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Prevalence and Risk Factors of Congenital Anomalies among the sick neonates of the Ladakh region of India

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Abstract: Congenital anomalies are the structural and functional irregularities at birth. In this progressive study, all the neonates who are admitted to the Neonatal Intensive Care Unit during the three year period from 1st June 2017 to 31 May 2020.

Aim: The study aims to examine the prevalence, type, and epidemiological factors of congenital anomalies among the population of Ladakh India.

Subject and methods: All the neonates during the study period were examined by pediatrics and questionnaire filled by the consent of the family. A total of 936 parents of neonates was agreed to participate in this study and among them, 524 are male neonate and 412 was female.

Results: Four and a half percent were diagnosed as being congenital malformed and the common system affected by congenital anomalies in the digestive system followed by the mucso-skeletal system. In this study, based on the logistic regression consanguineous marriage with OR of 9.862 (4.221; 23.041), P= <0.001, familial congenital anomalies in the family with OR of 17.008 (4.343; 66.606), P=0.001, an anaemic mother with OR of .124 (.029; .538). P = .005, Apgar score with .033 (.016: .067), P-value of <0.001 and paternal smoking with OR of 13.305 (5.558: 31.854) with P value of <0.001 had shown a very good significant correlation with the congenital anomalies.

Conclusion: The occurrence and distribution of congenital anomalies in Ladakh were reported. More active prenatal screening and the possible role of genomics study are major importance to uncovering the susceptibilities.

Keywords: Congenital anomalies, birth defects, Risk factors, Epidemiology, Neonates, Ladakh

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1. INTRODUCTION:

According to WHO, the congenital anomalies are also described as congenital disorders, birth defects, and congenital abnormalities that have well-defined structure or function anomalies that happen during intrauterine life. The congenital anomalies are due to the malfunctioning and faulty embryogenesis or intrinsic in the developmental process of the baby.[1] The occurrence of congenital anomalies shows the difference in various nations and globally, India contributes a burden of around 28% neonatal mortality due to congenital anomalies.[2]The pattern of congenital anomalies differ over time with the demographic data such as socioeconomic status, a complex dynamic interaction of genetic and environmental known and unknown factors.[3] In India the prevalence of congenital anomalies was reported as 1.91% to 4.08%.[4,5] The genetic and environmental factors play a significant role in the first trimester triggering congenital anomalies [6] and others showing some statistically significant in different studies. The classification of congenital anomalies based on which system they effect as some congenital anomalies may affect a single organ or multi organs in an individual. The congenital anomalies that affect the body system are nervous system, musculoskeletal system, urinary system, reproductive system, gastrointestinal system, the respiratory system and the circulatory system. [7] The exact cause of the occurrence of any congenital anomalies is unknown in about 40-60% of cases. However some factors that increase the risk of the congenital anomalies are genetic disorders lead by consanguinity, socioeconomic and demographic factors. These maternal factors are involved in congenital anomalies can be prevented once we have the evident for the association with incidence of congenital anomalies. So, the study of the pattern of congenital anomalies at the local level provides an effective tool for necessary intervention. The higher age of the mother augments the chance of various chromosomal defects, predominantly Down syndrome. Different studies have reported a statistically significant association between the higher age of mother and congenital anomalies. [4] Moreover, with advancing of age the non-disjunction of chromosomes increases hence results number of chromosomal abnormalities including Down syndrome.

The aim of this study was to estimate the incidence, type and the risk factors associated with congenital anomalies in Ladakh region of India.

2. MATERIAL AND METHODS:

Description of the study:

The study was conducted in Kargil district of Ladakh region of India. The town is located at elevation of 2,676 meter above sea level and having an average annual temperature of 8.6 with 318mm of precipitation. According to 2011 population census report, Kargil has a total population of 1.43 lakh from which 77,785 is male and 63,017 are female.

In this hospital based prospective study was conducted to study the prevalence and risk factors associated with congenital anomalies in the high altitude region of India. The study is for the period of three years that is from 1st June 2017 to 31 May 2020 in Neonatal Intensive Care Unit (NICU) of district hospital Kargil-Ladakh includes 936 newly born neonates. All the neonates during the study period were examined by paediatrics with the help of available

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necessary laboratory investigation. The diagnosis of the patients was made mainly on the basis of the clinical ground. All the data that includes demographic data, date of birth, baby's gender, parental consanguinity, familial malformation, premature birth, mother's professional status, , prematurity, birth by normal or caesarean section, mother's iron or folic acid intake during pregnancy, mother's calcium intake during pregnancy, mother's vitamins intake during pregnancy, mother's drug intake during pregnancy, mother's gestity, number of abortions, number of children and mother's age, malformation, Apgar score, and neonate's weight are recorded in the questioners.

Statistical analysis:

Data were entered and analysed using SPSS software, Descriptive results were presented using means, medium, mode, and standard deviation for continuous variable and percentage for the qualitative variable. Chi square test was used to compare between two or more percentages when fulfilled condition were satisfied. In addition, the odds ratio (OR) and the 95% confidence interval (CI) of individual for consanguinity, familial malformation, nature of birth, mother took calcium and vitaminsduring pregnancy, anaemic mother and paternal smokingwere calculated by logistic regression analysis.

The study was approved by Ethics committee of the Sher-i-Kashmir Institute of Medical Science Srinagar (Deemed University).

3. RESULTS:

During the period of three years 936 neonates were admitted to the NICU. Among 936, five hundred twenty four (56%) were male and four hundred twelve (44%) were female with the ratio of 1.27: 1. Among them six hundred thirty seven (68%) babies were born in the main hospital and two hundred ninety nine (31 %) were born in peripheral hospitals and were referred as well as home delivery cases. From the total nine hundred thirty six (936) neonates admitted, eight hundred thirty seven (89%) neonates were discharged, 8 leave against medical advice, 12 referred to specialised hospital in Kashmir valley and PGI Chandigarh and 79 (8.4%) expired. Among seventy nine expired neonates fourty two (53%) were male and thirty seven (46.8%) were females. Among the expiry cases fifty three (53) neonates were inborn that delivered at district hospital and twenty six (26) were born outside district hospital.

Out of the 936 admission of neonates at Neonatal Intensive care unit district hospital Kargil, Ladakh, 42 neonates had congenital anomalies with the percentage of 4.5% as showed in figure 1. The yearly incidences of the cases are showing in the chart 1 which shows the yearly case number admitted to NICU varies. When the identified congenital anomalies were classified according to the international classification of Disease, the most common affected was digestive system (cleft lip with or without cleft palate) followed by musco-skeletal system (clubfoot and dysplasia of hib), multiple congenital anomalies, chromosomal aberration (Down syndrome), metabolic, cardiovascular system (congenital heart anomalies, haemorrhagic anomaly) and respiratory system (pierre robin syndrome) as showed in figure 1.

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The mean of maternal age the neonates with congenital anomalies are 27.98 with the standard deviation of 5.89 and the mean of maternal age without congenital anomalies are 27.64 with 4.46 of standard deviation. The mean weight of the neonates at birth is 2.95 with the standard deviation of 0.55 for the neonates with congenital anomalies and 3.22 with 0.56 standard deviation for neonates without congenital anomalies. The mean of Apgar score based on the appearance, pulse, grimace (irritability), activity and respiration found to be 5.98 for neonates with congenital anomalies and 7.87 for without congenital anomalies as show in table 1. The Apgar score is showing significant in weight and the Apgar score of the neonates as show in table 1.

In this reports, there is very good evidence of a relationship between incidence of congenital anomalies due to consanguineous marriage with the chi square value of 41.24 and the p value is <0.001 (Table 2) and OR of 9.862 (4.221 ; 23.041), P=<0.001 (Table 3). Along with consanguinity, familial congenital anomalies in the family, anemic mother, Apgar score and paternal smoking has been showing very good evidence of a relationship with incidence of congenital anomalies as details mentioned in the table 2 and table 3.

4. DISCUSSION:

This prospective study involves 936 new born from the Neonatal Intensive Care Unit of district hospital Kargil, Ladakh from 1st June 2017 to 31 May 2020. Out of 936 neonates, 42 were born with congenital anomalies and the incidence rate is 4.5%. Most of the anomalies are with digestive system (22%). There are some high risk pregnancies which are the major health problem through out of the world. The current study was an attempt to evaluate the incidence, type, and risk factors that contributing for congenital anomalies in the local population. In this study the incidence of congenital anomalies was 4.5%, lower than the 6% that is the common reported percentage of the general Indian population. [8] The most common affected system was found to be the digestive system followed by musco-skeletal system, multiple congenital anomalies, chromosomal aberration, metabolic, cardiovascular system, and respiratory system. The results is different from other study done by Desai and Desai, Deshpande *et al.*, Ndibazza *et al.,* Sarkar *et al.,* Koumi *et al.*, Vinodh and Deepthy 2017 and Bhalerao and Garg that found musculoskeletal anomalies are the most widespread form of congenital defects.[9,10,11,3,12,13,14] Other study found circulatory system is common system affected by congenital anomalies followed by musculoskeletal system [15] and cardiovascular system is the common system followed by the central nervous system.[16] However in the year 2018, Jayasree *et al found*nervous system followed by the musculoskeletal system are the common effected system. [7]

It has been found that the higher incidences of congenital anomalies are found to be in low socioeconomic groups, [17] due to possible lack of access to balanced diet, quality health care facility, and time to time screening facility of the pregnant women due to their economic status. [18] However this study does not found any such evidence of association. Folic acid intake is crucial for the biosynthesis and methylation of deoxyribonucleic acid and ribonucleic acid [19]and lack of folic acid was found to be association with congenital anomalies. [18]A study done by Kurdi*et al*., in the year 2019 documented that folic acid

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fortification, preconception diabetes screening and consanguinity-related counselling have significant and comprehensive health benefits to prevention and care. [20] This study found consanguinity, familial congenital anomalies in the family, anemic mother, Apgar score and paternal smoking has very good evidence of a relationship associated with the incidence of congenital anomalies. Familial congenital anomaly in the family has been associated with an increased risk of having another child with congenital anomalies, with a recurrence rate especially for neural tube defects and Down syndrome. [12] In adding to all above listed risk factors, number of other factor also found to be associated with the incidence of congenital anomalies like higher number of time a women conceive a strong association with the occurrence of congenital anomalies. [21]

5. CONCLUSION:

The occurrence and distribution congenital anomalies in Ladakh were reported. The factors such as consanguineous marriage, familial congenital anomalies in family, anaemic mother, paternal smoking and lower Apgar value of neonates are found to be as risk factors as they are showed evident for the association with congenital anomalies. More active prenatal screening and possible role of genomics study are major importance to uncovering the susceptibilities.

6. LIMITATION:

This study confined to the neonates admitted to NICU of the district hospital Kargil for the period of three year. Therefore, the result cannot be generalized.

Conflict of interest: No conflict of interest.

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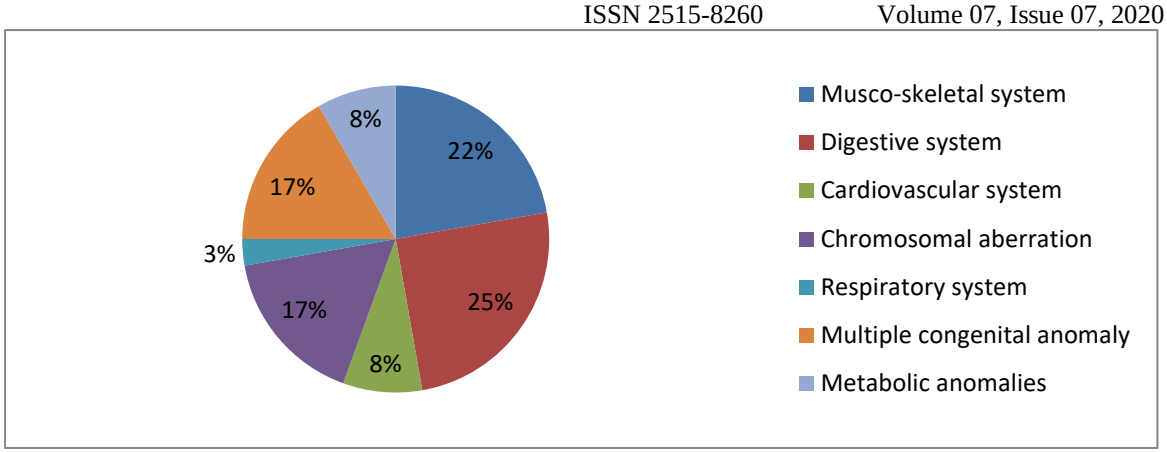

Figure 1: Distribution of congenital anomalies according to body system

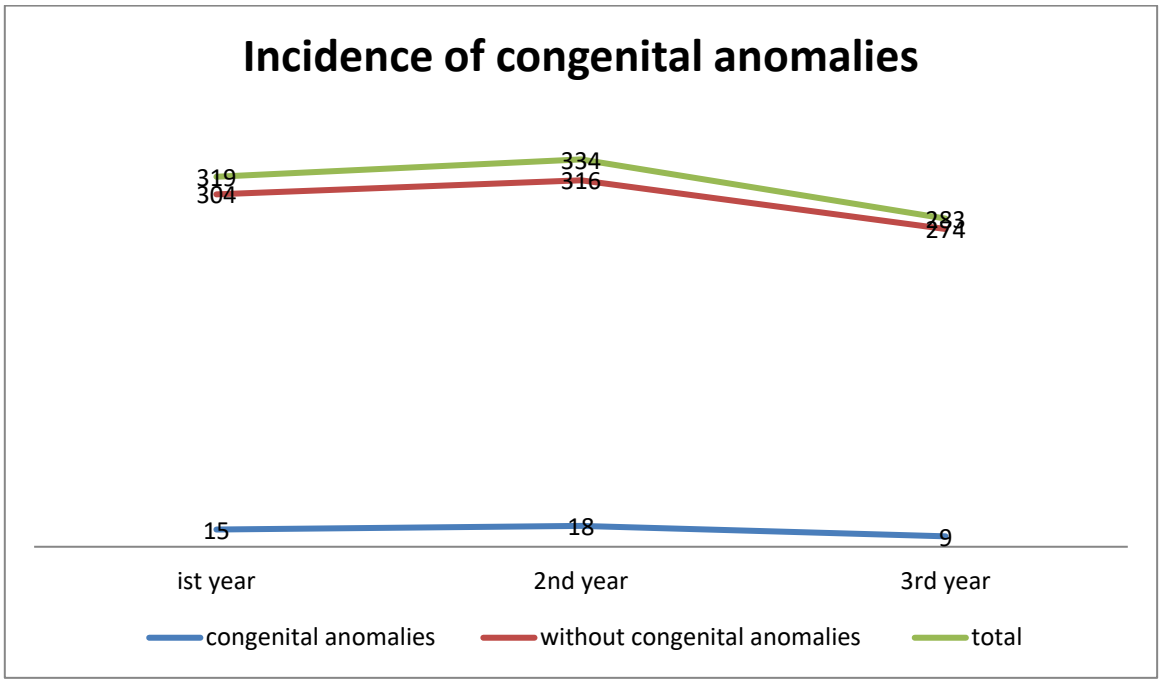

Chart 1: showing the incidence of cases of congenital anomalies

Table 1: Associated characteristics of births with and without congenital malformation

Characteristics	Congenital malformation N=42 Mean (standard deviation)	No congenital malformation N=894 Mean (standard deviation)	Means difference	p-value
Mother's age	27.98(5. 891)	27.63 (4.464)	0.341	0.021
Mother's number of live children	2.55(1.329)	1.77 (1.202)	0.775	0.193
Total number of pregnancy	3.66 (1.734)	2.54 (1.432)	1.123	0.069
Abortion	1.12 (0.354)	1.45 (0.552)		

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Weight of the baby (in kg)	2.95 (0.555)	3.22 (0.562)	-.267	<0.001
Apgar score out of 10	5.98 (1.506)	7.87 (0.886)	-1.891	<0.001

Table 2: Chi square test to births with or without congenital malformations

Characteristics		No congenital malformation N=894 (95.5%)	Congenital malformation N=42 (4.5%)	Chi square	df	p-value	Total N=936
District hospital		894	42				936
Gender	Male	500	24	.024	1	.877	524
	Female	394	18				412
Consanguinity	Yes	143	23	41.24	1	<0.001	166
	No	751	19				770
Familial malformation	Yes	53	13	38.32	1	<0.001	66
	No	841	29				870
Premature birth	Yes	74	6	1.853	1	.173	80
	No	820	36				856
Nature of Birth	Normal	681	31	.123	1	.726	712
	Caesareans	213	11				224
Mother took iron and folic acid tablet during pregnancy	Yes	854	40	4.452	2	.108	894
	No	12	2				14
	Don't know	28	0				28
Mother took calcium during pregnancy	Yes	730	37	1.124	1	.289	767
	No	164	5				169
Mother took vitamins during pregnancy	Yes	690	39	5.723	1	.017	729
	No	204	3				207
Mother took other drugs during Pregnancy	Yes	17	1	.049	1	.825	18
	No	877	41				918
Diabetes mother	Yes	3	1	2.823	1	.093	4
	No	891	41				932

Anaemic mother	Yes	276	3	10.796	1	.001	279
	No	618	39				657
Paternal smoking	Yes	132	23	46.444	1	<0.001	155
	no	762	19				781
Family status	BPL	694	27	6.530	1	.011	721
	APL	168	15				183
Apgar score	>7	855	19	174.19	1	<0.001	874
	<7	36	23				59
Mother age	<30	719	32	.496	1	.481	751
	>30	173	10				183

Table 3: Bivariate logistic regression analysis of factors associated with and without congenital malformation

Characteristics		Odds ratio	95% confidence interval	P value
Gender	Male	.759	.333 ; 1.726	.510
	Female			
Consanguinity	Yes	9.862	4.221 ;23.041	<0.001
	No			
Familial malformation	Yes	17.008	4.343 ; 66.606	<0.001
	No			
Premature birth	Yes	.578	.106 ; 3.146	.526
	No			
Nature of Birth	Normal	.972	.384 ; 2.458	.952
	Caesareans			
Mother took iron and folic acid tablet during pregnancy	Yes	1.293	.346 ; 4.835	.703
	No			
	Don’t know			
Mother took calcium during pregnancy	Yes	.048	.006 ; .401	.005
	No			
Mother took vitamins during pregnancy	Yes	23.052	2.315 ; 229.545	.007
	No			
Mother took other drugs during Pregnancy	Yes	.624	.028 : 14.104	.767
	No			
Diabetes mother	Yes	5.019	.189 ; 133.435	.335
	No			
Anaemic mother	Yes	.124	.029 ; .538	.005
	no			
Paternal smoking	Yes	13.305	5.558 ; 31.854	<0.001
	No			

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Family status	BPL	.924	.373 ; 2.289	.864
	APL			
Mother age	<30	.597	.263 : 1.358	.219
	>30			
Apgar score (10)	>7	.033	.016 ; .067	<0.001
	<7			