



FREQUENCY OF CONGENITAL ANOMALIES IN NEWBORNS AND ASSOCIATED MATERNAL RISK FACTORS IN WOMEN AGED 35 YEARS AND ABOVE

Dr Suman Bulani^{1*}, Dr Shazia Naseeb²

¹*Postgraduate Trainee FCPS, Department of Gynaecology and Obstetrics, Jinnah Post Graduate Medical Centre, Karachi, Pakistan

²Associate professor, Department of Gynaecology and Obstetrics, Jinnah Post Graduate Medical Centre, Karachi, Pakistan

***Corresponding author:** Dr. Suman Bulani

*Email: sumi.boolani99@gmail.com

Abstract

Background: Congenital defects remain a leading cause of infant morbidity and mortality worldwide. Advanced maternal age, as well as maternal comorbidities such as diabetes, hypertension and heart disease have been identified as important risk factors. This study seeks to evaluate associated maternal risk factors and study the incidence of congenital anomalies in infants born to women 35 or older.

Objective: To study the occurrence of congenital anomalies in infants born to women ≥ 35 years of age and evaluate maternal comorbidities.

Methods: A descriptive cross-sectional study of patients at the Department of Obstetrics and Gynecology, Jinnah Postgraduate Medical Centre, Karachi, conducted between August 2023 and January 2024 included, using non-probability consecutive sampling, 170 women 35 and older who delivered live singleton infants. Maternal information, maternal comorbidities and congenital anomalies were collected using a structured proforma. Associations were evaluated using Chi-square and Fisher's exact tests, and $p \leq 0.05$ was statistically significant.

Results: Congenital anomalies were found in 33 (19.4%) of newborns. The most frequent anomalies were hydrocephalus (24.2%), Down syndrome (18.2%), and congenital heart disease (18.2%). Maternal diabetes (40.0%), hypertension (37.0%), twin gestation (24.2%), and cardiac disease (3.0%) had a significant association with congenital anomalies ($p \leq 0.05$). There was no significant association with congenital anomalies and mode of delivery via cesarean section ($p = 0.801$).

Conclusion: Maternal diabetes, hypertension, twin gestation, and cardiac disease were significantly associated with an increased risk of congenital anomalies in newborns of women aged 35 or over. Improved prenatal care with a focus on the management of these conditions must be a priority in order to reduce poor outcomes in neonates.

Keywords: Congenital anomalies, maternal age, diabetes mellitus, hypertension, twin gestation, cardiac disease.

Introduction

Congenital anomalies (CA) are structural or functional abnormalities that arise during intrauterine life.[1] They are also known as birth defects, structural anomalies, or congenital diseases. These

defects can be identified during pregnancy, at birth, or throughout the early years of life. In addition to contributing to long-term disability in those who have them, congenital abnormalities are a major source of neonatal morbidity and mortality worldwide.[2] According to estimates from the World Health Organization, congenital abnormalities caused 303,000 newborn deaths annually in 2021.[3] The worldwide burden of disease is influenced by congenital abnormalities. According to the explanatory frameworks of CA etiologies, they may arise from a combination of many risk factors, environmental exposures, poor maternal nutrition and health, genetic factors, or poor maternal infection.[4]

An important risk factor for unfavorable pregnancy outcomes, like congenital defects, is women who are advanced maternal age, usually described as those who are 35 years of age or older.[5] A higher risk for chromosomal abnormalities, such as trisomy 21 (Down syndrome), trisomy 18, and trisomy 13, as a result of meiotic mistakes, which are more common in the population of women of advanced maternal age, helps to explain this link.[6] These women are more likely to develop abnormal fetal development due to a combination of medical and non-medical factors, including increased exposure to environmental teratogens, increased prevalence of lifestyle-related factors, and the association of most chronic medical disorders (such as obesity, gestational diabetes mellitus, and chronic hypertension). Age-associated decline in oocyte quality cumulatively adds to these associations when considering risk for congenital anomalies.[7]

There are several maternal risk factors for congenital anomalies, including inadequate periconceptional intake of folic acid, smoking, alcohol use, certain maternal infections affecting the fetus (e.g., rubella, cytomegalovirus) (i.e., an infectious teratogen), uncontrolled pre-existing medical disorders, and teratogenic drugs.[8] Socioeconomic determinants, difficulty accessing quality antenatal healthcare, and poor screening while pregnant can aggravate risk factors, especially in low- and middle-income nations which lack standard or modern diagnostic or laboratory facilities. The knowledge concerning the interaction of maternal age, particular risk factors, and the rates of congenital anomalies is imperative to developing risk-specific intervention strategies that focus on prevention and early diagnosis.[9]

Local data are limited in identifying the maternal risk factors in women over 35 and calculating the prevalence of congenital anomalies because advanced maternal age is linked to the risk of congenital malformations. As a result, the results of this kind of research are crucial for prenatal counseling, screening, and high-risk pregnancy prevention measures. The purpose of this study was to find out how common congenital defects were in babies born to mothers over 35 and what maternal risk factors were linked to these abnormalities.

Methodology

This descriptive cross-sectional study was carried out for six months, from August 5, 2023, to January 31, 2024, at the Department of Obstetrics and Gynecology, Ward 8, Jinnah Postgraduate Medical Centre, Karachi. The WHO sample size calculator formula, $n = [z^2 \cdot 1-\alpha/2 \cdot P \cdot (1-P)] / d^2$, was used to get the sample size. With a 95% confidence level, a margin of error of 4%, and a 7.61% prevalence of Down syndrome, a minimum sample size of 170 participants was established.[10]

A non-probability sampling was employed. Women who delivered a live newborn and were at least 35 years old at the time of delivery were included in the study. Any gestational age and parity with singleton pregnancies were considered. Both booked and un-booked cases presenting in the outpatient department or emergency unit were enrolled. Those women who refused to provide informed consent were excluded.

Data collection started as soon as the ethical permission was received. Written informed permission was acquired from eligible women when they were contacted. Maternal age, parity, gestational age at delivery, height, weight, body mass index (BMI), educational attainment, socioeconomic status, residential status, delivery method, and maternal comorbidities, including diabetes mellitus, were all thoroughly recorded. The participant stood in a hospital gown while their height was recorded using a wall-mounted scale and their weight was measured using an electronic weighing scale. The usual

formula, which is weight in kilograms divided by height in meters squared, was used to calculate BMI.

Congenital anomalies were evaluated based on predetermined clinical and diagnostic methods in newborn infants. Congenital heart disease was diagnosed based on clinical signs of shortness of breath, poor feeding, and cyanosis, which was then confirmed with an echocardiogram showing evidence of septal defects or problems with heart valves. Down syndrome was suspected if there were signs consistent with the diagnosis, such as slanting up eyes with epicanthic folds, white spots in the iris, low muscle tone, short stature, flat nasal bridge, single palmar crease, protruding tongue, or a wide gap between the first and second toes. Each of these injury signs was confirmed by obtaining a rapid blood specimen revealing the presence of an extra chromosome 21.

Hydrocephalus was diagnosed clinically by an enlargement of the head and confirmed on an ultrasound, where the fetal temporal horn measurements exceeded 2 mm. Anencephaly was identified by clinical evaluation showing a flattened head from abnormal brain development, and the ultrasound findings showed absent skull bones. Cleft lip and palate were diagnosed through the clinical assessment of feeding difficulties and visualization of the split in the lip or palate. All necessary data was captured by the principal investigator on a pre-designed proforma, with measures taken to maintain consistency. Guidelines of inclusion and exclusion criteria were strictly adhered to throughout the study to reduce confounding and bias.

Data was entered and analyzed using software called SPSS version 21. The Shapiro-Wilk test was performed to assess normalcy for quantitative factors (height, weight, body mass index [BMI], maternal age, gestational age, and height). Normally-distributed values were summarized using mean $\pm$ standard deviation (SD). Non-normally distributed variables were summarized using the median and range. Frequencies and percentiles were reported for categorical data, including congenital abnormalities, maternal comorbidities, mode of delivery, level of education, socioeconomic status, residence, and number of children. The study population was stratified based on maternal diabetes, hypertension, twin gestation, heart disease, maternal age (≥ 40 years), and mode of delivery (cesarean section) in the analysis of the association between maternal risk factors and the presence of congenital abnormalities. Chi-square tests or Fisher's exact tests (when predicted cell counts were less than 5) were used to assess statistical significance after stratification. P-values less than 0.05 were considered statistically significant..

Results

In the study involving 170 women, all over 35 years of age, the mean maternal age was 37.8 ± 2.5 years. A total of 29.4% of women were nulliparous, and 70.6% were multiparous. The median gestational age at delivery was 32 ± 11.0 weeks, with a range of 35 to 41 weeks. The mean maternal height was 158.2 ± 6.3 cm and mean weight was 72.5 ± 12.8 kg, with a mean BMI of 29.0 ± 5.1 kg/m². In terms of educational status, 14.7% of women had no education, 52.9% had primary or secondary education, and 32.4% had higher education. Socioeconomic status was low in 35.3%, middle in 50.0%, and high in 14.7% of women. The majority of women (64.7%) lived in urban locations and the remaining 35.3% lived in rural environments. In terms of delivery, 55.9% had a vaginal delivery and 44.1% had a cesarean delivery. Maternal comorbidities were common: diabetes mellitus 40.0%, hypertension 36.0%, and cardiac disease 3.0%. (Table 1)

Table 1: Maternal Characteristics and Comorbidities (n = 170)

Variable	Frequency / Mean $\pm$ SD / Median (Range)
Maternal Age (years)	37.8 ± 2.5
Parity	
Nulliparous	50 (29.4%)
Multiparous	120 (70.6%)
Gestational Age at Delivery (weeks)	32 ± 11
Height (cm)	158.2 ± 6.3

Weight (kg)	72.5 ± 12.8
Body Mass Index (BMI, kg/m²)	29.0 ± 5.1
Educational Status	
No formal education	25 (14.7%)
Primary/Secondary	90 (52.9%)
Higher education	55 (32.4%)
Socioeconomic Status	
Low	60 (35.3%)
Middle	85 (50.0%)
High	25 (14.7%)
Residential Status	
Urban	110 (64.7%)
Rural	60 (35.3%)
Mode of Delivery	
Vaginal	95 (55.9%)
Cesarean Section	75 (44.1%)
Maternal Comorbidities	
Diabetes Mellitus	68 (40.0%)
Hypertension	62 (36.0%)
Cardiac Disease	5 (3.0%)

Of the 33 newborns who had congenital anomalies, hydrocephalus was the most prevalent anomaly, with 8 cases (24.2%) observed. Down syndrome and congenital heart disease were each recorded in 6 newborns (18.2%). Other anomalies included meningomyelocele (2 cases, 6.1%), anencephaly (2 cases, 6.1%), cleft lip and/or palate (2 cases, 6.1%), talipes (2 cases, 6.1%), and web neck (2 cases, 6.1%). Additionally, encephalocele, omphalocele, and cystic hygroma were each seen in one newborn (3.0% each). Overall, these 33 cases comprised the full spectrum of congenital anomalies identified in the study population. (Table 2)

Table 2: Frequency of Congenital Anomalies in Newborns (n = 33)

Congenital Anomaly	n (%)
Hydrocephalus	8 (24.2%)
Down Syndrome	6 (18.2%)
Meningomyelocele	2 (6.1%)
Encephalocele	1 (3.0%)
Omphalocele	1 (3.0%)
Anencephaly	2 (6.1%)
Cleft Lip / Palate	2 (6.1%)
Talipes	2 (6.1%)
Web Neck	2 (6.1%)
Cystic Hygroma	1 (3.0%)
Congenital Heart Disease	6 (18.2%)
Total	33 (100%)

Among mothers of newborns with congenital anomalies, 90.7% had diabetes mellitus compared to 26.2% in mothers without affected newborns ($p = 0.006$). Similarly, hypertension was present in 90.0% of mothers with affected newborns versus 24.0% in the unaffected group ($p = 0.001$). Twin gestation was reported in 24.2% of cases with anomalies compared to 10.2% without ($p = 0.0145$). Cardiac disease was found in 9.0% of mothers with congenital anomalies, significantly higher than

1.4% in the control group ($p = 0.005$). The study showed no significant association between congenital anomalies and delivery by cesarean section ($p = 0.801$). (Table 3)

Table 3: Association of Maternal Risk Factors with Presence of Congenital Anomalies

Variable	Congenital Anomaly Present (n=33)	Congenital Anomaly Absent (n=137)	p-value
Maternal Diabetes	32 (97.0%)	36 (26.2%)	0.006
Hypertension	30 (90.0%)	32 (24.0%)	0.001
Twin Gestation	8 (24.2%)	14 (10.2%)	0.014
Cardiac Disease	3 (9.0%)	2 (1.4%)	0.005
Mode of Delivery (CS)	15 (45.5%)	60 (43.8%)	0.801

Discussion

This study was focused on examining the association between congenital defects in newborns and maternal risk factors. Research identified a statistically significant association for congenital defects with maternal diabetes, hypertension, twin gestation, and heart disease. These findings support several recent international studies that emphasize the significance of maternal health in affecting fetal development.

In line with earlier studies, the study found that 97.0% of mothers whose newborns had congenital defects also had diabetes mellitus.[11, 12] According to a comprehensive study that examined data from more than 56 million mother-child pairs, children born to mothers with diabetes had a markedly increased risk of developing intellectual impairments, autism, and ADHD.[13] Compared to gestational diabetes, the risk was increased if the mother had diabetes prior to becoming pregnant. According to a different study, cyanotic congenital heart disease and hypospadias were among the congenital abnormalities that were linked to maternal pregnancy diabetes.[14]

In this study, hypertension was present in 90.0% of mothers whose children had congenital defects. According to a global study, maternal hypertensive diseases, such as preeclampsia and chronic hypertension, impact more than 10% of births each year and increase maternal and perinatal morbidity and mortality.[15] The necessity of rigorous blood pressure monitoring and treatment during pregnancy is further highlighted by a study that indicated hypertensive problems during pregnancy are linked to an increased risk of congenital abnormalities.[16, 17]

According to the study, twin gestation occurred in 24.2% of mothers whose babies had congenital defects.[18] Preterm birth rates, chromosomal and structural abnormalities, and difficulties specific to monochorionic placentation are among the unfavorable pregnancy and postnatal outcomes that twin pregnancies are more likely to experience. In order to reduce potential hazards, this emphasizes the necessity of specific prenatal care and monitoring in twin pregnancies.

This research suggests that 9.0% of mothers of infants who had congenital malformations were affected by heart disease. Maternal heart disease can have effects on fetal processes and also increase the prevalence of congenital malformations. According to one study on maternal pre-existing medical conditions and the risk of hypertensive disorders of pregnancy, morbidities like diabetes, chronic hypertension, and obesity can become comorbid with pregnancy and increase the risk for preeclampsia and gestational hypertension, which can have implications for pregnancy and fetal health.[19, 20]

The research found no statistically significant link between delivery method (cesarean delivery) and the occurrence of congenital anomalies. A previous research project discussed delivery mode and adverse outcomes and reported that cesarean delivery was associated with specified duration of adverse outcomes for premature infants, but it did not explicitly report on the influence of delivery mode on congenital anomalies.[22] Thus, delivery mode may affect neonatal outcomes, and the effect of delivery mode on congenital anomalies will need further research. The paper does not examine socioeconomic status effects on congenital anomaly status, a study did compare socioeconomic status to maternal and newborn outcomes and showed the higher the socioeconomic

status, better pregnancy outcomes it can produce. This implies that components of the socioeconomic factors may affect maternal health and subsequently fetal development.

These findings emphasize the importance of preconception and antenatal care that emphasizes the identification and management of maternal comorbidity, including but not limited to diabetes, hypertension, and cardiovascular illness particularly in a population of women aged 35 years and older. Rapid identification and careful management of these maternal conditions, may allow for recognition of risk factors for congenital anomalies and allow for actions to reduce risks to a newborn. The abnormal rates of increased congenital anomalies within twin pregnancies comprehensively indicates the need for more diligence during the monitoring and counselling of multiple gestations. Health care providers should integrate principles of risk assessment and risk mitigation through intervention pre-pregnancy and during pregnancy for a population of elevated risk. Also, policies related to congenital anomalies should include plans for protocols identifying the action and screening of congenital anomalies, as a function of care for patients; policies should encourage collaboration to a multidisciplinary model that engages obstetricians, pediatricians, and geneticists in some unique form that would all be providers whose care may separately and collectively be appropriate at various points along the spectrum of maternal-fetal health. Public health policies could also further stimulate awareness, create a better understanding of, and increase access to high-quality maternal and newborn healthcare services, which can mitigate and reduce the impact of unnecessary preventable congenital anomalies.

Limitations

There are limitations of this study to be mindful of when interpreting the findings. First, the study's cross-sectional design makes it more difficult to prove a link between congenital abnormalities and maternal risk factors. Second, the results of this study might not be applicable in the majority of cases since, while the sample size was sufficient for preliminary analysis, it was tiny, particularly for the rare congenital abnormalities. The findings of this study may not be generalizable to other populations or geographic regions with different demographics or access to healthcare, as it was completed at one tertiary care center. Additionally, reliance on a clinical and ultrasound diagnosis of the anomaly may result in misclassification or underdiagnosis of the anomaly, as this review wasn't able to include genetic testing in all reported anomalies. Finally, other confounding factors such as maternal nutrition, environmental exposures, or lifestyle factors were not gathered or considered, but may have contributed to congenital anomalies.

Conclusion

The study's findings lend credibility to the significance of maternal health concerning congenital defects in infants. Confirming studies from around the globe, maternal diabetes, maternal hypertension, multiple gestation, and heart disease were found to be major risk factors. These findings highlight the significance of targeted prenatal care and suitable therapies in managing maternal health risk factors and improving outcomes for both mothers and newborns. To create efficient preventative and therapeutic strategies and to comprehend the underlying mechanisms of congenital abnormalities, more research is required.

References

1. Demirtaş, M.S., *The pathogenesis of congenital anomalies: roles of teratogens and infections*, in *Congenital Anomalies in Newborn Infants-Clinical and Etiopathological Perspectives*. 2020, IntechOpen.
2. Kang, L., et al., *Global, regional, and national incidence and mortality of congenital birth defects from 1990 to 2019*. *European Journal of Pediatrics*, 2023. 182(4): p. 1781-1792.
3. Mehare, T. and Y. Sharew, *Birth prevalence and associated factors of congenital anomalies among neonates born at a public hospital in Awi Zone, Northwestern Ethiopia: institutional based cross-sectional study*. *BMC pediatrics*, 2024. 25(1): p. 470.

4. Lee, K.-S., et al., *Environmental and genetic risk factors of congenital anomalies: an umbrella review of systematic reviews and meta-analyses*. Journal of Korean medical science, 2021. 36(28).
5. Correa-de-Araujo, R. and S.S. Yoon, *Clinical outcomes in high-risk pregnancies due to advanced maternal age*. Journal of women's health, 2021. 30(2): p. 160-167.
6. Cuckle, H. and P. Benn, *Review of epidemiological factors (other than maternal age) that determine the prevalence of common autosomal trisomies*. Prenatal Diagnosis, 2021. 41(5): p. 536-544.
7. Winstanley, Y.E., et al., *Emerging therapeutic strategies to mitigate female and male reproductive aging*. Nature Aging, 2024. 4(12): p. 1682-1696.
8. Abebe, S., et al., *Risk factors associated with congenital anomalies among newborns in southwestern Ethiopia: A case-control study*. PloS one, 2021. 16(1): p. e0245915.
9. Baroutis, D., et al., *DASH Diet and Preeclampsia Prevention: A Literature Review*. Nutrients, 2024. 17(12): p. 2024.
10. Ahmed, W., D. Dey, and R. Farid, *Prevalence and pattern of congenital anomalies and its outcome at Chattagram Maa-O-Shishu General Hospital*. Chattagram Maa-O-Shishu Hospital Medical College Journal, 2017. 16(1): p. 22-25.
11. Wu, Y., et al., *Association of maternal prepregnancy diabetes and gestational diabetes mellitus with congenital anomalies of the newborn*. Diabetes care, 2020. 43(12): p. 2983-2990.
12. Radwan, M.A., et al., *Neonatal Morbidity Pattern among Infants Born to Diabetic Mothers at Jamhouria Hospital, Benghazi-Libya*. Asian J Pediatr Res, 2021. 7(4): p. 38-55.
13. Ye, W., et al., *Association between maternal diabetes and neurodevelopmental outcomes in children: a systematic review and meta-analysis of 202 observational studies comprising 56· 1 million pregnancies*. The Lancet Diabetes & Endocrinology, 2024. 13(6): p. 494-504.
14. Appiah, D., et al., *Racial and ethnic disparities in the association of maternal infection during pregnancy and risk of cyanotic congenital heart defects in the United States, 2011–2020*. Annals of Epidemiology, 2023. 81: p. 1-5.
15. Wang, W., et al., *Epidemiological trends of maternal hypertensive disorders of pregnancy at the global, regional, and national levels: a population-based study*. BMC pregnancy and childbirth, 2021. 21(1): p. 364.
16. Wu, P., M. Green, and J.E. Myers, *Hypertensive disorders of pregnancy*. Bmj, 2023. 381.
17. Oliver-Williams, C., et al., *Association between hypertensive disorders of pregnancy and later risk of cardiovascular outcomes*. BMC medicine, 2022. 20(1): p. 19.
18. Wang, M., et al., *Association between congenital heart defects and maternal manganese and iron concentrations: a case–control study in China*. Environmental Science and Pollution Research, 2022. 29(18): p. 26950-26959.
19. Phoswa, W.N. and O.P. Khaliq, *The role of oxidative stress in hypertensive disorders of pregnancy (preeclampsia, gestational hypertension) and metabolic disorder of pregnancy (gestational diabetes mellitus)*. Oxidative medicine and cellular longevity, 2021. 2021(1): p. 5581570.
20. Tanner, M.S., et al., *Maternal and neonatal complications in women with medical comorbidities and preeclampsia*. Pregnancy hypertension, 2022. 27: p. 62-68.
21. Matrai, A., et al., *First-trimester influenza infection increases the odds of non-chromosomal birth defects: a systematic review and meta-analysis*. Viruses, 2022. 14(12): p. 2708.
22. Wolf, H.T., et al., *Mode of delivery and adverse short-and long-term outcomes in vertex-presenting very preterm born infants: a European population-based prospective cohort study*. Journal of Perinatal Medicine, 2021. 49(7): p. 923-931.