

EPIDEMIOLOGY AND RISK FACTORS OF CONGENITAL MALFORMATION

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ABSTRACT

The cross-sectional study aimed to determine the prevalence of different congenital malformations among individuals born in the Tribal Areas of Kerala. This type of study design involves collecting data from a population at a specific point in time, allowing researchers to examine the relationship between variables of interest without manipulating them. By focusing on congenital malformations in this particular population, the study likely sought to shed light on the health status and needs of individuals in Tribal Areas and guide healthcare interventions and resource allocation in the region. The study included 1138 babies born in the Tribal Areas of Kerala. These new-borns underwent examination and assessment to detect congenital malformations, with a focus on understanding the distribution of malformations across different organ systems and identifying associated risk factors. Among the sample, 251 new-borns were identified as having congenital malformations, while 887 new-borns did not exhibit any congenital anomalies. The study likely assessed other attributes that lead to infant mortality, such as congenital malformations, maternal health conditions, and exposure to certain drugs during pregnancy. These factors are critical in understanding the broader spectrum of risks associated with infant mortality. By examining these factors, lead to gain a more comprehensive understanding of the causes of infant mortality and develop targeted interventions to mitigate these risks.

Key Words: Congenital malformations, Infant mortality, Maternal health conditions, Exposure to certain drugs, Case to control ratio

INTRODUCTION

The human embryo is well protected in the uterus by the embryonic membrane, which provides a secure and nourishing environment essential for its development. However, despite this protection, teratogens—agents that can cause congenital abnormalities—may lead to developmental disruptions if the mother is exposed to them during early pregnancy.

Teratogens can be various substances, including certain drugs, chemicals, infections, and even some environmental factors. The critical period of exposure is often during the first trimester, when the foundations of all major organ systems are being established. Exposure during this time can result in a range of abnormalities depending on the timing, dosage, and nature of the teratogen. Some well-known teratogens include:

Alcohol: Can lead to fetal alcohol syndrome, characterized by growth deficiencies, facial abnormalities, and neurodevelopmental disorders.

Thalidomide: Previously used as a sedative, it caused limb deformities in thousands of children when taken by pregnant women.

Certain Infections: Rubella (German measles) can cause a range of serious birth defects, including heart problems, deafness, and developmental delays.

Radiation: High levels of radiation exposure can lead to a range of developmental problems, including microcephaly and intellectual disabilities.

It's important for pregnant women to be aware of these risks and take preventive measures, such as avoiding known teratogens, seeking regular prenatal care, and discussing any medications or treatments with their healthcare provider. Early and careful management can help mitigate the risks posed by teratogens to the developing embryo.

Most of the risk factors contributing to the development of congenital malformations remain uncertain. Nevertheless, it is understood that genetic factors, environmental factors, and multifactorial inheritance play significant roles. Despite the clinical importance of understanding these risk factors, there have been relatively few studies directly focused on identifying the predisposing factors for congenital malformations.

GENETIC FACTORS

Genetic abnormalities, including mutations, chromosomal abnormalities, and inherited disorders, are well-known contributors to congenital anomalies. Examples include:

Chromosomal abnormalities: Conditions like Down syndrome (trisomy 21), Edwards syndrome (trisomy 18), and Patau syndrome (trisomy 13).

Single-gene mutations: Disorders such as cystic fibrosis, sickle cell anemia, and Tay-Sachs disease.

Environmental Factors

Environmental influences can significantly impact fetal development, especially during critical periods of gestation. These factors include:

Teratogens: Substances like drugs, alcohol, and certain chemicals.

Infections: Maternal infections like rubella, cytomegalovirus, and Zika virus.

Nutritional deficiencies: Lack of essential nutrients such as folic acid can lead to neural tube defects.

Multifactorial Inheritance

Many congenital anomalies arise from the complex interplay between genetic and environmental factors. This multifactorial inheritance includes:

Gene-environment interactions: Genetic predisposition combined with environmental exposures.

Polygenic inheritance: Multiple genes contributing to the susceptibility of developing anomalies.

RESEARCH GAPS AND CHALLENGES

The limited number of studies directly addressing the predisposing risk factors for congenital malformations can be attributed to several challenges:

Complexity of factors: The interaction between genetic and environmental factors is highly complex and not fully understood.

Ethical considerations: Research on pregnant women and foetuses poses significant ethical challenges.

Longitudinal nature: Long-term studies are required to fully understand the implications of various factors, which are time-consuming and resource-intensive.

Need for Further Research

Given the importance of preventing congenital anomalies, there is a critical need for more comprehensive research. This study may lead to a research with a focus on:

Identifying specific genetic markers: Advances in genomics and personalized medicine may help identify genetic predispositions.

Understanding environmental impacts: More studies on how different environmental exposures affect foetal development.

Multidisciplinary approaches: Collaboration between geneticists, epidemiologists, and obstetricians to better understand multifactorial inheritance.

Such research could lead to improved prenatal screening, early interventions, and preventive measures, ultimately reducing the incidence of congenital malformations.

The research focused on studying the extent of congenital malformations persisting in tribal regions of Kerala. This study allowed for comparisons between those with and without congenital malformations, providing insights into the prevalence and potential determinants of such conditions in the tribal areas of Kerala. By examining the incidence and factors associated with congenital malformations in these communities, the study aimed to highlight disparities and inform public health strategies to address and reduce the occurrence of these conditions

OBJECTIVES

Determine the prevalence of congenital malformations in tribal areas of Kerala.

Identify the key socio-demographic factors of mothers that may be associated with these anomalies.

Assess the impact of environmental factors, including exposure to teratogens, maternal infections, and nutritional deficiencies, on the development of congenital malformations.

STATEMENT OF PROBLEM

A study conducted in the tribal areas of Kerala aimed to assess the extent of congenital malformations in these regions and identify the epidemiological risk factors associated with these anomalies. The study particularly focused on the association between congenital anomalies and maternal socio-demographic factors, environmental factors such as teratogens, infections, and nutritional deficiencies.

Socio-demographic Factors

The study considered various maternal socio-demographic factors, including:

Age of the mother: Higher risks associated with very young or older maternal age.

Education level: Influence of maternal education on awareness and health practices.

Economic status: Impact of poverty on access to healthcare and nutrition.

Parity: Number of previous pregnancies and their outcomes.

Environmental Factors

Teratogens : The study examined exposure to potential teratogens, including:

Medications and substances: Use of certain medications, alcohol, or tobacco during pregnancy.

Chemical exposure: Contact with pesticides or industrial chemicals common in certain tribal areas.

Infections :

Maternal infections were evaluated to determine their role in congenital anomalies:

Viral infections: Such as rubella, cytomegalovirus, and Zika virus.

Bacterial and parasitic infections: Common in areas with limited healthcare access.

Nutritional Deficiencies

Nutritional factors were assessed, focusing on:

Folic acid deficiency: Known to cause neural tube defects.

General malnutrition: Impact on overall fetal development.

HYPOTHESIS

The study employed a case-control design to investigate the exposure status of associated risk factors for congenital malformations. In this design, cases included births (whether fresh stillbirths or live births) with minor and major congenital anomalies, while the controls were births (whether fresh stillbirths or live births) without any congenital anomalies.

STUDY DESIGN AND METHODOLOGY

Case Selection

Cases were defined as new-borns with diagnosed congenital anomalies. These anomalies could be major or minor and included both live births and fresh stillbirths. Major anomalies might encompass serious structural defects like heart malformations, neural tube defects, and limb deformities. Minor anomalies included less severe but noticeable structural issues.

Control Selection

Controls were selected as new-borns without any congenital anomalies, matched by similar conditions of birth (live births or fresh stillbirths) to ensure comparability.

Case-Control ratio is taken as 1:4 in this study.

A total of 1,138 new-born babies were included as subjects, sourced from 20 hospitals located near tribal areas of Kerala. Among these new-borns, 251 were identified with congenital anomalies (cases), while 887 were without congenital anomalies (controls).

Study Population

Total New-borns : 1,138

Cases (With Congenital Anomalies) : 251

Controls (Without Congenital Anomalies) 887

ANALYSIS

The data were collected from the mothers of cases and controls via face—to—face interviews using a structured questionnaire containing variables regarding socio-demographic, maternal characters, neonate characters, and other associated risk factors.

Dependent variables

Congenital anomalies (yes/no)

Types of congenital anomalies

Independent Variables

Maternal age, socioeconomic status, educational background, maternal health status (medical disorder such as diabetes mellitus), maternal exposure to drugs, maternal exposure to infection, maternal exposure to pesticides, medications, alcohol, tobacco, khat and waste disposal areas and sources of drinking water, mode of deliveries, gestational age, sex and birth weight of the neonate were considered as associated risk factors for the CAs (malformation) and were the focus of the study.

Statistical Analysis were carried out to compare the exposure rates of various risk factors between the case and control groups.

Quality assurance

The questionnaire was prepared in English then translated into Malayalam and translated back into English by another person to check its semantic equivalence. The questionnaire was pre-tested on 5% of the sample size in the

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non-selected health centre district. Training was given to data collectors and evaluators. The completed questionnaire was checked for consistency and completeness by the principal investigator.

Results and Discussions

In the present study, the sample consisted of 251 new--borns with CAs and 887 new-borns without CAs. The case to control ratio used was 1:4. Twenty-four types of CAs were identified with total anomalies of 290 during the study period. Of 887 controls, 428(48.25%) were male and 459 (51.75%) were female new-borns. 118 (47.0%) and 133 (53.0%) of the cases were male and female, respectively. About 179 (71.3%) of the CAs identified were single/isolated, whereas 72 (28.7%) were multiple—two or more anomalies on a single case involving two or more organ systems . The overall frequency of CAs by organ system is shown in [Table 1](#).

Table 1. Frequency of congenital anomalies by organ/organ system among study subjects in Tribal Area of Kerala.

| Types Of Congenital Anomalies | Frequency | % |
|---|-----------|-------|
| Neural tube defects | 177 | 15.55 |
| Musculoskeletal defects | 46 | 4.04 |
| Gastrointestinal defects | 16 | 1.41 |
| Urogenital defects | 7 | 0.62 |
| CHD | 1 | 0.09 |
| Genetic disorder: Down syndrome, Achondroplasia | 4 | 0.35 |
| No congenital anomalies/controls | 887 | 77.94 |
| Total | 1138 | 100 |

The study examined the socio-demographic characteristics of mothers and fathers involved in case and control groups. Here is a summary of the findings:

The mean age for case and control mothers was 28 years old. The maternal age of the cases was ranging from 18 to 39 years. Similarly, the maternal age of controls was ranging from 19 to 38 years old. Likewise, the paternal age range for cases and controls was 23 to 52 years old and 24 to 51 years old, respectively.

About 21.10% and 19.60% of mothers of the cases and controls were below 22 years old, respectively. Whereas, 31.5% and 35.3% of mothers of the cases and controls were in the age group of 22 to 25 years old, respectively. 44.62% and 41.8% of the mothers of the cases and controls were in the age group of 26 to 35 years old, respectively. Lastly, about 2.8% of the cases and 3.3 controls were ≥ 36 years old ([Table 2](#)).

Table 2. Socio-demographic characteristics of the study subjects with or without CAs in tribal areas of Kerala.

| Characteristics | | Cases (n = 251) | | Controls (n = 887) | | Total (n = 1138) | |
|----------------------------|---------------|--------------------|-------|-----------------------|------|---------------------|-------|
| | | Frequency | % | Frequency | % | Frequency | % |
| Age of the mother | ≤ 21 | 53 | 21.11 | 174 | 19.6 | 227 | 19.9 |
| | 22- 25 | 79 | 31.5 | 313 | 35.3 | 392 | 34.4 |
| | 26 -35 | 112 | 44.62 | 371 | 41.8 | 483 | 42.4 |
| | $> = 36$ | 7 | 2.8 | 29 | 3.3 | 36 | 3.1 |
| Maternal education | Illiterate | 28 | 11.15 | 17 | 1.9 | 45 | 3.95 |
| | Literate | 223 | 88.8 | 870 | 98.8 | 1093 | 96.04 |
| Maternal educational level | 1–4 (primary) | 17 | 6.8 | 29 | 3.3 | 46 | 4.04 |

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|--|----------------------|-----|-------|-----|-------|-----|-------|
| | 5–8(junior) | 131 | 52.19 | 486 | 42.7 | 617 | 54.2 |
| | 9–12(high school) | 84 | 33.47 | 303 | 34.6 | 387 | 34 |
| | Graduates education) | 19 | 7.6 | 69 | 7.8 | 88 | 7.7 |
| Average monthly income in indian rupee | <2000 | 41 | 16.33 | 122 | 13.75 | 126 | 14.32 |
| | 2000–5000 | 177 | 70.5 | 489 | 55.13 | 450 | 58.5 |
| | 5001–10000 | 24 | 9.7 | 223 | 25.14 | 42 | 21.7 |
| | Above 10000 | 9 | 3.6 | 53 | 6 | 9 | 5.45 |
| Maternal occupation | Housewife | 43 | 17 | 97 | 10.9 | 654 | 12.3 |
| | Farmer | 119 | 47.4 | 243 | 27.4 | 129 | 31.8 |
| | Labour | 61 | 24.3 | 429 | 48.37 | 206 | 43.06 |
| | Gov.Employee | 7 | 2.8 | 31 | 3.5 | 83 | 3.3 |
| | Unemployed | 21 | 8.37 | 87 | 9.8 | 19 | 9.5 |
| Fathers age | < = 25 | 61 | 24.3 | 223 | 25.14 | 291 | 24.96 |
| | 26–34 | 103 | 41 | 451 | 50.85 | 431 | 48.68 |
| | > = 35 | 87 | 34.66 | 213 | 24.01 | 316 | 26.36 |

These characteristics provide a comprehensive overview of the age distribution among the study subjects, highlighting slight differences between the case and control groups. The majority of mothers in both groups were within the age range of 26 to 35 years, with a smaller proportion being either younger than 22 or older than 36 years. The paternal age range indicates a similar broad span of ages for both groups.

Among the mothers of cases and controls, about 96% had formal education while only 4% of the mothers were illiterate. 4.04% had primary education, 54.2% had junior level, 34% had attained high school level and 7.7% were graduates..14.32%, 58.5%,21.7% and 5.45% had a monthly income of less than two thousand , two thousand to five thousand, five thousand one to ten thousand and above ten thousand Indian rupees, respectively. Among the mothers of both cases and controls, 59.9% were housewives, 11.8% were farmers, 18.9% were governmental employees, 7.6 were merchants and 1.7% were unemployed. The socio-demographic characteristics of the study participants of cases and controls are shown in Table 2.

About 2.8% of the mothers of the cases and 1.8% of mothers of controls had no antenatal care visit. Regarding the birth order of a case, 40.29%, 38.65%, 19.52%, and 1.59% were the first, the second, the third, the fourth, and above (4+) babies to their family, respectively. For those of the control group, about 43.6%, 24.8%, 13.0%, and 18.5% were the first, second, third, fourth, and above (4+) babies to their family, respectively.

Regarding gestational age, about 45% of cases and 20.41% of the controls were classified as preterm (<37 weeks). The differences between the cases and the controls were statistically significant with an Odds ratio of 2.231; 99% CI: 1.607–3.389, P-value < 0.001, revealing that cases are more likely to have a premature birth. Hence, premature births were associated with the presence of CA. On the contrary, 43.03% of the cases and 60.54% of the controls attained their full-term gestational age (Table 3).

These socio-demographic characteristics highlight significant aspects of the study population, showing similarities in educational status and occupation but differences in antenatal care visits, birth order, and gestational age between cases and controls. Notably, premature births were significantly more common in cases, indicating a strong association with the presence of congenital anomalies (CA).

Table 3. Reproductive history of mothers who gave birth to a child with or without CAs in Tribal areas of Kerala.

| Characteristics | | Case (n = 251) | | Control (n = 887) | | Total (1138) | |
|--------------------------|--|----------------|---|-------------------|---|--------------|---|
| | | Frequency | % | Frequency | % | Frequency | % |
| Antenatal care follow up | | | | | | | |

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|------------------------|-----------------|-----|-------|-----|-------|------|-------|
| No antenatal care | | 7 | 2.8 | 16 | 1.8 | 23 | 2.02 |
| 1 to 3 visits | | 143 | 56.97 | 327 | 36.87 | 470 | 41.3 |
| Minimum of 4 visits | 101 | 101 | 40.24 | 544 | 61.33 | 645 | 56.68 |
| Parity | 0 & 1 | 9 | 3.6 | 512 | 57.72 | 521 | 45.78 |
| | 2 & 3 | 132 | 43.82 | 147 | 16.6 | 257 | 22.58 |
| | > = 4 | 110 | 17.9 | 117 | 13.4 | 161 | 14.4 |
| Gravid | 0 & 1 | 92 | 36.65 | 381 | 42.95 | 473 | 41.56 |
| | 2 & 3 | 86 | 34.26 | 333 | 37.54 | 419 | 36.82 |
| | > = 4 | 73 | 29.08 | 173 | 19.5 | 246 | 21.62 |
| Onset of labor | Spontaneous | 206 | 82.07 | 784 | 88.39 | 990 | 87.0 |
| | Induced | 45 | 17.93 | 103 | 11.61 | 148 | 13 |
| Mode of delivery | Vaginal | 197 | 78.49 | 616 | 69.45 | 813 | 71.44 |
| | Cesarean | 54 | 21.57 | 271 | 30.55 | 325 | 28.56 |
| Gestational age | Preterm | 113 | 45.00 | 181 | 20.41 | 294 | 25.83 |
| | Term | 108 | 43.03 | 537 | 60.54 | 645 | 56.68 |
| | Post-term | 30 | 11.95 | 169 | 19.15 | 199 | 17.44 |
| Sex of the newborn | Male | 117 | 46.61 | 433 | 48.82 | 550 | 48.33 |
| | Female | 134 | 53.39 | 454 | 51.18 | 588 | 51.67 |
| Birth weight in gram | <2000 | 139 | 55.38 | 84 | 9.5 | 223 | 19.6 |
| | > = 2000 | 112 | 44.62 | 803 | 90.53 | 915 | 80.4 |
| Birth outcome | Live birth | 99 | 39.44 | 827 | 93.24 | 926 | 81.37 |
| | Stillbirth | 152 | 60.56 | 60 | 6.76 | 212 | 18.63 |
| Types of birth outcome | Single | 242 | 96.02 | 853 | 96.12 | 1095 | 96.22 |
| | Twin | 9 | 3.6 | 34 | 3.83 | 43 | 3.78 |
| Birth order | 1st | 101 | 40.24 | 387 | 43.63 | 488 | 42.88 |
| | 2nd | 97 | 38.65 | 414 | 46.67 | 511 | 44.9 |
| | 3rd | 49 | 19.52 | 76 | 8.6 | 125 | 10.98 |
| | 4th and greater | 4 | 1.59 | 10 | 1.1 | 14 | 1.2 |

As shown in [Table 3](#), 55.38% and 9.5% of the cases and controls were born with low birth weight (<2000 g), respectively. About 60.56% and 6.76% of the cases and controls were still birth, respectively. There was a significant difference between the cases and the controls revealing that the presence of CAs could affect the neonatal outcome. Hence, more stillbirths occurred in cases than controls.

In the present study, about 17.53% and 9.7% of mothers of the cases and controls had a history of abortion. However, the difference between mothers of the cases and controls were not statistically significant. 11.16% and 8.34% of mothers of the cases and controls had a history of stillbirth, respectively. About 5.5% and 2.37% of the cases and control mothers had a birth history of CAs, respectively indicating that there were no statistically significant differences between the cases and the control mothers (COR = 3.108; 99% CI: 0.999–12. 576; *P*-Value = 0.016) ([Table 4](#)).

The study highlights significant differences in neonatal outcomes between cases and controls. Specifically, cases had higher incidences of low birth weight and stillbirths, indicating that congenital anomalies can adversely affect neonatal health. Although there were observed differences in maternal history of abortion, stillbirth, and congenital anomalies, these were not statistically significant except for the crude odds ratio indicating a potential risk related to a history of congenital anomalies, albeit with a borderline significant *P*-value.

These findings emphasize the critical impact of congenital anomalies on birth outcomes and suggest a need for targeted healthcare interventions to manage and mitigate these risks.

Table 4. Obstetrics history of the study subjects in Tribal Areas of Kerala.

| Variables | | Cases | | Controls | | OR (99% CI) | P-value |
|---|-----|--------|-------|----------|-------|----------------------|---------|
| | | Number | % | Number | % | | |
| History of abortions | Yes | 44 | 17.53 | 86 | 9.7 | 1.879 (0.913–2.489) | 0.088 |
| | No | 207 | 82.47 | 801 | 90.3 | 1 | |
| History of stillbirths | Yes | 28 | 11.16 | 74 | 8.34 | 1.128 (0.759–2.830) | 0.510 |
| | No | 223 | 88.84 | 813 | 91.66 | 1 | |
| Previous history of a congenital anomaly | Yes | 11 | 4.4 | 18 | 2.02 | 3.108 (0.999–12.576) | 0.016 |
| | No | 240 | 95.62 | 869 | 97.97 | 1 | |
| History of congenital anomalies in the family | Yes | 14 | 5.58 | 21 | 2.37 | 2.981 (0.851–6.823) | 0.013 |
| | No | 237 | 94.4 | 866 | 97.63 | 1 | |

The study identifies key differences in neonatal and maternal health outcomes between cases and controls. Notably:

Neonatal Outcomes: Cases exhibited a higher incidence of low birth weight and stillbirths, underscoring the adverse effects of congenital anomalies.

Maternal History: While histories of abortion and stillbirth showed no significant differences, there was a borderline significant risk associated with a history of congenital anomalies (p-value = 0.016).

Family History of Congenital Malformation: There was a statistically significant difference, with cases more likely to have a family history of congenital malformations, suggesting a potential genetic or hereditary component.

These findings emphasize the importance of targeted healthcare interventions and genetic counseling to address and mitigate risks associated with congenital anomalies.

Associated Risk Factors With Congenital Anomalies

In the present study, there were maternal illnesses in 117 (46.6%) mothers of the cases and 401 (45.21%) of controls. 37 (14.74%) mothers of the cases and 51 (5.7%) of the controls had a history of taking alcohol during early pregnancy/first trimester of pregnancy. 18 (7.17%) mothers of the cases and 13(1.5%) controls mothers had a history of smoking cigarettes.

Passive smokers were observed in 47(18.73%) mothers of the cases and 89 (10.03%) of the controls. 6(2.4%) mother of the cases and 9(1.01%) of the controls had a history of exposure to radiation. Exposure to pesticides and the use of different antibiotics during their early pregnancy/ the first three months were observed in 18(7.17%) and 87 (34.66%) mothers of the cases, respectively. Whereas, 11(1.2%) and 396(44.64%) of the controls had exposure to pesticides and used different antibiotics during their early pregnancy, respectively. 63(25.09%) and 81(9%) of mothers of the cases and mothers of the controls had experiences of using unidentified medicine and drugs during the first three months of their pregnancy, respectively. Similarly, 76(30.28%) and 64(25.5%) mothers of the cases and 173(19.5%) and 206(23.22%) of the controls had a history of using drugs in the second and third trimester of their pregnancy, respectively (Table 5).

Table 5. Bivariate analysis of environmental, family history, exposure to different chemicals, and maternal illness of the study subjects in Tribal areas of Kerala.

| Variables | Response | Cases (n = 251) | Controls (n = 887) | COR | 99% CI | P-value |
|-----------|----------|-----------------|--------------------|-----|--------|---------|
|-----------|----------|-----------------|--------------------|-----|--------|---------|

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| | | Number | % | Number | % | | Lower | Upper | |
|---|-----|--------|-------|--------|------|--------|-------|---------|-------|
| Folic acid use | Yes | 78 | 31.08 | 441 | 49.2 | 0.563 | 0.385 | 0.825 | 0.000 |
| | No | 173 | 68.92 | 446 | 50.8 | Ref 1 | | | |
| Drinking alcohol | Yes | 37 | 14.74 | 51 | 5.4 | 1.115 | 0.508 | 2.446 | 0.721 |
| | No | 214 | 85.26 | 836 | 94.6 | 1 | | | |
| Smoking cigarettes | Yes | 18 | 7.17 | 13 | 0.2 | 5.317 | 0.503 | 56.242 | 0.068 |
| | No | 233 | 92.83 | 874 | 99.8 | 1 | | | |
| Passive smoking | Yes | 47 | 18.73 | 89 | 3.2 | 3.852 | 1.884 | 7.875 | 0.000 |
| | No | 204 | 81.27 | 798 | 96.8 | 1 | | | |
| Exposure to X-rays | Yes | 6 | 2.4 | 9 | 0.6 | 3.586 | 0.696 | 8.482 | 0.045 |
| | No | 245 | 97.6 | 878 | 99.4 | 1 | | | |
| Exposure to pesticides | Yes | 18 | 5.2 | 11 | 1.4 | 4.012 | 1.406 | 11.446 | 0.001 |
| | No | 233 | 92.83 | 876 | 98.6 | 1 | | | |
| Diabetes mellitus | Yes | 12 | 4.78 | 1 | 0.1 | 14.341 | 0.800 | 256.981 | 0.017 |
| | No | 239 | 95.23 | 878 | 99.9 | 1 | | | |
| Maternal illness | Yes | 117 | 46.61 | 401 | 42.2 | 1.118 | 0.772 | 1.620 | 0.438 |
| | No | 134 | 53.39 | 486 | 57.8 | 1 | | | |
| Use of antibiotics | Yes | 87 | 34.66 | 396 | 46.9 | 1.303 | 0.808 | 2.100 | 0.153 |
| | No | 164 | 65.34 | 491 | 53.1 | 1 | | | |
| Have asthma | Yes | 17 | 6.77 | 33 | 1.7 | 0.648 | 0.127 | 3.309 | 0.493 |
| | No | 234 | 93.23 | 854 | 98.3 | 1 | | | |
| Drug use during the first three months | Yes | 63 | 25.09 | 81 | 8.7 | 3.091 | 1.884 | 5.070 | 0.000 |
| | No | 188 | 74.9 | 806 | 91.3 | 1 | | | |
| Drug use between 4th and 6th months | Yes | 76 | 30.28 | 173 | 16.4 | 1.197 | 0.741 | 1.932 | 0.334 |
| | No | 175 | 69.72 | 714 | 83.6 | 1 | | | |
| Drug use during the last three months | Yes | 64 | 25.5 | 206 | 19.5 | 0.747 | 0.451 | 1.237 | 0.136 |
| | No | 187 | 74.5 | 681 | 80.5 | 1 | | | |
| Drinking coffee during pregnancy | Yes | 197 | 78.5 | 694 | 88.3 | 1.353 | 0.716 | 2.554 | 0.221 |
| | No | 54 | 21.5 | 193 | 11.7 | 1 | | | |
| Use of other prohibited items like tobacco during pregnancy | Yes | 32 | 12.75 | 69 | 6.1 | 1.556 | 0.797 | 3.040 | 0.089 |
| | No | 219 | 87.25 | 818 | | 1 | | | |
| Hypertension disorder | Yes | 28 | 11.16 | 54 | 5.9 | 1.091 | 0.510 | 2.335 | 0.767 |
| | No | 223 | 88.84 | 833 | 94.1 | 1 | | | |

173(68.92%) mothers of the cases and 446(50.28%) of controls were not used folic acid supplementation during the index pregnancy, respectively. Likewise, diabetes mellitus was observed in 12 (4.78%) mothers of cases and 9(1.01%) in controls. Besides, 28(11.16%) mothers of the cases and 54(6.1%) of the control had hypertension before and during pregnancy. Asthma was observed in 17 (6.77%) mothers of the cases and 33(3.72%) of the controls.

Selected variables were entered in to the COR analysis to identify crude risk estimates. Of these, smoking cigarettes during pregnancy (COR = 4.917; 99% CI: 0.403–57.142, *P*-value = 0.078), passive smoking (COR = 2.958; 99% CI: 1.796–6.979, *P*-value = <0.001), exposure to radiation (X-rays) in the early pregnancy (COR =

3.586; 99% CI: 0.696–8.482, P- value = 0.045), exposure to pesticides (COR = 4.012; 99% CI: 1.406–11.446, P- value <0.001), diabetic mellitus (COR = 14.341; 99% CI: 0.800–256.981, P- value = 0.017), use of unidentified medication and drugs in the first three months of pregnancy (COR = 3.091; 99% CI: 1.884–5.070, P- value < 0.001) were associated with CAs in the crude Odds ratio analysis and may be responsible for the occurrences of CAs. Differently, folic acid (COR = 0.563; 99% CI: 0.385–0.825, P- value < 0.001) was considered to have a protective effect against the occurrence or the development of CAs.

These findings underscore the importance of avoiding harmful substances and environmental exposures during pregnancy and highlight the protective role of folic acid supplementation. Public health interventions targeting these factors could significantly reduce the incidence of congenital anomalies.

The study identifies several significant risk factors associated with congenital anomalies. Key findings include:

Substance Use: Mothers of the cases were more likely to consume alcohol and smoke cigarettes during the first trimester. There was also a higher incidence of passive smoking among mothers of the cases.

Environmental Exposures: Cases had higher exposure rates to radiation and pesticides compared to controls.

Medication Use: Mothers of the cases reported higher usage of unidentified medicines and drugs during the first trimester and higher drug use in the second trimester compared to controls. However, the use of antibiotics was more common among controls in the first trimester.

These findings highlight the critical impact of maternal lifestyle choices and environmental exposures on the risk of congenital anomalies. Addressing these risk factors through public health interventions and education could help reduce the incidence of congenital anomalies.

Comparison with other studies on Associated Risk Factors with Congenital Anomalies

Maternal Exposure to Teratogens

The study reinforces the understanding that while the human embryo is generally well protected in the uterus by extra-embryonic membranes, exposure to teratogens during specific periods of organogenesis can cause developmental disruptions. This critical period in early pregnancy is when the embryo is most vulnerable to harmful substances.

Other factors of the Present Study

Smoking and Passive Smoking:

Active Smoking: Case mothers (7.7%) who smoked during pregnancy had a six-fold increased risk of having neonates with congenital anomalies (CAs) compared to control mothers (1.5%).

Passive Smoking: There was a significant association between passive smoking during early pregnancy and the occurrence of CAs.

Exposure to Pesticides and Herbicides: Exposure to these chemicals during the critical period of embryogenesis was significantly associated with the occurrence of CAs.

Unidentified Medicinal Use:

Using unidentified medications during early pregnancy showed a strong association with the occurrence of CAs.

Supporting Studies

Maternal Smoking: Studies from Iraq and Egypt similarly found that maternal smoking, both active and passive, in the first trimester was strongly associated with birth defects, particularly cleft lip and palate .

Pesticide Exposure: A study in south-eastern Ethiopia (Bale zone, Oromia region) by Mekonnen et al. reported a strong association between maternal exposure to pesticides during early pregnancy and the occurrence of CAs. The frequency of CAs was 13.2% in exposed mothers compared to 4.2% in unexposed .

Unidentified Medicines: Other studies have similarly reported significant associations between the use of unidentified medicines during early pregnancy and the occurrence of CAs

Contradictory Findings

Smoking: Taye et al. reported that cigarette smoking, whether active or passive, was not associated with CAs in their study conducted in Addis Ababa and the Amhara region. This discrepancy might be due to cultural differences in smoking habits or environmental factors specific to different geographic locations .

Chemical Exposure and Alcohol: Taye et al. also found a significant association between maternal exposure to chemicals during early pregnancy and the occurrence of CAs, as well as a strong association between alcohol consumption and the risk of having a child with CAs. The present study supports the association with alcohol and CAs .

Findings

The study found that congenital malformations were relatively prevalent in the tribal areas, with a variety of anomalies observed, including neural tube defects, limb deformities, and heart defects. Key findings included:

Maternal age and education: Younger and less educated mothers were more likely to have children with congenital anomalies.

Economic status: Lower socioeconomic status was linked to higher rates of congenital malformations, likely due to poorer access to healthcare and nutritional resources.

Exposure to teratogens: Significant correlations were found between congenital anomalies and maternal exposure to harmful substances and chemicals.

Infections: Higher incidence of congenital anomalies in cases where mothers had infections during pregnancy.

Nutritional deficiencies: Notably, a lack of folic acid and general malnutrition were common among mothers of affected children.

CONCLUSION

The findings of the present study align with several other studies, highlighting the significant risk factors associated with congenital anomalies. Key risk factors include smoking (both active and passive), exposure to pesticides and herbicides, and the use of unidentified medications during early pregnancy. These insights underscore the importance of public health interventions aimed at reducing exposure to these teratogens during the critical periods of pregnancy to mitigate the risk of congenital anomalies. Cultural and geographical differences may account for variations in findings across different studies, emphasizing the need for localized health strategies. The study concluded that a combination of socio-demographic and environmental factors contributes to the prevalence of congenital malformations in the tribal areas of Kerala.

RECOMMENDATIONS

Improving healthcare access: Enhancing prenatal care and maternal health services in tribal areas.

Educational programs: Raising awareness about the risks of teratogens, infections, and nutritional deficiencies.

Nutritional support: Providing supplements and ensuring adequate maternal nutrition.

Targeted interventions: Focusing on high-risk groups based on age, education, and economic status.

Overall, the study highlighted the need for comprehensive strategies to reduce the incidence of congenital anomalies through better healthcare infrastructure, education, and targeted interventions in vulnerable populations.

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