their health, life expectancy, and physical or social capabilities. On the other hand, minor anomalies are characterized by having minimal to no effect on health or short- and long-term functionality.<sup>11</sup> Furthermore, parental ethnicity, socioeconomic status, and hyperthermia in early pregnancy are also recognized as potential risk factors for the development of congenital malformations.<sup>5</sup>

According to a study by Mohseni, the incidence of congenital anomalies at birth is higher among mothers aged over 40 years and under 19 years. Maternal age, as indicated by numerous studies, is indeed a crucial risk factor.<sup>2</sup> A study by Abebe et al. in southwestern Ethiopia identified risk factors like passive smoking, exposure to pesticides and chemicals, and the use of surface water in early pregnancy linked to congenital anomalies.<sup>5</sup> Shahmirzady et al. also found maternal illnesses and abnormal pregnancy history as significant factors. Understanding maternal risk factors is crucial to prevent congenital anomalies.<sup>12</sup> Feng et al. reviewed maternal lifestyle factors during pregnancy and their correlation with congenital heart defects in offspring, emphasizing the need for policymakers to focus on high-risk women and prevention strategies.<sup>13</sup> These studies enhance our knowledge of factors influencing congenital anomalies in newborns. There is a lack of information on predisposing risk factors for congenital anomalies, especially in Yazd.

An in-depth analysis of maternal socioeconomic status and its correlation with risk factors in congenital anomalies reveals a complex interplay of various components influencing infant outcomes. A key study underscores the impact of maternal education on infants with congenital malformations, highlighting the link between lower maternal education levels and adverse neonatal outcomes.<sup>14</sup> Another study identifies risk factors like passive smoking and exposure to certain substances during early pregnancy as significantly associated with congenital anomalies in infants. This underscores the importance of considering environmental factors alongside maternal socioeconomic status.<sup>5</sup> Understanding maternal risk factors is vital for preventing and managing congenital anomalies. Additionally, there is limited data on maternal risk factors related to congenital anomalies, especially in Yazd. Thus, this study examines the influence of maternal risk factors on the occurrence of congenital

anomalies in Yazd. The goal is to identify maternal risk factors connected to congenital anomalies in infants born at Yazd hospitals over four years.

## Materials and Methods

**Study design:** This cross-sectional and retrospective descriptive study aimed to investigate maternal risk factors associated with congenital anomalies in newborns in Yazd from 2018 to 2021. Data was collected from the National Mother and Newborn Health Registration System of Shahid Sadoughi University of Medical Sciences, Yazd, accessed through <https://qlik-view.health.gov.ir>. Maternal characteristics (age, parity, education) and pregnancy details (gestational age, delivery method) were extracted from an Excel file and structured.

**Study population:** The study population included mothers of newborns delivered in Yazd province hospitals from 2018 to 2021. Data was collected through a standardized questionnaire and entered into the system by skilled professionals. Participants with incomplete information were excluded. Over four years, data from about 122,098 mothers was documented in the maternal information registration system.

**Statistical analysis:** To perform statistical analysis on the data, the study information was entered into the statistical software SPSS version 21. Frequency and percentage were employed for presenting qualitative data, whereas mean  $\pm$  standard deviation was utilized for quantitative data. The comparison of qualitative variables was conducted using the Chi-square test.

## Results

**Maternal risk factors:** The distribution of congenital anomalies concerning both age range and maternal education level is shown in Table 1. The majority of mothers, about 53.9%, were aged between 25 and 35 years. In contrast, the smallest group was mothers under 19, accounting for around 6585 individuals (5.6%). Moreover, mothers aged 35 and above made up 23828 individuals (20.1%) in the study. An examination of the data indicated a significant increase in congenital anomalies among mothers under 19 compared to other age groups ( $p < 0.05$ ), with 1.2% of mothers in this category having such anomalies. Following this, mothers aged 20 to 24 had the second-highest prevalence of congenital anomalies at 0.93%. Lastly, mothers aged 35 and over exhibited the third-highest prevalence of congenital anomalies at 0.86%.

Table 1. Socio-Demographic Characteristics of the Study Subjects

	Congenital anomalies (n ≈937) Frequency (%)	Total (n ≈122098) Frequency (%)	P
Mothers' Education	n≈ 936	n≈ 118237	
Low-educated (Illiterate, primary)	370 (1.3)	28912 (24.45)	< 0.001
Educated (High school, university)	555 (0.62)	88951 (75.23)	
No response	11 (3)	374 (0.32)	
Mothers Age (year)	n≈978	n≈ 118235	
<19	79 (1.2)	6585 (5.6)	< 0.05
20-24	223 (0.93)	24090 (20.4)	
25-29	234 (0.74)	31705 (26.8)	
30-34	236 (0.74)	32027 (27.1)	
>35	206 (0.86)	23828 (20.1)	
Mode of delivery	n ≈937	n ≈122098	
Vaginal	348 (0.58)	59940 (49.1)	< 0.001
Cesarian	589 (0.95)	62158 (50.9)	

**Table 2.** Frequency of Pregnancy Risk Factors in Neonates with Abnormality and Total Population

Maternal risk factors	Mothers with complication (n = 122098)	Mothers with Newborns with Congenital Anomalies (n= 937)
Labor Pain	31050 (25.43)	236 (25.2)
Thyroid dysfunction	20580 (16.85)	145 (15.5)
Gestational diabetes	13243 (10.84)	114 (12.2)
Episiotomy	12721 (10.41)	105 (11.2)
Preterm birth	2327 (1.9)	92 (9.8)
Stained with meconium	5299 (4.33)	66 (7)
Abnormal fetal heart rate	2832 (2.32)	57 (6)
Pre-eclampsia and eclampsia	1834 (1.5)	26 (2.8)
Neurological and mental diseases	1097 (0.9)	22 (2.3)
Maternal hypertension	1866 (1.52)	16 (1.7)
Previous Diabetes	596 (0.5)	10 (1)
Hepatitis B	371 (0.3)	3 (0.32)

Among maternal participants, around 24.45% had limited educational attainment, such as primary education levels or being illiterate. Additionally, 75.23% of the mothers had higher education, like high school or university degrees, while 3% did not respond. In the group of educated mothers, the rate of congenital anomalies was 0.62%, whereas among mothers with lower education levels, it was higher at 1.3%, showing a significant difference between the two groups. The higher occurrence of congenital anomalies among mothers with limited education compared to those with higher educational backgrounds was statistically significant ( $p < 0.001$ ). We also evaluated the delivery method in our research. 49.1% of mothers chose vaginal childbirth, while 50.9% had a cesarean section. We discovered that the occurrence of congenital anomalies was 0.95 for cesarean section births and 0.58 for vaginal deliveries. Additionally, we observed a significantly higher prevalence of congenital anomalies among mothers who underwent a cesarean section compared to those who had a vaginal delivery ( $p < 0.001$ ).

**History of risk factors in mothers:** The frequency of maternal pregnancy risk factors in neonates with congenital anomalies delivered at hospitals in Yazd is detailed in Table 2. An investigation spanning from 2018 to 2021 analyzed the pregnancy and childbirth risk factors. Out of 122,098 individuals, 937 ( $\approx 0.77\%$ ) had congenital anomalies. The

primary issues in the group with abnormalities were compared with the general population. Key pregnancy risk factors included inducing or augmenting labor pain, thyroid irregularities, gestational diabetes, episiotomy, and premature delivery. The prevalence of inducing or augmenting labor pain was 25.43% in the total population and 25.2% in the abnormal cohort, showing no significant difference. Thyroid dysfunction was lower in the abnormal group at 15.5% compared to the total population (16.85%). However, other pregnancy risk factors were more prevalent in the abnormal cohort. Gestational diabetes and episiotomy rates were 12.2% and 11.2% respectively, in the abnormal group, higher than the general population's rates of around 10%. The most significant contrast was in the prevalence of premature birth, with 9.8% in the abnormal group and 1.9% in the general population, indicating a fivefold higher likelihood of preterm birth in mothers with anomalous neonates. Additionally, abnormal fetal heart rate prevalence was 6% in the abnormal group and 2.3% in the overall population.

## Discussion

The examination of maternal risk factors associated with congenital anomalies is crucial in understanding the occurrence of birth defects in neonates. Numerous studies have explored this area, shedding light on various factors that can affect the prevalence

and types of congenital anomalies observed in newborns. A study by Zhang et al. focused on the impact of China's two-child policy on maternal age and the prevalence of congenital anomalies, revealing a notable increase in both. This suggests the need for updated healthcare approaches to address these changes.<sup>15</sup> Ahn et al. conducted a systematic review and meta-analysis, quantifying the correlation between maternal age and susceptibility to birth defects, highlighting the heightened vulnerability in the offspring of middle-aged mothers.<sup>16</sup> Goetzinger et al. examined the connection between advanced maternal age and the risk of significant congenital anomalies, proposing an "all or nothing" phenomenon in embryonic development.<sup>17</sup> Furthermore, Aslam et al. investigated the frequency of various congenital anomalies and identified consanguineous marriage as a prevalent maternal risk factor.<sup>18</sup> These studies collectively enhance our understanding of the intricate relationship between maternal risk factors and congenital anomalies, emphasizing the necessity for tailored interventions and healthcare strategies to mitigate the consequences on neonatal well-being. Previous research in Yazd hospitals explored the frequency and types of congenital anomalies, with the cardiovascular system being the most prevalent, followed by musculoskeletal, gastrointestinal, and genital system anomalies.<sup>3</sup> Additionally, studies on prenatal screening and the positive predictive value of screening tests in expectant women in Yazd were conducted, including an analysis of maternal risk factors in the manifestation of abnormalities.<sup>19,20</sup>

The results of our investigation indicated a higher prevalence of preterm birth, gestational diabetes, neurological issues, and high blood pressure among mothers of neonates with abnormalities. Previous research has demonstrated the importance of considering both maternal and fetal risk factors, such as parental consanguinity, a positive family history of anomalies, malnutrition, low birth

weight, prematurity, and maternal obesity, which were significantly correlated with an increased occurrence of congenital anomalies.<sup>21,22</sup> Based on our study's findings, maternal age below 19 and limited maternal education were identified as factors contributing to the elevated risk of congenital anomalies in neonates. Common maternal risk elements outlined in existing literature encompass consanguineous unions, medication usage, maternal age, alcohol consumption, smoking, and maternal health conditions.<sup>23</sup> Maternal age is also a contributing factor to the likelihood of specific chromosomal abnormalities like Down syndrome.<sup>24</sup> Our research findings also suggest that extreme maternal age, very young (under 19), may correlate with an escalated probability of congenital anomalies in neonates. A study by Khan A. et al. revealed a higher incidence of anomalies among neonates born to mothers aged 26-30 years.<sup>25</sup>

Maternal diabetes represents a critical risk factor associated with congenital anomalies. Several studies have explored the repercussions of pregnancy on gestational diabetes mellitus (GDM) and pregestational diabetes mellitus (PGDM) on birth defects and adverse health outcomes for both the mother and the offspring. The literature has demonstrated that gestational diabetes mellitus is linked to unfavorable pregnancy results, underscoring the necessity for a more comprehensive assessment of prognostic indicators to precisely evaluate risks.<sup>26</sup> Additionally, scholarly investigations have revealed that maternal diabetes, encompassing PGDM and GDM, heightens the likelihood of significant congenital deformities.<sup>27</sup> Particularly, individuals with pregestational diabetes mellitus face the highest susceptibility to fetal congenital anomalies.<sup>28</sup> Some evidence also suggests a marginally elevated risk of major congenital malformations in women with GDM compared to the general population.<sup>29</sup> Furthermore, scholarly works have illuminated the connection between maternal

diabetes and specific birth abnormalities, such as congenital heart defects. Previous studies examined the frequency and risk factors related to gestational diabetes among women in Yazd.<sup>29</sup> Furthermore, it was observed that the prevalence of congenital heart diseases (CHD) and hypertrophic cardiomyopathy (HCM) was more pronounced in the offspring of diabetic mothers compared to nondiabetic counterparts in Yazd.<sup>30,31</sup> Similarly, another study underscored the significance of maternal glycemic regulation in achieving favorable pregnancy results and reducing the occurrence of birth anomalies in women with pregestational diabetes mellitus.<sup>32</sup> Moreover, findings suggest that documented links between GDM and birth defects might, to some extent, stem from undiagnosed metabolic disorders linked to obesity, highlighting the complex interplay between metabolic conditions and pregnancy outcomes.<sup>33</sup> The body of research emphasizes the substantial influence of maternal diabetes, whether pregestational or gestational, on the probability of congenital anomalies. Effective diabetes management in expectant women is paramount for alleviating these risks and ensuring enhanced maternal and neonatal health outcomes. This highlights the significant impact of maternal socioeconomic status on infant health results. Together, these researches show the vital role of maternal socioeconomic status in influencing the risk factors and outcomes related to congenital anomalies in newborns.

### Conclusion

Understanding maternal risk factors associated with congenital anomalies is essential for developing targeted interventions and strategies to reduce the incidence of these birth defects. It is crucial to address disparities and provide support to mothers from diverse backgrounds to improve infant health outcomes. Future research should explore the relationship between maternal factors and different anomaly types to enhance prenatal care for high-risk

populations. However, our study was limited by insufficient participant responses to the maternal and neonatal survey, resulting in a lack of maternal-related data. Larger studies are needed to fully understand the impact of maternal risk factors on congenital anomalies. By overcoming this limitation, we can offer more comprehensive information to guide public health policies and interventions aimed at reducing the burden of birth defects. Collaboration among healthcare providers, researchers, and policymakers is vital to ensure all mothers receive the necessary support for healthy pregnancies and babies.

### Conflict of Interest

The authors declare no conflicts of interest.

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### Ethical Considerations

The present study was approved by Shahed University Ethics Committee (IR.SHAHED.REC.1400.223).

### Author's Contribution

Conceptualization, S.R., M.M. and A.D.; methodology, S.E. and M.M.; formal analysis, E.D. and S.R.; investigation, E.D., A.D., S.R. and F.G.; resources, E.D. and F.G.; data curation, E.D. and S.E.; writing-original draft preparation, S.E.; writing- review and editing, S.R., M.M. and A.D.; supervision, M.M. and S.E. All authors have read and agreed to the published version of the manuscript.

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