

Is decline possible in congenital heart defects by adjusting avoidable risk factors?

Comment [n1]: No need for page number.

Abstract:

Introduction:

Congenital heart defects (CHD) are the leading causes of birth defects-associated morbidity and mortality with incidence variable with geographic locale, race, family history and gender of the baby.

Material and Methods:

This descriptive study was conducted on 96 infants after ethical approval; infants of both genders with diagnosis of CHDs were registered. After complete history and physical examination type of anomaly observed was confirmed by echocardiography. Data was analyzed by using SPSS 21.0 Chi square test was applied for comparison of categorical variables, $p < 0.05$ was considered significant.

Results:

During study period total 96 patients were examined. Significant association of various types of CHDs with cousin marriage, lack of folic acid intake and positive family history were observed on Pearson chi-square statically significant p -value (< 0.01) was observed shown in tables.

Conclusion:

Further studies on modifiable risk factors on big sample size will be very helpful in decreasing the load of CHDs, and patients can also be facilitated with early diagnosis and management.

Keywords:

CHDs, cousin marriage, folic acid, risk factors, Sindh

Introduction:

Congenital heart defects (CHD) are the leading causes of birth defects-associated morbidity and mortality. The incidence of CHD varies according to the geographic locale, race, family history and gender of the baby. About six to eight infants/1000 live births have CHD. They are associated with multiple risk factors; consanguinity, low birth weight, maternal diseases, lack of folic acid, family history of CHD. [1, 2]

Some environmental factors are also supposed to contribute in it such as maternal alcohol consumption and smoking, and medication in pregnancy like antidepressant drugs. Though, at present, disease prevention by risk factors is not well stated. Studies reveal that about 30% of CHDs can be prevented by adjusting /modifying risk factors easily with subsequent intervention. [3, 4]

Currently with improvement of health care awareness and facilities, diagnosis in earlier stages of pregnancy in utero or soon after birth provides better opportunity for earlier diagnosis and management. But as prevention is better than cure, no fruitful steps are taken in identification and preclusion of modifiable risk factors to decrease the graveness of CHDs. By determining pregestational diabetes, family history of CHDs, maternal addiction habits, obesity, use of antidepressants, pre-pregnancy use of folic acid significant decline is possible, if endeavored by public health programs. [5, 6]

The pattern of risk factors for CHD is different among different parts of the world. The role of consanguinity in the etiology of CHD is supported by inbreeding studies, which demonstrate an autosomal recessive pattern of inheritance of some congenital heart defects. Consanguineous marriages are fairly common in South Asia owing to religious or social rationale. In developing countries, consanguinity is relatively prevalent; Avoiding cousin marriages essentially when positive family history of congenital anomalies. [7]

The association of CHDs with several chromosomal anomalies is closely linked. Family history of CHDs and positive history in siblings is suggestive of genetic association; superadded by

Comment [n2]: The entire article should be written justified on both sides.

Comment [n3]: CHD [1, 2].

environmental factors such as cousin marriage doubles the risk. New trends of genetic analysis/mutations will play vital role in early identification of CHDs and thereby decreasing them. [8]

Cardiac teratology is seems to be occurring as diversion from normal embryogenesis in first trimester of pregnancy; when important event of cardiogenesis i.e. formation of heart tube and cardiac septa formation occurs. This period require critical monitoring of maternal well- being by avoiding possible teratogens can prevent CHDs. [9]

The data on perinatal risk factors is scare in our setup, moreover no such study was conducted among population of rural Sindh. Hence current study was conducted in order to conclude the risk factors associated with CHD in our setup as the burden of CHDs is quite high with no reliable statistics. This study reviews the risk factor portfolio for future direction of health care policies for prevention and management of such cases.

Material and Methods:

This descriptive study was conducted in Department of Pediatrics of Civil Hospital Mirpurkhas Sindh from January 2019 to December 2019 on 96 infants. After approval from Institutional ethical committee and informed consent from parents, infants of both genders with diagnosis of CHDs were registered. Complete history about weight, age of baby and mother at the time of pregnancy of this baby, gestational age, and history of use of any drug and folic acid, cousin marriage and congenital defect in family was taken. Thorough physical examination was completed. On physical examination type of anomaly observed was confirmed by echocardiography. Data was analyzed by using SPSS 21.0 Chi square test was applied for comparison of categorical variables, $p < 0.05$ was considered significant. [10]

Results:

During study period total 96 patients were examined. Significant association of various types of CHDs with cousin marriage, lack of folic acid intake and positive family history were observed. In this study 76% of infants born to mothers who had cousin marriage while 24% were to mothers who had no history of cousin marriage, on Pearson chi-square statically significant p-value (< 0.01) was observed shown in table 1. Positive family history of congenital anomalies

was observed in 61.4% while negative in 38.5% cases (table 2 & graph 1) in 80% mother no use of folic acid is reported only 20% mother give history of folic acid intake depicted in table 3.

Table no: 1 Association of congenital anomalies with cousin marriage

		congenitaldefects * cousinmarriage Crosstabulation		
Count		Cousin marriage		Total
		Yes	No	
Congenital defects	VSD, Hypospadiasis	6	0	6
	CHD, VSD	14	2	16
	CHD, TOF	7	0	7
	CHD, VSD, L.V	8	1	9
	Hypotrophy	4	1	5
	CHD	1	0	1
	CHD, Hypospadiasis	9	1	10
	CHD, TOF, PDA	0	1	1
	Cleft palate	3	0	3
	ASD, Left to right shunt	1	0	1
	Dextrocardia	4	1	5
	umblical hernia	0	3	3
	Meningocele	1	2	3
	Hemangioma	15	1	16
	PDA	0	10	10
	cleft lip and cleft palate			
Total		73	23	96

P value < 0.01

Table No:2 Association of congenital anomalies with history of folic acid intake

Congenital defects * history of folic acid intake Cross tabulation

Count		History of folic acid intake		Total
		No	Yes	
		Congenital defects	VSD, Hypospadiasis	
	CHD, VSD	14	2	16
	CHD, TOF	7	0	7
	CHD, VSD, L.V Hypotrophy	8	1	9
	CHD	4	1	5
	CHD, Hypospadiasis	1	0	1
	CHD, TOF, PDA	9	1	10
	Cleft palate	0	1	1
	ASD, Left to right shunt	3	0	3
	Dextrocardia	1	0	1
	umblical hernia	4	1	5
	meningocele	1	2	3
	hemangioma	3	0	3
	PDA	16	0	16
	cleft lip and cleft palate	0	10	10
	Total	77	19	96

P value <0.01

Pearson chisquare value = 59.429a

a. 24 cells (80.0%) have expected count less than 5. The minimum expected count is .20.

Table No: 3 Association of congenital anomalies with history of congenital disorder in family

congenitaldefects * history of congenital anomaly in family Crosstabulation

Count		History of congenital anomaly in family		Total
		yes	no	
Congenital defects	VSD, Hypospadiasis	6	0	6
	CHD, VSD	14	2	16
	CHD, TOF	7	0	7
	CHD, VSD, L.V Hypotrophy	8	1	9
	CHD	4	1	5
	CHD, Hypospadiasis	1	0	1
	CHD, TOF, PDA	9	1	10
	Cleft palate	0	1	1
	ASD, Left to right shunt	3	0	3
	Dextrocardia	1	0	1
	umblical hernia	0	5	5
	meningocele	0	3	3
	hemangioma	0	3	3
	PDA	6	10	16
	cleft lip and cleft palate	0	10	10
Total		59	37	96

P value <0.01

Pearson chisquare value = 61.851a

- a. 23 cells (76.7%) have expected count less than 5. The minimum expected count is .39.

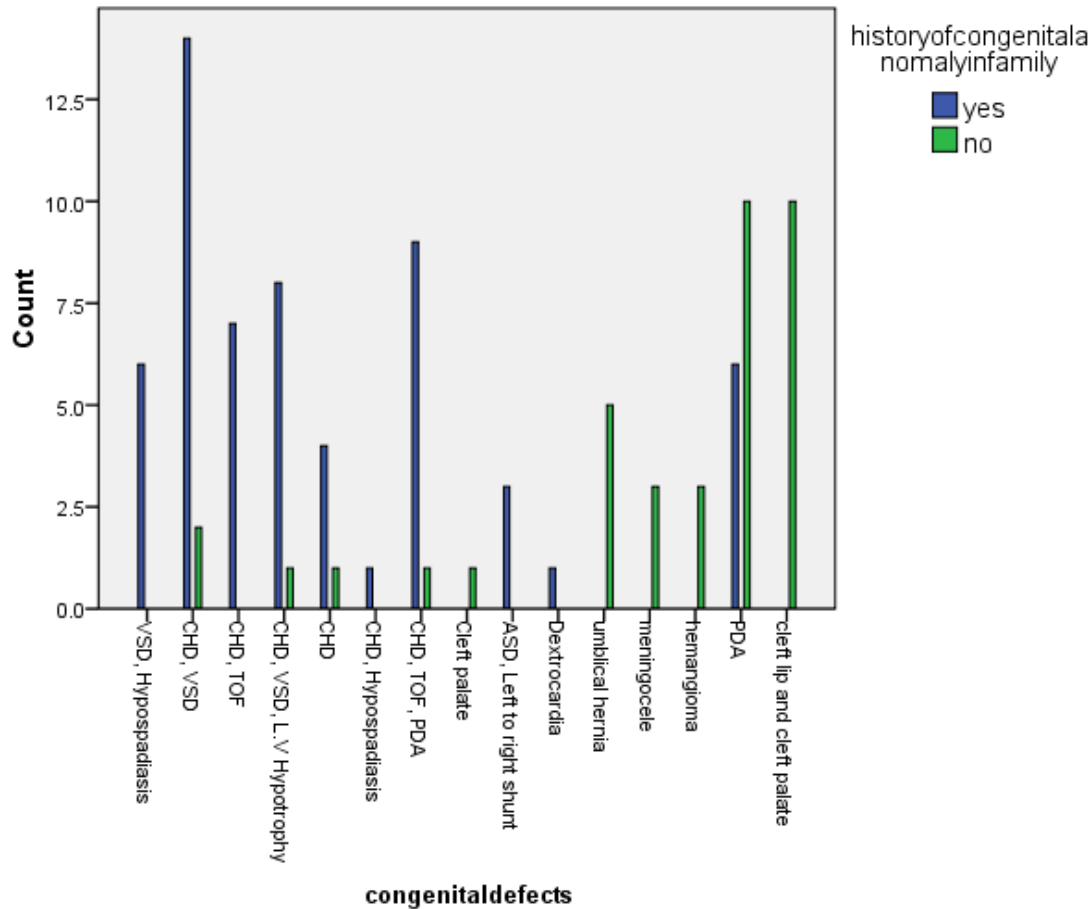


Fig 1: History of Congenital

Discussion:

CHDs not only increasing disease and deaths but also effects the psychological and economic status because of very expensive surgical interventions with poor outcomes in limited resources. Mortality due to CHDs is reported highest in Asia then other countries. This study reveals strong association between avoidable/modifiable risk factors. As majority of the study population is illiterate or less aware of health care and/ not facilitated by them. Moreover they have strong believes in myths and taboos, changes in rituals and customs are near sin to them which hamper them to avail health care facilities. Despite of having history of congenital anomaly in family, inter family marriages are not abided, no any medication including folic acid or any other

supplement is used in pregnancy or on the other hand self-medication. In this study higher incidence of cousin marriage, non-compliance in use of folic acid and positive family history are found linked with CHDs. [11]

This study reports 76% born to cousin married mothers and 61% with history of congenital anomalies in family. Al-Ani in from Iraq reports cousin marriage in (77.9%) very similar to this probably because of same social practices of interfamily marriages. While study from Egypt reveals cousin marriage in 44.6% cases and positive family history of CHD in 9.2% of cases and Haq et al. reports cousin marriage in 49% and positive family history in 14% The variances of results suggest difference in practices according to locale, study population and awareness regarding this issue and better healthcare system for early detection and management. [2, 12, 13] Regarding use of folic acid which is supposed to play role in prevention of CHD was taken by only 20% of mothers during pregnancy which was found significant with p value <0.01 Meta-analysis by Hassan et al and Feng reports intake of folic acid by mothers significantly decreased risk of CHDs. Another study reports marked decline in various CHDs including ventricular septal defect, tetralogy of Fallot, transposition of great arteries and atrial septal defect in infants born to mothers who had taken high doses of folic acid during the critical period of CHD development. [14, 15, 16]

Comment [n4]: The writing style is different.

Several studies suggests the role of avoidable factors in decreasing the disease from 14% to 30% But due to insufficient data and studies regarding this in various populations is controversial, which make it harder to refine any strategy and implication. [17, 18]

References:

1. Sehar T, Sheikh AM, Kanwal A. To identify pattern of congenital heart diseases in a newly developed tertiary care unit. Pak Armed Forces Med J 2019; 69 (4): 831-3
2. Haq F, Jalil F, Hashmi S et al. Risk factors predisposing to congenital heart defects Ann Pediatr Cardiol 2011;4:117-21
3. Khan AA, Khattak TA, Shah SHA, Roshan E, Haq AU (2012) Pattern of Congenital Anomalies in the Newborn. J Rawalpindi Med Coll 16: 1-3.

Comment [n5]: .

4. Soomro T, Tikmani SS (2016) Frequency of Birth Defects and its Relationship to Parents Having Interfamily Marriages at a Tertiary Care Hospital. *J Gen Pract (Los Angel)* 4: 265.
5. Chou HH, Chiou MJ, Liang FW, Chen LH, Lu TH, Li CY. Association of maternal chronic disease with risk of congenital heart disease in offspring. *CMAJ*. 2016;188(17-18):E438–46.
6. Liu S, Joseph KS, Lisonkova S, Rouleau J, Van den Hof M, Sauve R, et al. Association between maternal chronic conditions and congenital heart defects: a population-based cohort study. *Circulation*. 2013;128(6):583–9
7. Saidan MA, Ammari AN, Al Hashem AM, Al Rakaf MS, Shoukri MM, et al. (2015) Effect of Consanguinity on Birth Defects in Saudi Women: Results from a Nested Case-Control Study. *Birth Defects Res A Clin Mol Teratol* 103: 100-104
8. Asbagh PA, Rabbani A, Vafaei N, Rastegar SM, Moghadam A, Hojati V et al. Prevalence of Factors Associated with Congenital Heart Disease. *Multidiscip Cardio Annal*. 2021 January; 12(1):e106026.
9. Kloesel B, DiNardo JA, Body SC. Cardiac Embryology and Molecular Mechanisms of Congenital Heart Disease: A Primer for Anesthesiologists. *Anesth Analg*. 2016;123(3):551–569
10. Hotwani P, Goswami P, Kumar P, Das C. Spectrum and association of congenital heart defects with other congenital malformations in Sindh, Pakistan *RMJ* 2021;46(1):159-162
11. Jortveit J, Oyen N, Leirgul E, et al. Trends in mortality of congenital heart defects. *Congenit Heart Dis* 2016;11:160–8.
12. Al-Ani ZR (2010) Association of consanguinity with congenital heart diseases in a teaching hospital in Western Iraq. *Saudi Med J* 31:1021–1027
13. Al-Fahham MM, Ali YA. Pattern of congenital heart disease among Egyptian children: A 3-year retrospective study. *The Egyptian Heart Journal* (2021) 73:11
14. Hassan AF, Howsawi BM, Al Awwas MY, Alzein ZH, Alanazi FM, Faqehi HH, et al. The Correlation Between Infants' Congenital Heart Defects and Maternal Folic Acid Supplementation. *The Egyptian Journal of Hospital Medicine* (January 2018). 2018 Jan 5;70(5):771-6.

Comment [n6]: .

Comment [n7]: ?

Comment [n8]: The writing style is different.

Comment [n9]: ?

15. Feng Y, Wang S, Chen R, Tong X, Wu Z, Mo X. Maternal folic acid supplementation and the risk of congenital heart defects in offspring: a meta-analysis of epidemiological observational studies. *Scientific reports*. 2015 Feb 17;5:8506.
16. Czeizel AE, Vereczkey A, Szabó I. Folic acid in pregnant women associated with reduced prevalence of severe congenital heart defects in their children: a national population-based case-control study. *Eur J Obstet Gynecol Reprod Biol*. 2015 Oct; 193:34-9
17. Botto LD, Lin AE, Riehle-Colarusso T et al (2007) Seeking causes: classifying and evaluating congenital heart defects in etiologic studies. *Birth Defects Res A Clin Mol Teratol* 79:714–727.
18. Liu S, Joseph KS, Lisonkova S et al (2013) Association between maternal chronic conditions and congenital heart defects. *Circulation* 128:583–589.

UNDER PEER REVIEW