

AN EPIDEMIOLOGICAL STUDY OF CONGENITAL ANOMALIES IN CONSANGUINEOUS AND NON-CONSANGUINEOUS MARRIAGES AMONG PATIENTS ATTENDING PEDIATRIC WARD IN GGH, GUNTUR

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ABSTRACT: Marriage in Indian society is a religious duty. Consanguineous marriage has been a long standing habit among many Indian families. Many studies have suggested a strong association between consanguineous marriages and the incidence of autosomal recessive diseases and congenital anomalies. According to studies 30-40% of the marriages in Andhra Pradesh are consanguineous. Recently the awareness of consequences of consanguineous marriages among the educated families has led to change in attitudes of many people about this age old practice of interbreeding in the traditional Indian society. **OBJECTIVES:** This study is aimed at determining at the prevalence of consanguineous marriages, type of consanguinity and the prevalence of congenital anomalies among offspring of consanguineous and non-consanguineous parents and also to study the effect of consanguinity on foetal loss and neonatal morbidity and mortality. **MATERIALS AND METHODS:** Prospective longitudinal hospital based study conducted at the Government General Hospital (GGH), Guntur, A. P over a period of 2months from July to August 2012. We screened 1025 babies delivered in the obstetrics dept for malformations and relevant demographic and obstetric data was obtained from the parents. Infants with congenital anomalies of Indian nationality were included in the study. Babies of mothers having history of hereditary diseases, sexually transmitted diseases and exposure to drugs were excluded from the study. Institutional ethics committee approval was obtained. Out of 1025 infants screened, 200 babies had malformations. **RESULTS:** Malformed babies were noted in 33.8% of consanguineous marriages versus 15.1 % in controls (Non- consanguineous marriages) with P value of 0.0000001 which is statistically significant.

KEYWORDS: Consanguineous parentage, congenital anomalies, genetic and premarital counselling.

INTRODUCTION: Congenital malformations (CM) are also known as birth defects, congenital disorders or congenital anomalies. Congenital malformations (CM) began to emerge as one of the major childhood health problems and it refers to any structural or functional abnormality, whether genetic or not, which is present at birth. CM are important causes of childhood deaths, chronic illnesses, and disability in many countries. They affect an estimated 1 in 33 infants and result in approximately 3.2 million birth defect-related disabilities every year.¹ An estimated

2, 70, 000 newborns die during the first 28 days of life every year from congenital anomalies. In one study,² the prevalence of CM was 3% for single major anomaly and 0.7% for multiple major anomalies and it has also been shown that 12.3-32% of deaths that have occurred during the perinatal period are related to congenital anomalies. Treatment and rehabilitation of children with most of the CM is costly and complete recovery is usually impossible.³ While infections and

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malnutrition are the dominant causes of infant morbidity and mortality in the developing countries like India, congenital malformations^{1,4,5} contribute to significant proportion of childhood disability and deaths. Although congenital anomalies may be genetic, infectious or environmental in origin, approximately 50% of all congenital anomalies, cannot be linked to a specific cause, some known risk factors of CM are socioeconomic, infections, nutritional, genetic and environmental.

Consanguineous marriages have been described as an important factor contributing to increased congenital malformations.⁶ A consanguineous marriage can be characterized by the degree of relatedness between the spouses: Though there are several types of consanguinity, consanguineous marriage is defined as a marriage between two people who are second cousins or more closely related.⁷ Consanguinity may increase the chance of congenital malformations because the recessive genes present in both the parents may cause homogeneity for the character. Consanguinity also increases the risk for major malformations in children, leading to immediate death. Foetal loss is also more in consanguineous marriages, when compared to non-consanguineous marriages. Children born due to consanguinity may suffer from autosomal recessive genetic disorders.

Literature reports a historically high prevalence among the Middle East countries, North Africa and South Asia accounting for 20-50% of all marriages.^{8,9} According to earlier studies, about 30-40% of marriages in Andhra Pradesh are consanguineous marriages. The frequency of malformations in different patterns of consanguineous marriages can vary in different places, based on marital habits, socio-economic status and environment of different places.

There are 2 types of congenital malformations: Major and minor. Major congenital developmental disturbances are defined as structural defects of the body and/or organs that impair viability and require intervention. Minor morphogenetic errors are small structural developmental disturbances that do not impair viability and do not need to be treated. Preventive public health measures administered through pre- and peri-conception and prenatal health care services decrease the frequency of certain congenital anomalies including those due to consanguineous marriages.

This study aimed to determine the prevalence of consanguineous marriages, type of consanguinity and to determine the role of consanguinity on CM so as to create awareness about the ill effects of consanguineous marriages in people thereby decreasing the burden of CM related morbidity and mortality in our society to a large extent.

METHODS: This is a descriptive, cross section & observational study with consecutive sampling of 1025 newborn babies, who had been delivered at Obstetrics department, GGH, Guntur, AP during 2 months period from July to Aug 2012. All newborns who had been delivered in the hospital during this period were examined and screened for congenital malformations by pediatricians. Data collection was performed by means of a structured model and the variables which included maternal and paternal age, socioeconomic status, literacy, nutritional status, significant diseases during pregnancy, environmental factors like drugs, radiation, method of delivery, number of births, stillbirth and miscarriages, gravidity (Defined as the number of times a woman has been pregnant), parity (Defined as the number of times she has given birth to a foetus with a gestational age of 24 weeks or more, regardless of whether the child was born alive or stillborn), history of CM in other offspring and members of their family, and parental consanguinity were obtained by interviewing the mothers of the new born babies were recorded. Neonatal characteristics including sex, gestational

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age, existence of congenital malformation and the type of malformation were noted. Babies of mothers having history of hereditary diseases, sexually transmitted diseases and exposure to drugs were excluded from the study. Institutional ethics committee approval was obtained. Out of 1025 infants screened, 200 babies had congenital malformations.

The type of birth defects was classified by the diagnostic standardization of CM from the international classification of disease (ICD-10) codes. The data was entered into Microsoft Excel and then improvised in EPI INFO 2000 and calculations were done. The response to each question and the results of each test were recorded separately and analyzed. The rates of malformed newborns and malformations were compared using statistical T-test and the Chi-square tests. The level of significance was determined at $p < 0.05$.

RESULTS: Among 1025 cases screened, the mean maternal and paternal age was observed to be 26.78 ± 4.2 and 32.27 ± 7.4 respectively. 645(62.9%) and 380(37.07%) newborns were delivered by normal vaginal delivery (NVD) and caesarean section (CS) respectively.

Out of 1025 cases screened, 239 (23.3%) were from consanguineous marriages and 786 (77.6%) were from non-consanguineous marriages and 200 babies who had anomalies were admitted in the paediatric ward. Out of 200 infants with anomalies, 81 babies (33.8%) were from consanguineous marriages while only 119 (15.1%) were from non-consanguineous marriages. There was an increased incidence of anomalies in consanguineous marriages compared to non-consanguineous marriages (p value= < 0.0000001).

Among the studied babies with malformations, males were more as compared to females. When we studied the type of consanguinity, 2nd degree consanguineous was more. We studied the age distribution of mothers who delivered malformed babies. The risk of congenital anomalies in both consanguineous and non-consanguineous marriages was more when maternal age was >30 years.

	Total marriages	Number of anomalies	Percentage
Consanguineous	239	81	33.8%
Non-Consanguineous	786	119	15.1%

Different types of anomalies affecting the various systems are given below: (Anomalies were most commonly observed in the cardiovascular system).

System	Number	Percent
Cardiovascular system	48	24%
Musculoskeletal system	38	19%
Genitourinary system	38	19%
Gastrointestinal system	31	15.5%
Central nervous system	11	5.5%
Others	34	17%

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Different anomalies observed in each system are given below:

Anomalies	Number	Percent
Acyanotic	6	12.5%
Cyanotic	12	25%
Dextrocardia	12	25%
Complex Congenital heart diseases	12	25%
Asymmetric Ventricular septal hypertrophy	6	12.5%
Cardiovascular system		

Anomalies	number	Percentage
Sacrocoxygealteratoma	4	10.5%
Musculo skeletal anomalies	16	42.1%
RTA rickets	4	10.5%
Others	14	36.8%
Musculoskeletal system		

Anomalies	Number	Percentage
Hypospadias	12	31.6%
Undescended testis	10	26.3%
Hydronephrosis	6	15.85
Others	10	26.3%
Genitourinary system		

Anomalies	Number	Percentage
Cleft lip cleft palate	15	48.4%
Omphalocele	2	6.5%
Hirschprung's	4	12.9%
Anorectal	10	32.3%
Gastrointestinal system		

Anomalies	Number	Percentage
Hypoplasia of foot	5	45.5%
Macrocephaly	2	18.2%
Microcephaly	1	9.1%
Dandy walker's	1	9.1%
Meningomyelocele	2	18.2%
Central nervous system		

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Anomalies	Number	Percentage
Hernias	10	29.4%
Turner's syndrome	5	14.7%
Hydrocephalus	5	14.7%
Prune belly syndrome	4	11.7%
Down's syndrome	2	5.9%
Collodion baby	4	11.7%
Floppy infants	3	8.8%
Congenital Anaemias	3	8.8%
Thalassemia	2	5.9%
Others		

DISCUSSION: Consanguinity has a major effect on the occurrence of congenital anomalies. Congenital anomalies, when major, may cause immediate death and if they survive infancy are affected physically, mentally or socially and can be at increased risk of morbidity due to various health disorders. Minor anomalies may not cause any major problem, but it may be an indicator of significant anomalies affecting major systems of the body and sometimes can affect the normal life. The prevalence of consanguineous marriages is found to be very high in the region of study, probably due associated factors like low socioeconomic status, illiteracy and rural residence. In recent times, the situation appears better in urban areas. However, despite medical advancements, literacy rate and urbanization all over the world, still, this family linked traditions are not able to be broken.

The present study shows prevalence of consanguinity, type of consanguinity and the role of consanguinity on incidence of congenital anomalies, mostly the major congenital anomalies with the objective of taking remedial steps to create awareness among people of this region about consequences of consanguinity which would be helpful in decreasing the CM problem in the society.

The total number of patients screened during the period of study was 1025, out of which 239 were consanguineous marriages and 786 were non-consanguineous. The prevalence of consanguineous marriages was 23.3%. The total no. of anomalies in consanguineous marriages was 81, where as in non-consanguineous they were 119. The prevalence of CM was 33.8% among the total consanguineous marriages where as it was only 15.1% (99 out 786). This shows that there is increased occurrence of congenital anomalies in consanguineous marriages than in non-consanguineous marriages. Increased incidence of CM in the offspring of consanguineous couples most likely arises from the homozygous expression of recessive genes inherited from their common ancestors.

While the prevalence of congenital anomalies at birth in developed countries is reported to be between 3-5%, those reported in Taiwan are said to be approximately 4.3%, 7.92% reported for the United Arab Emirates, 2.46% for Oman, 2.7% for Bahrain, and 3.6% for India.¹⁰⁻¹⁴ The frequency of malformations in this study was higher compared with other studies probably because of environmental factors, nutritional status, habits and low socio economic status of many individuals, besides high prevalence of consanguinity in this region. In this study, among the babies with malformations, males were more as compared to females. These findings are consistent with those reported by Gorgan et al, where male newborns were more affected than females.¹⁵

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The results are in agreement with results from the study by Tayebi N et al.¹⁶ We did not see if there was relationship between malformation and the degree of relation of the parents. But Mehrabi et al. (2205) showed that although the consanguinity for malformed patients was high, there was no significant relationship between malformation and the degree of relation of the parents.¹⁷ Also, in a study by Bromiker et al in Palestine, no statistically significant difference was found in the incidence of congenital malformation with the degrees of parents relation.¹⁸

In view of high prevalence of consanguinity in our region and its significant role in causing CM, preventive public health measures administered through pre- and peri-conception and prenatal health care services are highly recommended to decrease the frequency of congenital anomalies. Primary prevention of congenital anomalies includes mass campaigning about ill effects of consanguineous marriages as well as medical genetic screening and counselling besides other measures like improving the diet of women throughout their reproductive years, ensuring an adequate dietary intake of vitamins and minerals and particularly folic acid and iodine, abstaining from or restricting intake of harmful substances, particularly the use of alcohol., controlling pre-conceptional and gestational diabetes through counselling, weight management, diet and the administration of insulin when needed., avoiding exposure to hazardous environmental substances (e.g. heavy metals, pesticides, some medications) during pregnancy, improving vaccination coverage, especially against the rubella virus, for children and women and increasing and strengthening education to health staff and others involved in promoting birth defects prevention. Newborn screening with clinical examination and screening for haematological, metabolic, and hormonal disorders, screening for deafness and heart defects as well as early detection of other birth defects can facilitate life-saving treatments and prevent the progression towards some physical, intellectual, visual or auditory disabilities.

WHO is working with many national and international agencies for improving laboratory capacity, to provide needed technical expertise and trying to establish a global policy by bringing together birth defect surveillance and research programmes from around the world in order to investigate and prevent birth defects and to lessen the impact of their consequences.

CONCLUSION: In conclusion, consanguinity may play an important role in the high rates of malformation in children. For a possible prevention, genetic counselling before marriage must be applied, not only for consanguineous couples but also for any couples that may have a family history of genetic disorders. India needs to take a big leap in this direction with consanguineous marriages being more prevalent. The need of the hour is setting up infrastructure with basic research, mass campaigning at community level and good medical facilities with genetic testing and counselling especially to young people in the age group of 18-25 years.

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