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Congenital Heart Diseases: Frequency of Different Acyanotic and Cyanotic Lesions in Children

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Abstract—

Introduction:

Cardiac diseases of congenital origin are the most frequent diseases affecting children especially in first year of life. The most common congenital heart disease is the Ventricular septal defects. OBJECTIVE: To determine the frequency of simple acyanotic and complex cyanotic lesions among children presenting with congenital heart diseases in a tertiary care hospital Nawabshah.

Study Design*: This study was cross sectional.*

Setting*: This research was carried out at Pediatrics unit of PMCH Nawabshah.*

Duration*: January 2017 to December 2017.*

Subject and Methods*: Data of 165 patients collected who admitted to department of Pediatrics at PMCH Hospital, Nawabshah. Patient's personal information like age, gender, family history of heart disease, collected and a questionnaire was filled. After clinical examination, Echocardiography was performed to confirm for findings of congenital heart disease.*

Results:

Sixty-three children (63%) had cyanotic CHD and 102(61.8%) had simple cyanotic CHD. TOF (Tetralogy of Fallot) was the commonest noted in 64(38.8%), followed by VSD (ventricular septal defect) in 48 (29.1%), ASD (atrial septal defect) in 15 (9.09%), tricuspid atresia in 19 (11.5%), pulmonary stenosis in 15(9.1%) and pulmonary atresia in 9 (5.5%) patients.

Conclusion*:*

Acyanotic CHD was the most common lesion than cyanotic CHD. Our study showed a high prevalence of CHDs in pediatric patients with genetic defects. VSD, AVSD, PDA, and ASD are the commonest CHDs in our study. We observed increased prevalence of congenital heart ailments in children. VSD, AVSD, PDA, and ASD were the frequent CHDs observed in current study.

Keywords— *Simple acyanotic, Complex cyanotic lesions, Congenital heart diseases*.

I. INTRODUCTION

Cardiac diseases of congenital origin still remain the most widespread diseases of heart affecting children especially in first year of life [1-4]. Worldwide 34.3 million children were affected according to 2013 estimates, and approximately every 8-76/1000 live births per year are affected leading to increased neonatal or infant's morbidity and mortality [3-7]. In infants 10.4% mortality has been reported due to cardiovascular malformation in a population based study due to malformation or its treatment [3].

The most common congenital heart disease was Ventricular septal defect seen in 37.2%. Pulmonary stenosis, Patent ductus arteriosus, Atrial septal defect each were observed in 12.6% of subjects. Tetralogy of fallot in 8.2% and coarctation of aorta was noted in 0.2% of subjects in order of frequency respectively. However, some studies have reported TOF (27.7 %) as the most common congenital heart disease [8]. Recent study at NICVD Karachi in 2016 has shown 60.6% simple acyanotic and complex CHDs 38.6% in subjects. Septal defect (simple) observed in 64.9% and obstructive lesions seen in 11.0% patients. In addition, they found TOF to be the most common congenital defect in 24.4%, VSD was in 21.5%, ASD in 9.3%, PDA in 8.6% and pulmonary stenosis seen in 3.1% of subjects respectively. [9], [10]

Respiratory distress in the children is the most common complain which can be life threatening and needs an urgent recognition and aggressive management. Symptoms usually present in early life while some remain asymptomatic and present later on. Chelon et al. had found 87.6% patients

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presenting with dyspnea, 50.5% with cough, and 81.4% with heart murmur on physical examination in CHD [6]. However, some reported respiratory problems like shortness of breath, cyanosis, decreased appetite, fatigue, peri-orbital puffiness, and palpitations. Clinical examination and screening together with Echocardiography are the important tools that aid in diagnosis of congenital malformation.

Therefore, we aimed in current research to determine the frequency of CHDs in children presenting with respiratory difficulty in general population, in order to investigate and identify the affected children by echocardiography as well as to explore the overall health burden of our society related to heart disease.

Objective

To conclude the occurrence of simple acyanotic as well as complex cyanotic lesions among children presenting with cardiac diseases of congenital origin at tertiary care hospital Nawabshah.

Operational Definition:

Congenital heart disease: CHD is a structural anomaly of the heart present since birth and diagnosed through echocardiography. It will include patients with simple acyanotic and complex cyanotic heart diseases.

Complex cyanotic heart disease: Presence of any one of the following will be labeled as Complex cyanotic heart disease. is present otherwise not present.

1. Tetralogy of Fallot (TOF): Characterized by four features by direct visualization through echocardiography these are:
   a. Ventricular Septal Defect (VSD)
   b. Right Ventricular Outflow Tract Obstruction (RVOTO)
   c. Overriding aorta
   d. Right Ventricular Hypertrophy
2. Truncus Arteriosus (Persistent): Pulmonary and systemic circulation both are supplied by a single trunk. Normally there are separate trunks for both pulmonary and aorta.
3. Tricuspid atresia: Agenesis of tricuspid valve detected on echocardiography.
4. Pulmonary atresia (PA): Among right ventricular outflow tract (RVOT) and pulmonary trunk there is absolute obstruction on echocardiography.
5. Pulmonary Stenosis: The RVOT (right ventricular outflow tract), pulmonary valve or pulmonary artery are narrowed as detected on echocardiography.

Simple acyanotic heart disease: Presence of any one of the following will be labeled as simple acyanotic heart disease.

Ventricular septal defect: Direct visualization of defect in the interventricular septum by echocardiography.

Atrial septal defect: Direct visualization of defect in the interarterial septum by echocardiography.

II. Material and Methods

Study Design: This study was cross sectional.

Setting: This research was carried out at Pediatrics unit of PMCH Nawabshah.

Duration: January 2017 to December 2017.

Sample size: After fulfilling the inclusion criteria, 165 patients of CHD were recruited in study, sample size was determined by 95% CI (confidence interval) and margin of error 7.5% taking prevalence of 38.6% of complex cyanotic heart disease. [9]

Sampling technique: Non-probability consecutive sampling technique was applied.

Sample selection:

Children of either gender between the ages from 2 months to 12 years admitted with congenital heart disease will be enrolled. History of asthma, or any other respiratory illness like; bronchitis, lung abscess, pneumonia by radiograph, history and examination, other causes of anaemia and those refused for consent were excluded from study.

Data collection procedure:

Information was gathered as of subjects admitted in department of Pediatrics at PMC Hospital, Nawabshah after meeting inclusion criteria and declaration of Ethical committee review study was done. Written informed authority was obtained from patient's parent or next to kin by researcher. Patient's personal information like age, gender, family history of heart disease, filled in questionnaire. After clinical examination, Echocardiography by cardiologist and technician was performed to confirm for findings of congenital heart disease.

Data analysis:

Computer based software SPSS version 20.0 was applied for analysis of collected data. Descriptive statistics presented for qualitative and quantitative variables. Frequencies and percentages calculated for gender, family history of heart disease, simple acyanotic and complex cyanotic heart diseases. Mean ± SD for age, weight were calculated. Effect modifiers as age, weight, gender, family history of heart disease be managed by stratification, post stratification and chi-square test were used keeping $P \leq 0.05$ as considerable.

III. Results

A total 165 subjects with confirmed CHD were enrolled in current study, out of them 87 (52.7%) boys and 78 (47.3%) were girls. Mean age of study subjects was 4.22 years (range 2 months to 12 years). The majority of the patients were underweight with mean weight of 15.9 kg (5.4-29 kg). Table 1

Family history for heart diseases was obtained in 72.1% (119) children. Sixty-three (38.2%) children had cyanotic CHD and 102(61.8%) had simple cyanotic CHD. TOF (Tetralogy of Fallot) detected in 64 (38.8%), VSD (ventricular septal defect) in 48 (29.1%), ASD (atrial septal defect) in15 (9.09%), tricuspid atresia in 19 (11.5%), pulmonary stenosis in 15(9.1%) and pulmonary atresia was found in 09 (5.5%) patients as shown in Figure 1.

Complex cyanotic lesions were more in male children 33(37.9%) as compared with female children 30(38.5%) and statically no significant difference was found with (P=0.94). Children with family history of heart disease had significantly more complex disease 49 (41.2%) than children presenting without family history of heart disease 14 (30.4%). Significant

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effect of family history of heart disease in children was observed with (P= 0.04).

Children who were underweight 40(44.9%) were likely to have a complex cyanotic lesions and 49 (55.1%) had simple acyanotic lesions with significant difference (P =0.05). Children with age of more than five years complex cyanotic heart disease was seen in 32.5% (25), and 56.8% (50) had simple acyanotic diseases, Children having five or less than five years of age (n = 38, 43.2%) had complex cyanotic and 52(67.5%) had simple acyanotic diseases. (P = 0.15).Table 2.

Table 1. Descriptive statistics. n=165

Variables	n	Mean	Std. Deviation
Age	165	4.22	2.97
Weight	165	15.9	5.41

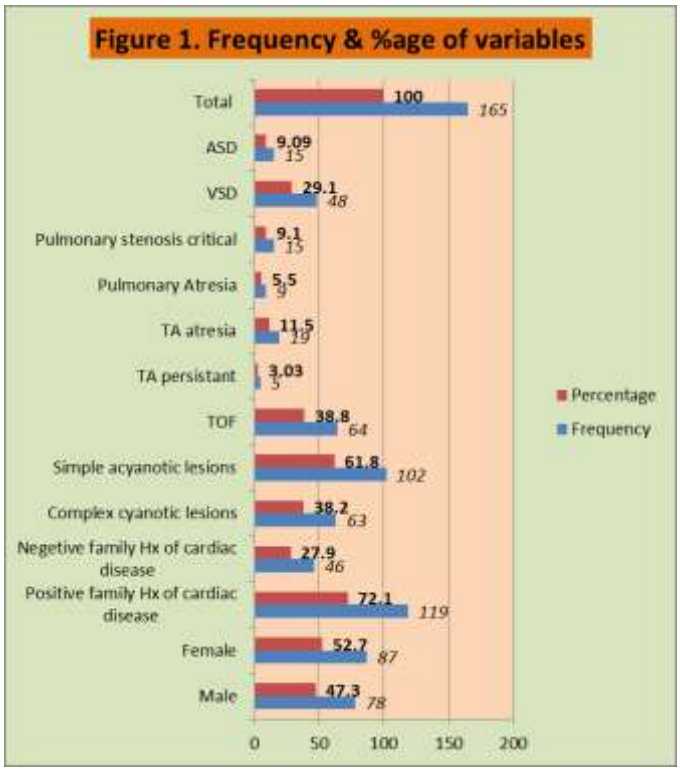

Table 2. Stratification for pattern of CHD with respect to effect modifiers. n=165

Variables		Complex Cyanotic Lesions	Simple Cyanotic Lesions	Total	P-value
Gender	Female	30(38.5%)	48(61.5%)	78(100%)	0.94**
	Male	33(37.9%)	54(62.1%)	87(100%)	
Family H/o Heart Disease	Yes	49(41.2%)	70(58.8%)	119(100%)	0.04*
	No	14(30.4%)	32(69.6%)	46(100%)	
Under Weight	Yes	40(44.9%)	49(55.1%)	89(100%)	0.05*
	No	23(30.3%)	53(69.7%)	76(100%)	
Age	</=5 yrs.	38(43.2%)	50(56.8%)	88(100%)	0.15**
	>5 yrs.	25(32.5%)	52(67.5%)	77(100%)	

IV. Discussion

Undiagnosed CHD convey an extreme danger of avoidable morbidity, mortality, and eternal disability. [11] Besides that inability to flourish, repeated infections, and under nourishment unfavorably influences the long haul wellbeing of these youngsters.

Limitations in everyday achievements also have a significant impact on social development of these children. The economic and social impacts on families are also significant in the absence of state-sponsored social support.

In this study, the distribution of CHD was quite similar to the previously documented data. Male predominance found in this study that also had been documented in previous regional studies. [12]

This may highlight a possible change in genetic substrate in South Asian populations resulting in higher incidence in males rather than equal gender distribution in Western population. Another factor is cultural wherein; a male child gets more attention and is more likely to be brought to attention earlier than a female child. The mean age of diagnosis from various developing countries has been recorded much higher (median 4 years) emphasizing the need for proper screening programs in developing countries. [13]Almost 60% children belonged to rural areas, a figure consistent with the general population, figures of rural population of Pakistan (62%) as well as South Asia (65%).[14]

Nearly two-third of all children with CHD were having severe malnutrition with no significant difference between children with cyanotic and acyanotic CHD (P = 0.5). The incidence of malnutrition with weight below third centile was much higher than international literature. Malnutrition is prevalent in the region (26%), however, our data suggests a significantly higher prevalence in children with CHD. [15]

Delayed diagnosis and late management not only compromised the optimal timing for intervention but also compounded by malnutrition that was significantly higher in children with delayed presentation when compared with normal population in this part of the world. [16]

This puts these patients at an added risk of morbidity and mortality from congenital heart surgery. [17]

This fact emphasizes additional need for nutritional and social support for these children as well as early interventions to prevent secondary complications from malnutrition itself.

In current study, acyanotic children had a much more delayed diagnosis than cyanotic children did. This finding was similar to the previous local data. [18] This difference could partly be because of clear finding of cyanosis in the children with CHD prompting early medical attention by the parents for the attending to specialist. On the other hand, acyanotic CHD with increased pulmonary blood flow were frequently misdiagnosed as pneumonia and accordingly managed until alternate diagnosis of CHD was established.

Parental education is an important determinant of delayed diagnosis of CHD. Literacy rate among mothers of children with CHD was only 54.0%. Mother's illiteracy was significantly associated with delayed diagnosis of children

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(179 vs. 13, P < 0.001). Interestingly, literacy rate among fathers was much lower than the national statistics (27% vs. 69%). This low literacy rate was probably related to socioeconomic status of the family. Delayed presentation in children with CHD was significantly associated with father's literacy (P < 0.001). This factor had also reported in the previous studies. [19] Hence, universal education for all is of utmost importance as literacy is equally important for mothers as well as fathers for proper care of their children and general awareness. [20]

It had been documented in a number of studies with smaller family size having a positive effect on better upbringing and optimal development of children. [21] Evidently, families with larger number of children can't focus socially or economically on one kid while ignoring others. [22]

Home deliveries by untrained birth attendants accounted for 77.1% of all deliveries and amounted to 88.6% of all children with delayed diagnosis. Almost all patients delivered at home (97%) had a delayed diagnosis. [23]

Distance from medical facility was an important factor in timely diagnosis of these children. [24]

Antenatal diagnosis by fetal echocardiography is a useful screening tool for recognizing an early CHD and thus preventing neonatal morbidity and mortality. Antenatal diagnosis is getting universal in developed countries. [25] Training the sonographers in a standard four-chamber and great vessels view on routine antenatal scans can increase the yield of a possible CHD significantly. [26]

In a local study high incidence of delayed diagnosis was 97%, [27] and this delay was mainly caused by difficult approach to a physician (37.2%) as most children with delayed diagnosis were residents of rural areas (60%) and belonged to poor socioeconomic strata (66%) and seek advice from unqualified, self proclaimed. [19]

Delayed diagnosis by a health professional (22.5%) is also a major reason. Lack of awareness among primary care medical professionals has been highlighted; additional training advocated timely and again avoiding missing such children in the previous studies. [23, 28]

Saxena et al. [19] also reported poverty, difficult access to tertiary care facility, and large family size as some of the factors responsible for delayed treatment of CHD in India. Chromosomal disorders, mutations, insertion or deletion at specific genes are usually related with CHDs and in one fourth of these patients had extra cardiac anomalies. [29-32] Logos observed that 68% of known genetic diseases were related with congenital heart diseases. [33] Down syndrome was the frequent; whereas Marfan´s, Noonan´s, Edwards, Prune Belly, Apert, Ellis-van Creveld and congenital rubella were the other syndromes observed. Genetic anomalies were seen in 64 subjects of CHD diagnosed on echocardiography. Trisomy 21 isolated in 71.2% of the study subjects with genetic defects. All these facts are supported by the prior studies, [29, 31, 34] but occurrence of CHD in down syndrome was more in Ghana and S Africa. [35-37]

Congenital heart diseases as AVSD, VSD, PDA, and ASD were the most common clinical abnormalities observed in subjects with Down's syndrome, [38] In Edwards anomaly CHD had been observed in 90% of subjects and in Patau syndrome CHD was seen in 80% of subjects along with dextro position. [39-41] Subjects with Turner had bicuspid aotic valve and aortic co-arctation (50% and15-30%) respectively [42]. An uncommon neuro developmental anomaly known as Williams Beuren and DiGeorge syndrome a velocardiofacial disease resulting due to 22q11 deletion present with classical features were also seen in subjects presenting with CHD. [34, 43-45]

AVSD, ASD and PS were common in Noonan syndropme. [46] Pulmonary stenosis was frequent in CHD subjects with Noonan syndrome. [47, 48]

V. CONCLUSION

Acyanotic CHD was the most common lesion than cyanotic CHD. Current research demonstrated a high prevalence of congenital heart diseases with genetic defects in pediatric subjects. In addition, the VSD, AVSD, PDA, and ASD were the frequent congenital heart diseases in this study. Mortality and morbidity can be avoided to an extent by improving poverty, early and appropriate screening and timely referral of these subjects to specific cardiac unit. CHDs are frequent in our population and it is observed that early diagnostic rates are inclining.

Furthermore, the general practitioners and pediatricians are make the diagnoses referral of CHD at earlier, and are conscious of the complications of CHD if referred not on time. The increased prevalence of CHD could be due to genetic grounds. Moreover, these positive facts it could not be disregarded that trouble of CHD is rising and a suitable populace based studies on a huge extent are required to approximate the frequency perfectly. It is also required to initiate extra cardiac units to facilitate early appropriate treatment.

REFERENCES

[1] Oster ME, Lee KA, Honein MA, Riehle-Colarusso T, Shin M, Correa A. Temporal trends in survival among infants with critical congenital heart defects. Pediatrics 2013;131:e1502-8.

[2] Peterson C, Ailes E, Riehle-Colarusso T,Oster ME, Olney RS, Cassell CH, et al. Late detection of critical congenital heart disease among US infants: estimation of the potential impact of proposed universal screening using pulse oximetry. JAMA Pediatr 2014;168:361-70.

[3] Wren C, Irving CA, Griffiths JA, O'Sullivan JJ, Chaudhari MP,Haynes SR, et al. Mortality in infants with cardiovascular malformations. Eur J Pediatr 2012;171:281-7.

[4] Mendis S,Puska P,Norrving B. World Health Organization. Global Atlas on Cardiovascular Disease Prevention and Control (PDF). WHO 2011;3:60.

[5] Milunsky A, Milunsky JM. Genetic disorders and the fetus: diagnosis, prevention, and treatment. John Wiley & Sons; 2015 Nov 9.

[6] Chelo D, Nguefack F, Menanga AP, Um SN, Gody JC, Tatah SA et al. Spectrum of heart diseases in children: an echocardiographic study of 1,666 subjects in a pediatric hospital, Yaounde, Cameroon. CardiovascDiagTher 2016;6(1):10-19. doi:10.3978/j.issn.2223-3652.2015.11.04.

[7] Mohammed NB,Chinnaiya AK. Evolution of foetal echocardiography as a screening tool for prenatal diagnosis of congenital heart disease. J Pak Med Assoc Sep 2011;61(9):904-9.

[8] Humayun KN, Atiq M. Clinical profile and outcome of Cyanotic congenital heart disease in Neonates. J Coll Physicians Surg Pak May 2008;18(5):290-3.

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[9] Pate N, Jawed S, Nigar N, Junaid F, Wadood AA, Abdullah F. Frequency and pattern of congenital heart defects in a tertiary care cardiac hospital of Karachi. *Pak J Med Sci*. 2016;32(1):79-84. doi:10.12669/pjms.321.9029.
[10] BakhtyarZahid S, Zeb Jan A, Ahmed S, Achakzai H. Spectrum of congenital heart disease in children admitted for cardiac surgery at Rehman Medical Institute, Peshawar, Pakistan. *Pak JMed Sci* 2013;29(1):173-76. doi:10.12669/pjms.291.2910.
[11] Massin MM, Dessy H. Delayed recognition of congenital heart disease. Postgrad Med J. 2006;82:468–70.
[12] Shirazi H, Haider N, Hassan M. Pattern of heart diseases in children. Ann Pak Inst Med Sci. 2008;4:50–5.
[13] Mocumbi AO, Lameira E, Yaksh A, Paul L, Ferreira MB, Sidi D. Challenges on the management of congenital heart disease in developing countries. Int J Cardiol. 2011;148:285–8.
[14] Rural population (% of total population) Available at: data.worldbank.org/indicator/SP.RUR.TOTL.ZS .
[15] Shah SM, Selwyn BJ, Luby S, Merchant A, Bano R. Prevalence and correlates of stunting among children in rural Pakistan. Pediatr Int. 2003;45:49–53.
[16] Vaidyanathan B, Nair SB, Sundaram KR, Babu UK, Shivaprakasha K, Rao SG, Kumar RK. Malnutrition in children with congenital heart disease (CHD) determinants and short-term impact of corrective intervention. Indian Pediatr. 2008;45:541–6.
[17] Panni RZ. Earlier surgical intervention in congenital heart disease results in better outcome and resource utilization. BMC Health Services Res. 2011;11:353.
[18] Khan IU, Muhammad A, Muhammad T. Pattern of congenital heart disease at Lady Reading Hospital, Peshawar. Gomel J Med Sci. 2011;9:174–7.
[19] Saxena A. Congenital heart disease in India: A status report. Indian J Pediatr. 2005;72:595–8.
[20] Children's HeartLink. Linked by a common purpose: Global efforts for improving pediatric heart health; A report by Children's HeartLink. 2007. Retrieved from: http://www.childrensheartlink.org/docs/globalreport .
[21] Juhn C. The quantity-quality trade-off and the formation of cognitive and non-cognitive skills: National Bureau of Economic Research. 2015
[22] Mughal AR, Sadiq M, Hyder SN, Qureshi AU, A Shah SS, Khan MA, Nasir JA. Socioeconomic status and impact of treatment on families of children with congenital heart disease. J Coll Physicians Surg Pak. 2011;21:398–402.
[23] Liberman RF, Getz KD, Lin AE, Higgins CA, Sekhavat S, Markenson GR, Anderka M. Delayed diagnosis of critical congenital heart defects: Trends and associated factors. Pediatrics. 2014;134:e373–81.
[24] Guy R, Donald J, Bijoy K, Eric R, Walter J, James B, et al. Remote telemedical interpretation of neonatal echocardiograms: Impact on clinical management in a primary care setting. JACC. 34;1;99:241–5.
[25] Brown KL, Ridout DA, Hoskote A, Hoskote A, Verhulst L, Ricci M, et al. Delayed diagnosis of congenital heart disease worsens preoperative condition and outcome of surgery in neonates. Heart. 2006;92:1298–302.
[26] Rychik J, Ayres N, Cuneo B, Gotteiner N, Hornberger L, Spevak PJ, et al. American Society of Echocardiography guidelines and standards for performance of the fetal echocardiogram. J Am Soc Echocardiogr. 2004;17:803–10.
[27] Ramegowda S, Ramachandra NB. An understanding the genetic basis of congenital heart disease. Indian J Hum Genet. 2005;11(1):14-23.
[28] Schultz AH, Localio AR, Clark BJ, Ravishankar C, Videon N, Kimmel SE, et al. Epidemiologic features of the presentation of critical congenital heart disease: Implications for screening. Pediatrics. 2008;121:751.
[29] Nisli K, Oner N, Candan S, Kayserili H, et al. Congenital heart disease in children with Down's syndrome : Turkish experience of 13 years. Acta cardiol. 2008 Oct;63(5):585-589.
[30] Hoe TS, Chan KC, Boo NY. Cardiovascular malformations in Malaysian neonates with Down's syndrome. Singapore Med J. 1990 Oct;31(5):474-476.
[31] Thienpont B, Mertens L, de Ravel T, Eyskens B, et al. Submicroscopic chromosomal imbalances detected by array-CGH are a frequent cause of congenital heart defects in selected patients. Eur Heart J. 2007 Nov;28(22):2778-2784.
[32] Johnson MC, Hing A, Wood MK, Watson MS. Chromosome abnormalities in congenital heart disease. Am J Med Genet. 1997 Jun 13;70(3):292-298.
[33] Ferencz C, Neill CA, Boughman JA, Rubin JD, et al. Congenital cardiovascular malformations associated with chromosome abnormalities: an epidemiologic study. J Pediatr. 1989 Jan;114(1):79-86.
[34] Meberg A, Hals J, Thaulow E. Congenital heart defects--chromosomal anomalies, syndromes and extracardiac malformations. Acta Paediatr. 2007 Aug;96(8):1142-1145.
[35] de Rubens Figueroa J, del Pozzo Magana B, Pablos Hach JL, Calderon Jimenez C, et al. Heart malformations in children with Down syndrome. Rev Esp Cardiol. 2003 Sept;56(9):894-899.
[36] Molteno C, Smart R, Viljoen D, Sayed R, et al. Twenty-year birth prevalence of Down syndrome in Cape Town, South Africa. Paediatr Perinat Epidemiol. 1997 Oct;11(4):428-435.
[37] Arthur JT. Cardiac lesions in "Trisomy 21" Ghanaian children. Ghana Medical Journal. 1995;29(1):617-620.
[38] Abbag FI. Congenital heart diseases and other major anomalies in patients with Down syndrome. Saudi Med J. 2006 Feb;27(2):219-222.
[39] Naguib KK, Al-Awadi SA, Moussa MA, Bastaki L, Gouda S, et al. Trisomy 18 in Kuwait. Int J Epidemiol. 1999;28: 711-716.
[40] Maeda J, Yamagishi H, Furutani Y, Kamisago M, et al. The impact of cardiac surgery in patients with trisomy 18 and trisomy 13 in Japan. Am J Med Genet A. 2011 Nov;155A(11):2641-2646.
[41] Rosa RF, Rosa RC, Lorenzen MB, de Oliveira CA, et al. Trisomy 18: frequency, types, and prognosis of congenital heart defects in a Brazilian cohort. Am J Med Genet A. 2012 Sept;158A(9):9:2358-2361.
[42] Donadille B, Rousseau A, Zenaty D, Cabrol S, et al. Cardiovascular findings and management in Turner syndrome: insights from a french cohort. Eur J Endocrinol. 2012 Oct;167(4):517-522.
[43] Del Pasqua A, Rinelli G, Toscano A, Iacobelli R, et al. New findings concerning cardiovascular manifestations emerging from long-term follow-up of 150 patients with the Williams-Beuren-Beuren syndrome. Cardiol Young. 2009 Dec;19(6):563-567.
[44] Eronen M, Peippo M, Hiippala A, Raatikka M, et al. Cardiovascular manifestations in 75 patients with Williams syndrome. J Med Genet. 2002 Aug;39(8):554-558.
[45] Lawrenson JB, Kalis NN, Pribut H, Hewitson J, et al. Why are some South African children with Down syndrome not being offered cardiac surgery? S Afr Med J. 2006 Sept;96(9Pt2):914-919.
[46] Mutesa L, Muganga N, Pierquin G, Ngendahayo L, et al. Clinical and cytogenetic profile of Down syndrome in Rwandan patients: Interest of prenatal diagnosis. Rwanda Medical Journal. 2007 March;66(1):5-10.
[47] Marino B, Digilio MC, Toscano A, Giannotti A, et al. Congenital heart diseases in children with Noonan syndrome: An expanded cardiac spectrum with high prevalence of atrioventricular canal. J Pediatr. 1999 Dec;135(6):703-706.
[48] Burch M, Sharland M, Shinebourne E, Smith G, Patton M, et al. Cardiologic abnormalities in Noonan syndrome: phenotypic diagnosis and echocardiographic assessment of 118 patients. J Am Coll Cardiol. 1993 Oct;22(4):1189-1192.