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EFFECT OF ADVANCED PATERNAL AGE ON DEVELOPMENT OF CONGENITAL MALFORMATION

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ABSTRACT:

Background: Congenital malformations not only affects the diseased but also extends to many at risk individuals as well as to their families and adds to the socio-economic burden of the society. Recent investigations are reaching cause from all direction and paternal factors are much given importance as they too lead to notable genetically based malformations. **Methodology:** Present descriptive, cross sectional; hospital based study was conducted in Krishna Hospital Karad. The study included all the Pregnant Mother diagnosed to have congenital birth defected fetus through antenatal examinations, delivered baby with diagnoses of congenital malformation, who were admitted at Tertiary care hospital Karad or came for reference services. Among all data, paternal age was segregated to study in depth about effect on congenital malformation. **Results:** In this study considering the prevalence with number of birth, it is 1.4% and calculating with number of neonates admitted its prevalence rate is 5.3%. As per as paternal age is concerned, 73 % of fathers of the malformation babies were are above 26 years of age and 25 % were above 36 years of age. Considering the mothers age maximum anomalies 116 (41%) were to the mothers with age of 21 to 25 years. There are 52 (18.4%) mothers between age group of 31 to 35 and 54 (19.1%) mothers above 6 years of age. **Conclusion:** Even though some of previous study results supports our study findings, however, the etiological causes for these malformations could not be advanced paternal age but the risk factors associated with age must not be ruled out.

Key words: Maternal, paternal, age, congenital malformations

Introduction:

Birth defects are also known as congenital malformation are responsible considerable amount of maternal as well as neonatal morbidity and mortality. According to WHO Congenital anomalies are defined as structural or functional anomalies, including metabolic disorders which are present at the time of birth[1]. Around 40%- 60% of congenital anomalies are of unknown etiology[2, 3]. 20-25% of anomalies the cause is multifactorial.10-13% are because of environment and 12-25 % are attributed to genetic causes. Among the risk factors are advanced maternal and paternal age, consanguinity, teratogenic agents and nutritional deficiencies[4]. Congenital malformations not only affects the diseased but also extends to many at risk individuals as well as to their families and adds to the socio-economic burden of the society. The causes for malformations are genetic or no genetic. Genetic cause would be considered direct cause due to defective gene where are non-genetic causes are varying with geographical location, socio-economic-cultural factors and

individuals health status. Genetic abnormalities or family history of birth defects are easily identifies as a etiological factors, where as non- genetic causes is quite difficult to point out as there are wide variety of influencing factor the mother and father exposed during preconception, conception and pregnancy.

Much concentration was paid to maternal factors than paternal in identifying etiology for birth defect. Recent investigations are reaching cause from all direction and paternal factors are much given importance as they too lead to notable genetically based malformations. As per maternal age is concern, it is well established that, advanced maternal age is important risk factors for many malformations, but, Genetic studies proved that many genetic syndromes are paternal origin. It has been stated that advanced paternal age causes mutation during spermatogenesis leading to increase the number of birth defects in their offspring[5]. However less research provides support to these hypotheses. There are studies with small samples; hence generalization is not possible for all genetic disorders and malformations. In many studies the definition for advanced paternal age is deferent and its co relation with maternal age is very less. Only few studies show relation of advanced paternal age with congenital malformation considering maternal age in a normal range. Few large scale studies shows that advanced paternal age increases the risk for specific malformation[6, 7], neural tube defects, congenital cataracts, upper limb reduction and Down's syndrome[8]. Study from National Birth Defects Prevention Study (NBDPS), analyzing data from 1997–2004, considering paternal and maternal age as continuous variables and while carefully controlling for maternal age suggest that paternal age may be a risk factor for some multifactorial birth defects.

Methodology:

Present descriptive, cross sectional; hospital based study was conducted in Krishna Hospital Karad, which provides specialist's tertiary care services to patients largely belonging to lower/middle socio-economic strata of the society with both rural and urban background. The study included all the Pregnant Mother diagnosed to have congenital birth defected fetus through antenatal examinations, delivered baby with diagnoses of congenital malformation, who were admitted at Tertiary care hospital Karad or came for reference services. Data was collected to assess the prevalence and risk factors of congenital malformation among mothers attending tertiary care unit hospital. Among all data, paternal age was segregated to study in depth about effect on congenital malformation. Data was collected assessed from September 2016 to august 2017. The study was initiated after approval of the Institutional Ethics Committee of Krishna Institute of Medical Sciences Deemed University's.

Results:

1. Prevalence of congenital malformation

Surveillance done all over the world has shown that the prevalence of congenital defects varies from country to country. These variations may be explained by social, racial, ecological and economic differences. In the present study we have gathered the data from two units, Pediatric and Maternity unit.

Pediatric unit included pediatric outpatient department, pediatric ward and Neonatal Intensive Care Unit where 75136, 4092 and 774 patients were assessed respectively. Prevalence is being maximum in the Neonatal Intensive Care Unit 41 (5.3%), followed by Pediatric Ward 14 (0.3%) and pediatric Outpatient Department 45 (1%).

Maternity unit included Maternity Outpatient Department, Maternity ward which also included labor room. In the Maternity Outpatient Department 50856 patients were visited in that 131 patients had the diagnosis of having congenital malformation fetus contributing to 0.3%. Whereas maternity ward had 3847 patients among those 52 (1.4%) had delivered congenital malformed babies. When considering the prevalence, many studies considered prevalence with number of birth / number of delivery or number of neonates admitted in Neonatal Intensive Care Unit. In my study considering the prevalence with number of birth, it is 1.4% and calculating with number of neonates admitted its prevalence rate is 5.3%.

2. System wise distribution of congenital malformation

Distribution of congenital malformation according to International Classification of Disease (ICD – 10) carries out after collecting data which shows, maximum Congenital malformations were belongs to the nervous system 63(22%), followed by circulatory system 57 (20%) and deformations of the musculoskeletal system 47 (17%). Other deformities includes Cleft lip and cleft palate 29 (10%), malformations of the digestive system 23 (8%), malformations of genital organs 19 (7%), malformations of the urinary system 21 (7%), other congenital malformations 2 (1%), Chromosomal abnormalities, not elsewhere classified 15 (5%) malformations of the respiratory system 5 (2%) and Congenital malformations of eye, ear, face and neck 2 (1%).

Table: 1 number of malformations and age of parents

Sl no	Age of Father	Age of Father	
		Frequency F	Percentage %
1.	Below 20 Year	3	1.06
2.	21 To 25 Year	60	21.20
3.	26 To 30 Year	72	25.44
4.	31 To 35 Year	78	27.56
5.	Above 36 Year	70	24.73

Total 283 congenital malformation cases were diagnosed in one year of duration. As per as paternal age is concerned, 73 % of fathers of the malformation babies were are above 26 years of age and 25 % were above 36 years of age.

Table: 2- Description of age of the father and system of congenital malformations.

SL NO	ICD CODE	System of malformation	≤ 20 Year	21 To 25 Year	26 To 30 Year	31 To 35 Year	Above 36 Year	TOTAL	Percentage
1	Q00-Q07	Malformations of the nervous system	1	14	12	17	19	63	22%
2	Q10-Q18	Malformations of eye, ear, face and neck	0	0	0	2	0	2	1%
3	Q20-Q28	Malformations of the circulatory system	0	5	18	19	15	57	20%
4	Q30-Q34	Malformations of the respiratory system	0	1	2	0	2	5	2%
5	Q35-Q37	Cleft lip and cleft palate	2	11	6	3	7	29	10%
6	Q38-Q45	Malformations of the digestive system	0	4	6	11	2	23	8%
7	Q50-Q56	Malformations of genital organs	0	8	4	6	1	19	7%
8	Q60-Q64	Malformations of the urinary system	0	9	0	1	11	21	7%
9	Q65-Q79	Malformations and deformations of the musculoskeletal system	0	17	11	12	7	47	17%
10	Q80-Q89	Other malformations	0	0	0	2	0	2	1%
11	Q90-Q99	Chromosomal Abnormalities, not elsewhere classified	0	0	2	5	8	15	5%
		Total	3	69	61	78	72	283	100%
		Percentage	1%	2%	21%	27%	25%	100%	

When considered advanced paternal age, (above 36 years) table explains that 72 (25%) of congenital malformed babies born from these age group. Among these maximum malformations were from nervous system 19 (6%), followed by cardiovascular system 15 (5%), urinary system 11(9%). 8 (3%) babies had chromosomal abnormalities and Cleft lip & cleft palate and deformations of the musculoskeletal system found in 7 (2.4%) babies.

The pattern of circulatory system malformation indicates that, 25 to 35 years of aged father had highest (13%) malformation rate. Between 20 to 25 years of aged fathers the most common anomalies were nervous system 14 (5%), Cleft lip and cleft palate 11 (9%) and deformations of the musculoskeletal system 17 (5.5%).

Discussion:

In our study considering both maternal and paternal age congenital malformations were classified. There is no direct co relation in increase of anomalies due to advanced age in both mother and father. The prevalence is uniformly distributed in all age group. This indicates that there are many other factors, than age, for development of malformations. For example risk factor for neural tube defect is not only paternal advanced age by also low intake of folic acid during pregnancy. There are other risk factors for all types of malformations such as exposure to teratogen, low nutrition, maternal smoking or alcohol use. However the advanced mother's age and father's age both gave birth to some malformation which needs not to be neglected in considering as advanced age as a risk factor. The discussion is carried out keeping in those anomalies born to advanced aged father. As we observed, the no correlation between advanced paternal age and malformations were not found in studies by, Polednak[9] and Lian et al[10]. Kazaura et al[11] found that Neither advanced paternal age nor older maternal age was identified as a risk factor for birth defects among offspring. 72 (25%) of congenital malformations are belongs to advanced age group fathers. Among these maximum malformations were from nervous system 19 (6%), followed by cardiovascular system 15 (5%), urinary system 11(9%) and chromosomal abnormalities in 8 (3%) babies. 7 (2.4%) babies had Cleft lip & cleft palate and deformities of the musculoskeletal system.

One of the large scale study conducted in USA by Q. Yang[12] using the 1999–2000 birth registration data, found that advanced paternal age was related to an increased risk in the cardiovascular malformations, respiratory anomalies, tracheo-oesophageal fistula/ oesophageal atresia, other musculoskeletal/ integumental anomalies, Down's syndrome and other chromosomal anomalies. Some studies have found associations between advanced paternal age and several birth defects, including cleft lip and palate [13,14, 15], orofacial clefts[16,17,18,19] hydrocephalus and pulmonary Stenosis [17], situs inversus[20] neural tube defects, limb reduction defects and congenital cataracts [21], hypospadias and craniosynostosis[22], malformations of the extremities[23], tracheo-esophageal fistula/esophageal atresia[24], atrial septal defects (ASDs) and ventricular septal defects (VSDs)[25], congenital heart defects (overall)[25]. This evidence supports our study results.

Summary:

Even though some of previous study results supports our study findings, however, the etiological causes for these malformations could not be advanced paternal age but the risk factors associated with age must not be ruled out. Genetic council must be targeted both maternal as well as paternal age for preventing risk for malformation.

Weakness of this study:

There are very few samples where paternal age information provided by the mother and could not be verified. There is no study or guidelines which specifies what age constitutes advanced paternal age.

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