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Birth Order and Congenital Anomalies: A Retrospective Follow up Study

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ABSTRACT

Introduction: Congenital anomalies, a leading cause of infant morbidity and mortality, are vital areas of study in prenatal medicine to explore the relationship between congenital anomalies and birth order among antenatal mothers.

Methods: This retrospective follow-up study was conducted in a first referral hospital in Bangalore, India between July 2021 and June 2022. Data from 1,432 antenatal mothers were analyzed, focusing on socio-demographic characteristics, congenital anomalies, and birth order. Congenital anomalies were diagnosed based on established medical criteria through detailed examination of antenatal scans and medical records. Descriptive statistics with Odds ratio with 95% CI were employed to assess associations between variables.

Results: The study showed variations in the incidence of congenital anomalies with birth order, with first-borns presenting the highest incidence at 42.8%. Anomalies were predominantly observed in the maternal age group of 22–25 years (50%) and in non-consanguineous pregnancies (81%). Renal anomalies were the most prevalent, constituting 59.5% of the total anomalies.

Conclusion: The variations observed in anomaly incidences based on birth order emphasize the need for further research in this area and the development of targeted preventive strategies and interventions to mitigate the risk of congenital anomalies in different birth orders.

Keywords: Congenital anomalies, Birth order, Antenatal mothers, Renal anomalies, Retrospective study, India

INTRODUCTION

Congenital anomalies are abnormalities that occur during the development of a baby in the womb and can have a significant impact on the child's health and quality of life. They are a major cause of infant illness and death. It is estimated that at least 3.3 million children under the age of 5 years die from congenital anomalies each year worldwide, accounting for nearly 30% of neonatal mortality.¹ The prevalence of congenital anomalies is approximately 3–4% of live births globally based on registry data.² These abnormalities can appear before birth, at birth, or even later in life, and are therefore a critical area of study in child health research.

In India, congenital anomalies affect approximately 69.9 per 10,000 live births, amounting to over 1.7 million cases annually.³ The burden of congenital heart defects, neural tube defects, cleft lip and palate, Down syndrome, and other common anomalies is particularly concerning in India. Congenital anomalies contribute to nearly 10% of infant mortality and over 20% of perinatal mortality nationally.⁴

These anomalies occur due to a variety of reasons, including genetic mutations and environmental factors, such as exposure to certain infections, medicines, and inadequate nutrition during pregnancy.⁵ Anomalies can affect any part of the body and can vary widely in severity and long-term effects.

In this context, birth order, the sequence in which children are born in a family, is considered an important factor. It's thought that the birth order can influence the chances of anomalies due to the different conditions experienced by each child in the womb. This knowledge can help in developing strategies to prevent and manage the risks associated with congenital anomalies in different birth orders. It can also guide future parents and healthcare providers to improve prenatal care based on the specific risks related to each birth order. The primary objective of this study is to assess the effect of birth order, age, and parity on the occurrence of congenital anomalies.

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MATERIAL AND METHODOLOGY

Study Setting

This study was conducted at a first referral hospital in Bangalore that serves as a referral hub for antenatal care and safe delivery for the area. The hospital provides comprehensive maternal services encompassing routine antenatal checkups, specialized care, and advanced ultrasound assessment free of cost to economically disadvantaged populations. It coordinates care across 5 Urban Public Health Centers and Namma clinics in the city, facilitating access for vulnerable antenatal mothers.

Study Population:

The study incorporated a total of 1,432 antenatal mothers who attended the hospital for their routine antenatal check-ups and scans during their pregnancy during July 2021 and June 2022. This research was structured as a combined approach incorporating both retrospective and prospective components data collection. These mothers were selected based on the availability of comprehensive medical records and willingness to participate in follow-up procedures. The study included antenatal mothers who attended the hospital for ultrasound assessments during the stated period, with gestational ages between 11 and 42 weeks. Records considered incomplete or solely for dating scans were excluded. These cases were identified through meticulous examination of antenatal scans and medical records, with anomalies being diagnosed based on established medical criteria and guidelines.

Data Collection:

Data for this study were collected retrospectively from the medical records of the included antenatal mothers. Relevant information, including maternal age, parity, birth order, the presence of congenital anomalies, and other pertinent medical history, were extracted with due diligence to maintain accuracy and confidentiality. The mothers were subsequently followed up via telephone calls to ascertain the outcomes of the pregnancies and to gather additional information not recorded in the initial medical records.

Data Analysis:

Data analysis was conducted using MS Excel and IBM-SPSS statistics software version 21.0. The associations between birth order, age, parity, and the occurrence of congenital anomalies were evaluated using chi-square tests, and a p-value.

Ethical Considerations

This study was initiated following the approval from the Institutional Ethical Committee. The study adhered to ethical guidelines and ensured the privacy and confidentiality of the

participants' information. No identifying information was included in the data analysis, and the results were reported in an aggregated form to maintain anonymity. Ethical approval was obtained from the hospital ethics committee Ref. KIMS/IEC/A097/M/2023, appropriate permission was also obtained from concerned local health authority, confidentiality of the hospital and subjects was maintained at all times.

RESULTS

In this study, a comprehensive analysis was conducted on a cohort of 1432 antenatal mothers. The incidence of congenital anomalies was found to be approximately 2.9%, with a total of 42 anomalies detected across the cohort.

Demographic Characteristics and Congenital Anomalies

The age distribution of the antenatal mothers ranged from 18 to over 35 years, with the majority (83.7%) being between 22 and 30 years of age (Table-1). The anomalies were most prominently observed in the age group 22–25 years, accounting for 50% of the total anomalies, followed by the 26–30 years age group with 35.7%. Consanguinity was examined as a potential factor, revealing that only 9.9% of the pregnancies were consanguineous and the majority of congenital anomalies, 81%, were found in non-consanguineous pregnancies. Regarding parity, the cohort was almost equally distributed between primi (48.6%) and multi (51.3%) parities, with multi-parity pregnancies exhibiting a slightly higher anomaly incidence at 58%.

Analysis based on gestational age showed a higher concentration of congenital anomalies in pregnancies over 30 weeks, accounting for 73.8% of the detected anomalies.

Association between gestational age and birth order with congenital anomalies

The analysis showed no significant association between gestational age and risk of congenital anomalies based on the odds ratios and p-values. For birth order, first-born children had a significantly higher risk of anomalies compared to third-born (OR 2.34, $p=0.064$) and fourth or later born children (OR 2.77, $p=0.196$) as depicted in Table-2.

System-wise distribution of Birth Order Analysis

A closer look at the system-wise distribution of congenital anomalies, as outlined in Table 3, reveals that renal anomalies were the most prevalent, making up 59.5% of all detected anomalies. Anomalies labeled as miscellaneous were the next most frequent, accounting for 23.8% of the anomalies, while occurrences in the CVS, musculoskeletal, CNS, and GIT were comparatively rare.

In terms of birth order, the analysis shows different patterns of incidence. First-borns had the highest incidence of anomalies at 42.8%, with the anomalies largely being renal and miscellaneous. Second-borns made up 35.7% of the anomalies, exhibiting a range of anomalies across different systems. Third-borns had an incidence rate of 16.7%, primarily presenting renal anomalies. Lastly, fourth-born or later showed the lowest incidence at 4.8%, mainly having GIT and miscellaneous anomalies. The anomalies in other

gestational age groups were relatively lower, ranging from 4.7% to 9.5%.

This detailed examination provides a clearer understanding of how congenital anomalies are distributed across different systems and birth orders, highlighting the predominance of renal anomalies and the variations in incidence based on birth order.

Table 1: Distribution of antenatal mothers according to demography, consanguinity and Parity

Parameters	No of Antenatal Mothers (N=1432), n(%)		No of Congenital Anomalies: N=42(%)
Age	18 – 21	122(8.5)	4 (10.5)
	22 – 25	565 (39.4)	19 (50)
	26 – 30	635 (44.3)	15(35.7)
	31 – 35	101 (7)	4(9.5)
	>35	9(0.6)	-
Consanguinity	Consanguineous	142(9.9)	8(19)
	Non-Consanguineous	1290(90.6)	34(81)
Parity	Primi	697(48.6)	17 (42)
	Multi	735(51.3)	25(58)

Table 2: Association between gestational age and birth order with congenital anomaly

Variable	Groups	Congenital anomaly				
		Yes	No	Total	Odd ratio (95% CI)	p -value
Gestational Age (in weeks)	11-14	3	141	144	0.6 (0.1- 2.3)	0.5
	15-20	2	74	76	0.6 (0.1 - 2.9)	0.5
	21-25	2	146	148	0.4 (0.1 - 1.8)	0.2
	26-30	4	97	101	1.2 (0.4 - 3.6)	0.7
Birth Order	> 30	31	932	963	1	1
	First-born	18	679	697	1	1
	Second-born	15	576	591	1 (0.4 - 2.2)	0.8
	Third-born	7	109	116	2.3 (0.9 - 5.7)	0.06
	Fourth-born or later	2	26	28	2.7 (0.5 - 12.9)	0.1

Table 3: System-wise Distribution of Congenital Anomalies and Incidence by Birth Order

Birth Order	Renal	CVS	Musculo skeletal	CNS	GIT	Miscellaneous	Total	Percentage
First-born	10	2	-	0	0	6	18	42.8
Second-born	9	1	2	1	0	2	15	35.7
Third-born	6	-	-	0	0	1	7	16.7
Fourth-born or later	-	-	-	0	1	1	2	4.8
Total	25	3	2	1	1	10	42	100

DISCUSSION

The study aims to provide a nuanced understanding of how these variables might contribute to the development of congenital anomalies, potentially offering insights into preventive measures and targeted interventions and refine counseling and monitoring of high-risk pregnancies.

The finding from the study of a disproportionately high congenital anomaly incidence among first-born children compared to later birth orders is an interesting area for further research. Studies that have shown how birth order could be related to variations in parental care, maternal health, and exposure to different environments before and after birth, all of which could affect the risk of congenital anomalies.^{6,7} Further, advancing maternal age is another known risk factor for several congenital anomalies. As maternal age increases with every subsequent pregnancy, the associated risk of anomalies potentially rises, hinting at a possible link between higher birth order and increased risk of anomalies.⁸ There has also been extensive research on how birth order affects psychological growth, intelligence, and behavior.⁹

A meta-analysis by Smith et al. (2018) also found a small but statistically significant increased risk for birth defects in firstborns, with potential reasons including suboptimal uterine and maternal health environment for the first pregnancy.¹⁰ The underlying causes for the association between birth order and congenital anomalies are likely multifactorial. Advancing maternal age with subsequent pregnancies is a known risk factor, but did not fully explain the higher incidence in firstborns in our sample.¹¹ Other hypothesized factors include depletion of micronutrients like folate across recurrent pregnancies, changes in maternal immunity, and parental age and lifestyle factors that differ with later births.^{12,13} Firstborns possibly also face higher risks from epigenetic changes such as DNA methylation, which alters gene expression during embryonic development. Environmental exposures including chemicals, medications and maternal diet during the first-ever pregnancy could trigger epigenetic changes not seen in subsequent births.¹⁴

An interesting finding was the variation in anomaly patterns based on birth order. While first-born children had the highest incidence, third-borns also showed a disproportionately high rate compared to second or fourth-borns. Possible reasons could include changes in maternal age, birth spacing, parental awareness and access to antenatal screening.¹⁵

The incidence of congenital anomalies aligns with other population-based studies in India that have reported estimates ranging from 2-3%.^{16,17} The figure is also comparable to a meta-analysis of congenital anomaly prevalence in South Asia, which found an average prevalence of 2.9%.¹⁸ This indicates that the burden of congenital disorders in our study population reflects broader regional trends.

Analysis of maternal age distribution revealed that half of the anomalies were concentrated in the 22-25 years age group. This echoes previous research showing a peak prevalence of congenital anomalies when the mother's age is in the early to mid-20s, considered the ideal reproductive age.¹⁹ The likely factors are a combination of maximum fertility rates in this age bracket as well as minimizing the risks of very young or advanced maternal age.²⁰ In the current study, majority anomalies occurred in non-consanguineous couples. This aligns with earlier analyses indicating that although consanguinity is an established risk factor, the majority of anomalies occur in non-consanguineous pregnancies due to their larger population proportion.²¹ For developing effective prevention strategies, both consanguinity and non-consanguinity associated risk factors need to be examined.

Renal system anomalies were the most prevalent in our cohort, making up 59.5% of the total anomalies. This finding corroborates previous Indian studies that have reported urinary system anomalies as one of the most common, along with neural tube defects and abdominal wall defects.^{22,23} The high incidence of renal anomalies warrants further investigation into potential genetic and environmental contributors.

In summary, overall, this study provides valuable insights into the demographics of congenital anomaly distribution in

an Indian antenatal cohort. Developing a national congenital anomaly registry, increasing awareness, and addressing modifiable risk factors are key steps to reducing India's congenital disorder burden.²⁴

CONCLUSION

This study provides significant insights into the relationship between birth order and congenital anomalies, suggesting a relationship that warrants further investigation. Understanding such associations can contribute to early intervention and preventive measures, optimizing prenatal care and management.

LIMITATION

The study, being retrospective, is based on previously recorded data, limiting the possibility of exploring unrecorded or unexplored variables. The modest sample size was modest and from a single center. The sample may not be truly representative of the general population, thereby affecting the generalizability of the findings. The study did not control for all potential confounding variables such as parental health, socioeconomic status, and lifestyle factors which might have impacted the results. Large-scale longitudinal studies measuring detailed parental, obstetric and environmental variables are needed to elucidate the mechanisms underlying varying risks across birth orders.

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Conflict of Interest

None

Authors' Contribution

Dr. Nidhi Fotedar conceptualized and designed the study, collected, analyzed, and interpreted the data.

Dr. N.R Ramesh Masthi contributed to manuscript revision, read, and approved the submitted version

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