

**PREVALENCE OF ACYANOTIC CONGENITAL HEART DISEASE
AND IT'S ASSOCIATED FACTORS AMONG INBORN NEONATES - A
CROSS-SECTIONAL STUDY AT A TERTIARY CARE HOSPITAL IN
NORTH INDIA**

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ABSTRACT

OBJECTIVE: To study the prevalence of acyanotic congenital heart disease(CHD) and it's associated maternal and neonatal factors among inborn neonates.

STUDY DESIGN: This was hospital based retrospective cross sectional descriptive study, conducted over the period of 13 months in neonatal intensive care unit of a government teaching hospital.

MATERIALS AND METHODS: During this period, 4955 babies were born,50 newborns were found to have acyanotic CHD.The acyanotic CHD was confirmed by 2-dimensional echocardiography in accordance with standard transthoracic echocardiography guidelines by the cardiologist. Parents were individually administered a structured questionnaire consisting of personal and demographic information.The obstetric and neonatal variables were noted on a predesigned proforma. Data was analysed by using statistical package for social science software and p value <0.05 was considered significant to see the association between factors and non adherence.

RESULTS: The prevalence of acyanotic CHD was 10/1000 neonates. Atrial Septal Defects(ASD) was the commonest defect(64%) followed by Patent Ductus Arteriosus(PDA)(24%), Ventricular Septal Defects(VSD)(8%) and PFO(Patent Foramen Ovale)(4%). ASD and PDA were observed more in preterm neonates as compared to term and VSD was more in term neonates (p=0.023)).

Low birth weight babies had statistically significant association with CHD($P=0.04$). Maternal risk factors associated with acyanotic CHD were advanced age ($p=0.023$), upper lower and lower socioeconomic status($p=0.013$).

CONCLUSION: The prevalence of acyanotic was 10 per 1000. Predominant CHD was ASD. The acyanotic CHD was more in male, preterm and low birth weight babies. The mothers with advanced age, upper lower and lower socioeconomic status had increased prevalence of acyanotic CHD. ASD had statistically significant association with antenatal risk factors.

KEY WORDS: Prevalence, Congenital Heart Disease, Neonate

INTRODUCTION

The prevalence of congenital heart disease(CHD) in neonates is 5-8/1000 live births and accounts 28% of major congenital anomalies. It is a leading global health problem.[1-3]. CHD is a group of abnormalities in the heart structure or cardiovascular function occurring from birth, even if diagnosed later. These cardiac defects range from minor lesions with no clinical manifestations to potentially fatal conditions [4]. The incidence of CHD in India is increasing, probably due to increase of birth. 7% of the neonatal deaths are due to congenital malformations, 25% of which are cardiovascular. In India, 10% of the present infant mortality may be accounted for by CHD as reported by Saxena et al [5]. In developing countries like Jordan, though the incidence of CHD was high but majority were mild acyanotic CHD[6]. CHD are categorized into trivial, moderate and severe lesions or acyanotic vs. cyanotic defects according to the pathophysiology and affected heart structure [7].

Cyanotic heart diseases consist of tetralogy of fallot(TOF), pulmonary atresia, double outlet right ventricle (DORV), transposition of great arteries (TGA), single ventricle, pulmonary vein anomalies, truncus arteriosus, atrioventricular septal defects (AVSD), aortopulmonary window (AP Window). Acyanotic heart diseases consist of atrial septal defect(ASD), ventricular septal defect(VSD), patent ductus arteriosus(PDA), pulmonary stenosis (PS), coarctation of the aorta (CoA), aortic stenosis (AS), right and left ventricular hypertrophy (RVH and LVH), and mitral valve prolapse (MVP)[8]. All types of CHDs may severely reduce the quality of life of all family members, impose high costs on the health care system, necessitate adulthood follow-ups, repeated surgical

procedures [9].CHD appears to be a multifactorial disease caused by environmental and genetic factors [10].Environmental factors include a history of maternal illness during pregnancy, a positive familial history, the number of pregnancies, maternal hypertension, and medication exposure during pregnancy[11].This study aimed to describe the prevalence of acyanotic heart disease and its associated sociodemographic, obstetric and neonatal variables.

SUBJECTS AND METHODS :

This was hospital based retrospective cross sectional descriptive study, conducted in Government Medical College and Rajindra Hospital Patiala, Punjab over the period of 13 months from April 2022 to April 2023. During this period, 4955 babies were born,50 newborns were found to have acyanotic CHD.Informed consent was taken from parents.The acyanotic heart disease was confirmed by 2-dimensional echocardiography. Echocardiography was performed in accordance with standard transthoracic echocardiography guidelines[8] by the cardiologist. Parents were individually administered a structured questionnaire consisting of personal and demographic information, Obstetric variables like number of pregnancies, live birth, type of delivery, single or multiple gestation, pregnancy complications (Fever, Drug intake, Radiation exposure, Pregnancy Induced Hypertension(PIH),Gestational Diabetes Mellitus (GDM),Premature Rupture of Membranes (PROM) , Oligohydramnios(OHD) , Polyhydramnios(PHD), Anaemia and Hypothyroidism were noted. Neonatal variables like Gestation, Apgar score at birth , Babies weight (weighed on an electronic scale), Duration and type of oxygen therapy, acyanotic heart disease like Patent ductus arteriosus(PDA) Atrial septal defect(ASD), Ventricular septal defect(VSD),Patent foramen ovale(PFO) etc and Duration of hospital stay and final outcome i.e. survival at discharge was noted on a pre-designed proforma.Preterm were babies born before completed 37w.Appropriate for Gestational Age (AGA) were babies with birth weight between 10 -90th percentile for that gestation.Small for Gestational Age(SGA) were babies with birth weight less than 10th percentile for that particular gestation.Data was analysed by using statistical package for social science software and p value <0.05 was considered significant to see the association between factors and non adherence.

RESULTS:

The study was conducted in a tertiary care hospital in Punjab, India. 50 neonates were enrolled in this study. Among all acyanotic heart disease neonates, ASD was the most common diagnosis, seen in 64% of patients followed by PDA seen in 24% of the patients. Among 50 neonates, 4 (8%) had VSD and 2 (4%) neonates had PFO. (Table 1)

Table 1: Distribution of neonates by the type of CHD

CVS defect	Patients n =50	Percentage
ASD	32	64%
PDA	12	24%
VSD	4	8%
PFO	2	4%

It was observed that 59.8% (n=19) of the males had ASD as compared to 40.63% females (n=13) who had ASD. PDA and VSD was seen in 66.67% (n=8) and 75% (n=3) of males respectively as compared to 33.3% (n=4) and 25% (n=1) of females with p value of 0.19 that was statistically not significant.

This study revealed that ASD (75%) and PDA (83.3%) were more seen in preterm neonates as compared to term neonates and VSD was seen in 75% of term neonates and 25% of preterm neonates with p value of 0.02, that was statistically significant. The incidence of ASD, PDA, PFO and VSD was more among urban neonates as compared to rural area, that was statistically not significant (p=0.156). 65.6% of ASD, 33.3% of PDA and 50% of VSD were seen in neonates weighing 1500-2499 gm whereas 25% of ASD, 50% of PDA and 100% of PFO were in neonates weighing >2500 gram. It showed that the incidence of ASD and VSD was more in very low birth weight babies but the incidence of PDA and PFO were more in babies weight more than and equal to 2500 gram, that was statistically significant with p value of 0.03 (Table 2).

Table 2: Correlation of neonatal factors with acyanotic congenital heart disease

	ASD n=32	PDA n=12	PFO n=2	VSD n=4	X ²	p value
Sex						
Male	19 (59.38%)	8 (66.67%)	0 (0%)	3 (75%)	4.808	0.191
Female	13 (40.63%)	4 (33.33%)	2 (100%)	1 (25%)		
Gestational Age						
Term	8 (25%)	2 (16.67%)	1 (50%)	3 (75%)	5.771	0.023
Preterm	24 (75%)	10 (83.33%)	1 (50%)	1 (25%)		
AGA	27 (84.38%)	7 (58.33%)	2 (100%)	2 (50%)	5.398	0.157
SGA	5 (15.63%)	5 (41.67%)	0 (0%)	2 (50%)		

Birth weight						
1000-1499 gm	3 (9.38%)	2 (16.67%)	0 (0%)	2 (50%)	13.250	0.04
1500-2499 gm	21 (65.63%)	4 (33.33%)	0 (0%)	2 (50%)		
≥2500 gm	8 (25%)	6 (50%)	2 (100%)	0 (0%)		
Perinatal Asphyxia						
Yes	4 (12.50%)	1 (8.33%)	0 (0%)	0 (0%)	0.93	0.82
No	28 (87.50%)	11 (91.67%)	2 (100%)	4 (100%)		
Meconium Aspiration						
Yes	2 (6.25%)	0 (0%)	0 (0%)	0 (0%)	1.17	0.68
No	30 (93.75%)	12 (100%)	2 (100%)	4 (100%)		
Sepsis						
Yes	13 (40.63%)	6 (50%)	2 (100%)	2 (50%)	2.82	0.52
No	19 (59.38%)	6 (50%)	0 (0%)	2 (50%)		
O ₂ Req. by						
Prongs	20 (62.50%)	7 (58.33%)	1 (50%)	1 (25%)	5.072	0.76
CPAP	3 (9.38%)	3 (25%)	0 (0%)	1 (25%)		
Ventilator	9 (28.13%)	2 (16.67%)	1 (50%)	2 (50%)		
Duration of Stay						
<15 Days	21 (65.63%)	9 (75%)	0 (0%)	3 (75%)	4.46	0.64
16-30 Day	11 (34.38%)	3 (25%)	2 (100%)	1 (25%)		
>1 Month	0 (0%)	0 (0%)	0 (0%)	0 (0%)		
Condition at Discharge						
Satisfactory	27 (84.38%)	11 (91.67%)	2 (100%)	4 (100%)	3.27	0.642
Left in Between	1 (3.13%)	1 (8.33%)	0 (0%)	0 (0%)		
Death	4 (12.50%)	0 (0%)	0 (0%)	0 (0%)		

ASD (12.5%) and PDA (8.33%) were seen in neonates having perinatal asphyxia with p value of 0.92 (statistically not significant). Only 6.25% of ASD was seen in neonates with meconium aspiration with p value of 1.17, statistically not significant. Oxygen requirement among acyanotic heart disease neonates via prongs were 62.50% of ASD, 58.33% of PDA, 50% of PFO and 25% of VSD whereas mechanical ventilation was required in 28.13% of ASD, 16.7% of PDA, 50% of PFO and 50% of VSD neonates, that was statistically not significant with p value of 0.76 (table 2).

84.38% of ASD neonates, 91.67% of PDA, all the PFO and VSD patients were discharged under satisfactory condition, 12.50% of ASD patients were expired. (p value=0.642).

Most of the acyanotic heart disease occurred in the newborns whose mother age more than 30 years old (ASD 81.25%, PDA 91.67%, PFO 100% and VSD 75%), it was statistically significant with p value of 0.023. The mothers who belonged to upper lower and lower class had more incidence of congenital heart disease among newborns (ASD 37.50%, VSD 75%, PFO 100%, VSD 75% and ASD 62.50%, PDA 25% respectively) as compared to middle and high socioeconomic status mothers with p value of 0.013 (statistically significant as shown in table 3).

ASD was more seen in the neonates whose mother had fever (6.25%), history of drug intake (9.38%), Pregnancy induced hypertension (6.25%), Gestational diabetes mellitus (9.38%), Premature rupture of membrane (6.25%), Oligohydramnios (25%), Anaemia (21.88%), Hypothyroidism (15.63%) whereas PDA was seen among neonates whose mother had Anaemia (15.63%), Hypothyroidism (6.25%), Oligohydramnios (9.38%). It was statistically significant with p value of 0.02. Neonates who were born by cesarean had ASD (40.63%), PDA (25%), PFO (50%) and VSD (75%) while neonates born by normal vaginal delivery had ASD (59.38%), PDA (75%), PFO (50%) and VSD (25%) with p value of 0.455, that was statistically not significant.

Table 3: Correlation of maternal factors with acyanotic congenital heart disease

	ASD n=32	PDA n=12	PFO n=2	VSD n=4	X ²	p value
Age						
<20 Years	1 (3.13%)	1 (8.33%)	0 (0%)	1 (25%)	10.032	0.023
20-30 Years	5 (15.63%)	0 (0%)	0 (0%)	0 (0%)		
>30 Years	26 (81.25%)	11 (91.67%)	2 (100%)	3 (75%)		
Socioeconomic status					10.749	0.013
Upper	0 (0%)	0 (0%)	0 (0%)	0 (0%)		
Upper Middle	0 (0%)	0 (0%)	0 (0%)	0 (0%)		
Upper Lower	12 (37.50%)	9 (75%)	2 (100%)	4 (100%)		
Lower	20 (62.50%)	3 (25%)	0 (0%)	0 (0%)		

Antenatal factors						
Fever	2 (6.25%)	0 (0%)	0 (0%)	0 (0%)	51.55	0.02
Drug Intake	3 (9.38%)	0 (0%)	0 (0%)	0 (0%)		
Radiation Exposure	0 (0%)	0 (0%)	0 (0%)	0 (0%)		
Pregnancy induced hypertension(PIH)	2 (6.25%)	0 (0%)	0 (0%)	1 (25%)		
Gestational diabetes mellitus(GDM)	3 (9.38%)	1 (3.13%)	0 (0%)	0 (0%)		
Premature rupture of membrane(PROM)	2 (6.25%)	0 (0%)	0 (0%)	1 (25%)		
Oligohydramnios(OH)	8 (25%)	3 (9.38%)	2 (100%)	1 (25%)		
Polyhydramnios(PHD)	0 (0%)	1 (3.13%)	0 (0%)	0 (0%)		
Anaemia	7 (21.88%)	5 (15.63%)	0 (0%)	1 (25%)		
Hypothyroidism	5 (15.63%)	2 (6.25%)	0 (0%)	0 (0%)		
Pregnancy Type						
Single	25 (78.13%)	10 (83.33%)	2 (100%)	3 (75%)	0.716	0.869
Twin	7 (21.88%)	2 (16.67%)	0 (0%)	1 (27%)		
Triplet	0 (0%)	0 (0%)	0 (0%)	0 (0%)		
Mode of Delivery						
Cesarean	13 (40.63%)	3 (25%)	1 (50%)	3 (75%)	3.25	0.455
Normal vaginal delivery	19 (59.38%)	9 (75%)	1 (50%)	1 (25%)		

DISCUSSION:

This cross sectional and descriptive study was conducted in a tertiary care hospital in Punjab. In this study, 50 neonates were enrolled from April 2022 to April 2023. The prevalence of CHD was 10 per 1000 live birth in present study. The birth prevalence of CHD was 8 per 1000 live birth in a study done by Parvar SY et al [12]. It included both acyanotic and cyanotic CHD. The prevalence rate of CHD varies from as low as 1.3 per 1000 to as high as 13.28 per 1000 children in India [13].

Our study observed that ASD was most common acyanotic heart disease, seen in 64% of patients followed by PDA (24%) and then VSD (8%). Similar observation was seen in the study conducted by Parvar SY et al in 2023[12]. In this study, the most common acyanotic defects were ASD (85 in 1000 neonates), followed by PDA and VSD. In the study conducted by Rahim et al [14], Nikyar et al [15] and Pan et al [16], ASD was the most common acyanotic heart disease whereas in the study conducted by Kapoor and Gupta et al[17], VSD was seen in 21.3% and ASD in 18.0% of the cases and Meshram et al[18] reported VSD in 20.7% and ASD in 19% of the cases. But in our study, the second most common acyanotic heart disease was PDA. Naik et al [19] and Wanni et al [20] reported PDA as the second most common CHD. A study by Kafian et al that examined 300 neonates reported a PDA prevalence of (12.8%) as the second most common type of CHD[21].

It was observed that male had higher incidence of ASD (40.63%), VSD (75%) and PDA (66.67%) with p value of 0.19 that was statistically not significant. Elshazali H et al in 2020 conducted a study and observed male preponderance among neonates with congenital heart disease[22]. Wu et al[23], Nikyar B et al[24] and Zhao QM et al[25] also reported the higher incidence of congenital heart disease among male neonates as compared to female neonates.

Most of the acyanotic heart diseases occurred in the newborns whose mother age was more than 30 years old (ASD 81.25%, PDA 91.67%, PFO 100% and VSD 75%), it was statistically significant with p value of 0.023. In the study conducted by Reefhuis J et al[26] revealed the advanced maternal age may increase the possibility of new mutations in genes encoding some transcription factors associated with heart development. The mothers who belonged to upper lower and lower class had more incidence of congenital heart disease among newborns (ASD 37.50%, VSD 75%, PFO 100%, VSD 75% and ASD 62.50%, PDA 25% respectively) as compared to middle and high socioeconomic status mothers with p value of 0.013 (statistically significant). Similar results were seen in the study conducted by Xiaocheng Liu et al in 2015[27].

ASD was more seen in the neonates whose mother had fever (6.25%), history of drug intake (9.38%), Pregnancy induced hypertension (6.25%) Gestational diabetes mellitus (9.38%) Premature rupture of membrane (6.25%) Oligohydramnios (25%) Anaemia (21.88%) Hypothyroidism (15.63%) whereas PDA was seen among neonates whose mother had Anaemia (15.63%) Hypothyroidism (6.25%) Oligohydramnios (9.38%). It was statistically significant with p value of 0.02. It has been reported that the prevalence of fetal CHD cases with diabetic mothers was 3–5%[28]. Islam MN et al[29] revealed that maternal disease like diabetes mellitus, maternal infection, hypertension and some drugs might increase occurrence of heart disease in neonates.

The present study has some limitations. The neonates who could not survive after resuscitation at birth were excluded. Some acyanotic diseases may not manifest in neonatal age group. The study does not reflect the community data. However, burden of acyanotic heart diseases can guide the policy makers to focus on preventive steps.

CONCLUSION: The prevalence of acyanotic congenital heart disease was 10 per 1000. Predominant congenital heart defect was Atrial Septal Defect. The acyanotic CHD was more in male, pre-term and babies with low birth weight. The mothers with advanced age, upper lower and lower socioeconomic status had increased prevalence of acyanotic CHD. Atrial Septal Defects had statistically significant association with antenatal risk factors.

CONTRIBUTORS: AK conceptualized the study and collected the data. AK and MS analyzed and interpreted the data. MS wrote the manuscript and AK critically revised it. Both the authors approved the final manuscript.

Funding: Nil

Conflicts of Interest: None

Competing Interest: None

REFERENCES:

1. Dolk H, Loane M, Garne E. For the European Surveillance of Congenital Anomalies (EU-ROCAT) working Group. Congenital heart defects in Europe: prevalence and perinatal mortality, 2000- 2005. *Circulation*. 2011;123:841-9.
2. Samanek M, Voriskova M. Congenital heart disease among 815,569 children born between 1980 and 1990 and their 15 year survival: a prospective Bohemia survival study. *Pediatr Cardiol*. 1999;20:411-17.
3. Wren C, Richmond S, Donaldson L. Presentation of congenital heart disease infancy: implications for routine examination. *Arch Dis Child Fetal Neonatal Ed*. 1999;80:49-53.
4. Behrman RE, Kliegman RM, Jenson HB. Congenital heart disease. In: Behrman RE editor. *Nelson textbook of Pediatrics*, 16th edn. Eds., Harcourt Asia Pvt. Ltd;2000.p.1362-63.
5. Saxena A. Congenital heart disease in india: a status report. *Ind J Ped*. 2005;72:595-8.
6. Khasawneh W, Hakim F, Abu Ras O, Hejazi Y, Abu-Aqoulah A. Incidence and Patterns of Congenital Heart Disease Among Jordanian Infants, a Cohort Study From a University Tertiary Center. *Frontiers in pediatrics*. 2020;8:219. doi:10.3389/fped.2020.00219
7. Hoffman JIE, Kaplan S. The incidence of congenital heart disease. *J Am Coll Cardiol*. 39:1890–900. doi: 10.1016/S0735-1097(02) 01886-7.
8. Lancellotti P, Tribouilloy C, Hagendorff A, Bogdan AP, Thor Edvardsen, Luc AP, et al. Recommendations for the echocardiographic assessment of native valvular regurgitation: an executive summary from the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging*. 2013;14(7): 611-644.
9. Pinto Júnior VC, Branco KMPC, Cavalcante RC, Waldemiro CJ, Jose Rubens CL, Silvia DF, et al. Maria et al. Epidemiology of congenital heart disease in Brazil. *Revista Brasileira de Cirurgia Cardiovascular*. 2015;30(2):219-224.
10. Vecoli C, Pulignani S, Foffa I, Andreassi M. Congenital heart disease: the crossroads of genetics, epigenetics and environment. *Curr Genomics*. 2014;15(5):390-399. doi:10.2174/1389202915666140716175634

11. Ogeng'o JA, Gatonga PM, Olabu BO, Nyamweya DK, Ong'era D. Pattern of congestive heart failure in a Kenyan paediatric population. *Cardiovasc J Afr.* 2013;24(4):117-120. doi:10.5830/cvja-2013-015
12. Parvar SY, Ghaderpanah R, Naghshzan A. Prevalence of congenital heart disease according to the echocardiography findings in 8145 neonates, multicenter study in southern Iran. *Health Sci Rep.* 2023 Apr 4;6(4):e1178. doi: 10.1002/hsr2.1178.
13. Saxena A, Mehta A, Sharma M, Salhan S, Kalaivani M, Ramakrishnan S, Juneja R. Birth prevalence of congenital heart disease: A cross-sectional observational study from North India. *Ann Pediatr Cardiol.* 2016 Sep-Dec;9(3):205-9. doi: 10.4103/0974-2069.189122.
14. Rahim F, Ebadi A, Saki G, Remazani A. Prevalence of congenital heart disease in Iran: a clinical study. *J Med Sci.* 2008;8:547-552. doi:10. 3923/jms.2008.547.552
15. Nikyar B, Sedehi M, Mirfazeli A, Qorbani M, Golalipour MJ. Prevalence and pattern of congenital heart disease among neonates in Gorgan, Northern Iran (2007-2008). *Iran J Ped.* 2011;21(3): 307-312.
16. Pan F, Li J, Lou H, et al. Geographical and socioeconomic factors influence the birth prevalence of congenital heart disease: a population-based cross-sectional study in eastern China. *Curr Probl Cardiol.* 2022;47(11):101341.
17. Kapoor R, Gupta S. Prevalence of congenital heart disease, Kanpur, India. *Indian Pediatr* 2008;45(04):309–311.
18. Meshram RM, Gajimwar VS. Prevalence, profile, and pattern of congenital heart disease in Central India: A prospective, observational study. *Nig J Cardiol* 2018;15:45–49.
19. Naik S, Irshad M, Kachroo A, Ahmed M. A study of prevalence and pattern of congenital heart disease at Sopore, Kashmir, North India. *Int J Contemp Pediatr* 2019;6(02):275–279.
20. Wanni KA, Shahzad N, Ashraf M, Ahmed K, Jan M, Rasool S. Prevalence and spectrum of congenital heart diseases in children. *Heart India* 2014;2:76–79.
21. Kafian Atary S, Mirshahi A, Amouzesi A, Abbas AR, Zahra SK, Babak B, et al. Epidemiologic study of congenital heart diseases and its related factors in children referred to the pediatric cardiac clinic of Birjand University of Medical Sciences, Iran. *Int J Pediatr.* 2019;7(12):10455-10463.
22. Elshazali H, Elshazali O, Elshazali H. The relationship between birth weight and congenital heart disease at Ahmed Gasim Cardiac Centre, Bahri, Sudan. *Sudan J Paediatr.* 2017;17(2):49-55. doi:10. 24911/sjp.2017.2.6
23. Wu W, He J, Shao X. Incidence and mortality trend of congenital heart disease at the global, regional, and national level, 1990-2017. *Medicine.* 2020;99(23):e20593. doi:10.1097/md.00000000000020593
24. Nikyar B, Sedehi M, Mirfazeli A, Qorbani M, Golalipour MJ. Prevalence and pattern of congenital heart disease among neonates in Gorgan, Northern Iran (2007-2008). *Iran J Ped.* 2011;21(3): 307-312.
25. Zhao QM, Liu F, Wu L, Ma XJ, Niu C, Huang GY. Prevalence of congenital heart disease at live birth in China. *J Pediatr.* 2019;204: 53-58. doi:10.1016/j.jpeds.2018.08.040

26. Reefhuis J, Honein MA. Maternal age and non-chromosomal birth defects, Atlanta – 1968-2000: teenager or thirty-something, who is at risk? *Birth Defects Res A Clin Mol Teratol* 2004;70: 572–79.
27. Xiaocheng Liu, Gongshu Liu, Ping Wang, Yunzhou Huang, Enqing Liu, Dongbei Li, et al. Prevalence of congenital heart disease and its related risk indicators among 90 796 Chinese infants aged less than 6 months in Tianjin *International Journal of Epidemiology*, 2015, 884–893
28. Gao Y, Huang GY. Advance in the etiology and the epidemiology of congenital heart disease. *Chin J Evid Based Pediatr* 2008;3:213–22.
29. Islam MN, Hussain MA, Khaleque MA, Das MK, Khan MRH, Bari MS et al. Prevalence of congenital Heart Disease in Neonatal in a Tertiary Level Hospital. *NJMS*. 2013;2(2):91-5.