ORIGINAL ARTICLE
THE ROLE OF PULSE OXIMETRY IN THE EARLY DETECTION OF CONGENITAL HEART DISEASE IN NEONATES BEFORE HOSPITAL DISCHARGE

Abdollah Dehvari[1], Noor Mohammad Noori[1], Tahereh Boryri[1], Alireza Teimouri[1], Fatimah Davoudi[1]

[1]**Children and Adolescents Health research Center, Research Institute of Cellular and Molecular Science in Infectious Diseases, Zahedan University of Medical Science's, Zahedan, Iran**

Objectives: Infant screening for congenital heart disease (CHD) includes a straightforward bedside test called pulse oximetry. Low degrees of oxygen in the blood can be an indication of a critical CHD. The aim of the present study was to evaluate the role of pulse oximetry in the early detection of asymptomatic CHD in new borns before discharge from Hospital.

Methodology: This cross-sectional study conducted on 3151 term neonates first stage of SPO2 was performed 2-12 hours after birth. If SPO2 was < 95%, premeasured within the first 12 to 24 hours of life. If the neonates maintained their SPO2 <95, they shifted to pediatric cardiologist for echocardiography. For the statistical analyses, SPSS 18.0 (SPSS Inc., Chicago, IL) was used. The significant level considered less than 0.05.

Results: From 3151 neonates, 29 individuals had SPO2<95% in which 26 went under echocardiography and 3 missed. In these neonates 22 had CHD. The SPO2 had a diagnostic value of 85%. Maternal age and neonates' height at birth not changed based on healthy status and SPO2 levels. Gestational age had no association with healthy status and SPO2 levels, when maternal Diseases and weight at birth had a significant association with SPO2 levels at the second stage and health status.

Conclusion: From the present study concluded that a high and acceptable diagnostic value of 85% found for SPO2 to detect CHD in neonates in the first 24 hours of life. The factors of maternal diseases and weight at birth had a significant effect in this issue.

Keywords: early detection, CHD, pulse oximetry, neonates

INTRODUCTION

Congenital heart disease (CHD) is a set of heart structural abnormalities occurring during fetal development and is the most common type of birth defect leading death.[1] CHD can be subdivided in non-cyanotic and cyanotic. The cyanotic sometimes called critical CHD (CCHD) and in other side, can be further classified into 3 different types of lesions: right heart obstructive lesions, left heart obstructive lesions, and mixing lesions.[1-4] Most newborns are born with healthy heart and have enough oxygen in their blood. However, about 1% of newborns are born with a CHD in which a quarter of them are with CCHD.[5] Has been reported that newborns with CCHD are most at risk of death if not recognized and treated early.[6] The etiology of CHD is still unknown but recognized many cases are mufti-factorial and resulted from a combination of genetic predisposition and environmental risk factors.[7] At the same time, the CCHD is a high risk factor that threating neonates' life and is associated with systemic low cardiac output (LCO) requiring surgery or catheter-based intervention in the first year of life.[8]

Critical CHD included of; HLHS, coarctation of the aorta (COA) / interrupted aortic arch (IAA), TGA, TAPVR, critical aortic stenosis (AS), pulmonary atresia (PA) and tricuspid atresia (TA).[9]

Pulse oximetry is a simple, fast, inexpensive, and noninvasive method which can be used to show oxygen saturation in blood[10] and in this regards, has been reported that it is highly specific for detection of CCHD with moderate sensitivity.[11] The rationale and the main reason of using this method is that most CCHDs have a degree of hypoxaemia that would not necessarily produce visible cyanosis and therefore might not be clinically detectable. Although health-care systems and governments around the world are considering pulse oximetry as a screening strategy for newborn babies', but uncertainty exists about false-positive rates and test accuracy.[12] Strong evidence exists for health-care systems to consider pulse oximetry as a screening test for CCHD in asymptomatic newborn babies.[11]

Recently, several large European studies have strengthened and demonstrated that pulse oximetry as an adjunct to existing screening can increase CCHD detection rates to over 90%.[13] Notably, many studies also have reported detection of secondary targets, that is, test positive babies who have either non-critical CHD or serious non-cardiac illness such as congenital pneumonia, early-onset sepsis and pulmonary hypertension. In recent studies, between 30% and 70% of the false positives fell into this category.[14] As some of these conditions are potentially as deadly as a CCHD, this is a key and additional advantage of the test.[15] A recent systematic review and meta-analysis of 13 studies on 230 000 babies concluded that pulse oximetry is a highly specific (specificity 99.9%), moderately sensitive (sensitivity 76.5%, to 83.5%) test that meets the criteria for universal screening.[11]

Considering the matters mentioned above, the present study aimed to evaluate the role of pulse oximetry in the early detection of asymptomatic CHD in newborns before discharge from Hospital.

METHODOLOGY

According to the hospital birth registration system, 7272 neonates were delivered in the Ali Ebne Abitalib Hospital during the year of 2019. From these neonates, 5912 were term with gestation age higher than 37 weeks. From these term neonates, 3151 entered to the study because of inclusion and exclusion criteria. The study included consecutive infants born at our hospital, irrespective of mode of delivery, newborns with lung diseases or whose parent or guardian did not sign the informed consent excluded. Newborns with a gestational age < 37 weeks, sick babies admitted to neonatal units also were excluded from the survey. Due to a policy of early discharge in our hospital, the maximum age at pulse oximetry screening was 24 hours. Therefore, this cross-sectional study, conducted on 3151 term neonates. For the subjects, some measures recorded in a check list after birth such as sex, weight at birth, height at birth, gestation age, maternal diseases and age. First stage of pulse oximetry was performed 2-12 hours after birth by the well-experienced nursery personnel. Whether arterial oxygen saturation (SPO2) was < 95%, the measure rechecked after 12 to 24 hours (second phase). In the second phase, if the measure of SPO2 persisted to remain < 95% considered abnormal, shifted to pediatric cardiologist for electrocardiograph and more detailed examinations on the same day.

Saturation of peripheral oxygen (SPO2) was measured using a portable Rad-5™ handheld pulse oximeter with multisite sensor that prevents the pulse wave from hanging with the neonate's movements. This pulse oximeter signal is obtained by subtraction, making it more reliable than other equipment (Nellcor N-395, Nova Metrix MARS, and Philips Viridia 24C Rev BO), and has higher sensitivity and specificity. The measurement was taken during two minutes in the left lower extremity (post-ductal) until the reading remained the same in two determinations; the measurement was performed under physiological sleep and by only one member of the study team.

After the second phase screening, if the neonates had SPO2<95% referred to the cardiac center for echocardiography. An expert and experienced pediatric cardiologist performed the echocardiography to detect CHD.

The study approved by research committee of Zahedan University of medical sciences and coded as ir.zaums.rec.1398.067.

For the statistical analyses, SPSS 18.0 (SPSS Inc., Chicago, IL) used. The categorized variables are expressed as counts (percentages) and the continuous variables as means ± SD. The continuous variables were compared using the Mann-Whitney U test because data distribution were free, and the association between two categorized variables tested using non-parametric Chi-square test. The significant level considered less than 0.05.

RESULTS

The study aimed to diagnose CHD among neonates during the first 24 hours of life by pulse oximetry. In the first stage of measuring SPO2, the neonates categorized based on SPO2 ≤ 85%, Between 86%-90%, 91%-94% and ≥ 95% frequented of 5 (0.2%), 14(0.4%), 89(3.00%) and 3039 (96.4%) respectively. For those neonates with SPO2 <95%, the Pulse oximetry measuring repeated after 12 hours (The second step). In the second step of SPO2 measuring, from 5 neonates who had SPO2 ≤ 85%, an increase observed in 3 neonates to the level of 86-90%. From 14 neonates with SPO2 between 86-90%, an increase observed in 7 neonates to the level of 91-94% and one neonate had a jump to the normal level of SPO2. From 93 neonates that their SPO2 was between 90-94% levels, 82 had an increase to the normal status (≥ 95%). Therefore, in the second stage of SPO2 measuring, 2 neonates had SPO2 ≤ 85%, 9 neonates had PSO2 between 85-90%, 18 neonates had SPO2 between 90-94% and remained neonates (3122) had PSO2 ≥95%. From those 29 neonates with SPO2<95% that went under echocardiography, two were in SPO2≤ 85% level such that one had tricuspid atresia and one had transposition of the great arteries with intact ventricular septum (TGA+IVS). From those 9 neonates with SPO2 between 85-90%, one had

complete atrioventricular septal defect (AVSD), 4 had TGA, 3 had TOF and 1 missed echocardiography. From those 18 neonates with PSO2 between 90-94%, 4 were free of CHD and 2 missed echocardiography, 3 had AVSD, 2 had TOF, one had coarctation of aorta the remained (6 neonates) had VSD. In total, from 29 neonates with SPO2<95%, three refused echocardiography and from those 26 neonates that went under echocardiography, 22 neonates had CHD. It shows that Pulse oximetry can diagnose 86% of heart diseases.

Table 1 showed that from 3151 neonates, about 50.5% were boys. About 48.8% had gestation age of 37-38 weeks. About 59 (1.9%) and 60 (1.9%) and 7 (0.2%) of the mothers had diabetes mellitus, systemic hypertensions and diabetes mellitus with systemic hypertensions respectively. In total 22 (0.7%) of the neonates had heart diseases. About 184 (5.8%) were in low birth weight. Mother mean age at birth was 27.90±6.65 years. The mean weight at birth was 3086.63±384.34g. the mean of height at birth was 49.83±1.80 cm. Gestation age mean was 38.60±1.15 weeks.

Table 1: Descriptive statistics of the study variables based on their categorization

Statistics	Summary
Total (N)	**3151**
Sex	
Boys	1592 (50.5%)
Girls	1559 (49.5%)
Gestation Age (week)	38.6 ± 1.15
37-38 weeks	1538 (48.8%)
38-40 Weeks	1404 (44.6%)
>40 Weeks	209 (6.6%)
Mother diseases during pregnancy	
Diabetes mellitus	59 (1.9%)
Hypertension	61 (1.9%)
Diabetes mellitus and Hypertension	7 (0.2%)
Type of CHD in Neonate with SPO2<95%	
Healthy	3126 (99.21%)
Atrioventricular septal defect (AVSD)	4 (0.13%)
D-Transposition of the Great Arteries (dTGA)	5 (0.16%)
Tetralogy of Fallot (TF)	5 (0.16%)
Tricuspid atresia (TA)	1 (0.03%)
Coarctation of the aorta	1 (0.03%)
Ventricular septal defect (VSD)	6 (0.19%)
Refused to do Echocardiography	3 (0.1%)
Weight at Birth (g)	3086.63 ± 384.34
<2500g	184 (5.8%)
2500-3000g	1181 (37.5%)
3000-4000g	1760 (55.9%)
>4000	26 (0.8%)
Mother age at Birth (years)	27.9 ± 6.65
Height at birth (cm)	49.83 ± 1.8
SPO2 (2-12 h) %	96.86 ± 1.73
SPO2 (12-24 h) %	97.98 ± 1.11

Table 2 showed a comparison of maternal age and height at birth in health and CHD neonates as well as SPO2 levels. Resulted that maternal age and neonates' height at birth not changed based on healthy status and SPO2 levels.

Table 2: Maternal Age and height at birth comparison in neonates based on healthy status and SPO2 levels

	Participants		SPO2	
	Healthy	**CHD**	**<95%**	**≥95%**
Maternal Age				
Mean	27.8881	28.7097	28.38	27.89
Standard deviation	6.63972	7.60786	7.6	6.64
P-value	0.603		0.846	
Height at Birth				
Mean	49.8171	50.7419	50.28	49.82
Standard deviation	1.79079	2.12866	1.75	1.8
P-value	0.039		0.846	

Table 3 showed the association of maternal diseases, weight at birth and gestational age in healthy status and SPO2 levels. Resulted that gestational age had no association with healthy status and SPO2 levels, when Maternal diseases and weight at birth had a significant association with SPO2 levels at the second stage and health status.

Table 3: Maternal Disease, weight at birth and Gestational Age association with healthy status and SPO2 levels in neonates

Statistics	Total	Participants			SPO2	
		Healthy	**CHD**	**Missed ECHO**	**<95%**	**≥95%**
Total (N)	**3151**	**3126**	**22**	**3**	**29**	**3122**
Maternal Diseases						
Diabetes mellitus	59 (1.9%)	56 (1.8%)	3 (13.6%)	0 (0%)	3 (10.3%)	56 (1.8%)
Hypertension	61 (1.9%)	61 (2%)	0 (0%)	0 (0%)	1 (3.4%)	60 (1.9%)
Free of illness	3024 (96%)	3004 (96.1%)	17 (77.3%)	3 (100%)	23 (79.3%)	3001 (96.1%)
Diabetes mellitus and Hypertension	7 (0.2%)	5 (0.2%)	2 (9.1%)	0 (0%)	2 (6.9%)	5 (0.2%)
P-value	-	<0.001			<0.001	
Weight at Birth						
<2500g	184 (5.8%)	184 (5.9%)	0 (0%)	0 (0%)	0 (0%)	184 (5.9%)
2500-3000g	1181 (37.5%)	1176 (37.6%)	5 (22.7%)	0 (0%)	7 (24.1%)	1174 (37.6%)

3000-4000g	1760 (55.9%)	1742 (55.7%)	15 (68.2%)	3 (100%)	20 (69%)	1740 (55.7%)
>4000	26 (0.8%)	24 (0.8%)	2 (9.1%)	0 (0%)	2 (6.9%)	24 (0.8%)
P-value	-	0.001			0.001	
Gestation age						
37-38	1538 (48.8%)	1527 (48.8%)	10 (45.5%)	1 (33.3%)	13 (44.8%)	1525 (48.8%)
38-40	1404 (44.6%)	1392 (44.5%)	10 (45.5%)	2 (66.7%)	14 (48.3%)	1390 (44.5%)
>40	209 (6.6%)	207 (6.6%)	2 (9.1%)	0 (0%)	2 (6.9%)	207 (6.6%)
P-value	-	0.92			0.91	

DISCUSSION

Congenital heart diseases (CHD) are the leading causes of infant deaths in the world such that delay in diagnosis is associated with a worse preoperative condition[16] such that their early diagnosis and timely intervention can significantly reduce the likelihood of an adverse outcome.[17]

The present study aimed to detect CHD in new borns baby by screening pulse oximetry and resulted that in the first phase SPO2 (within 2-12 hours after birth), 3.4% of the neonates had SPO2<95%. In the second phase, 22(0.70%) of neonates had SPO2<95%. These neonates were referred to the cardiac center to assess their probable CHD and found that from them, 6 neonates had VSD, 5 neonates had TOF, 4 neonates had AVSD, 5 neonates had dTGA, and from 2 remained neonates, one had coarcation and one had TA.

Movahedian et al.[10], conducted a study on 3,846 newborns to detect CHD by screening SPO2. They resulted that at the first phase (at least 2 hours after birth) measuring SPO2, 7.9% (384) had SPO2< 95%. For every neonate, the second saturation measurement performed 2 hours later that neonates with SPO2 < 95% decreased to 2.7% (104). In their study, from these 104 neonates with SPO2<95%, 14 neonates had CHD, 67 were free of CHD when 23 neonates missed the study due to unknown reasons. This pattern showed, a prevalence of 3.6 in 1000 live birth. Of 14 CHD neonates 11 had critical CHD with the prevalence of 2.86 in 1000 live birth.

Taksande et al.[16], led a study on 2110 neonates to detect CCHD by pulse oximetry. They measured the SPO2 in two phases, the first phase performed within first 4 hours of life and resulted that 8 neonates had SPO2<90% and 102 had 90-95%. The second phase of SPO2 measured on 102 neonates such that, 98 neonates had an increase in SPO2 to 95% and 4 neonates had SPO2<95%. Overall, 12 neonates referred to cardiologist. Of 8 neonates from the first phase, one had TAPVC, one had TOF, 3 had dTGA, 2 had TA and one was free of CHD. Of 4 neonates from the second phase, one had VSD, one had PDA and two were normal. In overall, 9 neonates had CHD that shows the prevalence of 4.3 in 1000 live births.

Slitine et al.[18], measured pulse oximetry to find CHD on 10451 live birth. From 8013 eligible neonates, 15 had SPO2<95% in which 5 had CCHD, 5 had other types of CHD with the prevalence of 1.25 in 1000 live birth. The 5 remained neonates had other type of diseases such as persistent pulmonary hypertension and sepsis. Campbell et al.[16], measured pulse oximetry to evaluate the CCHD and concluded that mandatory pulse oximetry screening legislation did not change the late CCHD postnatal diagnosis rate in their cohort. The vast majority of newborns with CCHD were diagnosed prenatally. Of those diagnosed postnatal, most were diagnosed early postnatal. a small number; three subjects were diagnosed with dTGA, four with total anomalous pulmonary venous return, one with aortic coarctation and one with interrupted aortic arch.

In the Tekleab et al.[19], study, during the initial screening, from all neonates that entered to the study, 13.1% and 7.4% had foot and right arm SPO2 <95%respectively. In the second or third phase, 39.4% had SPO2 of <95%. Echocardiography examination was done for those newborns and resulted that 11 neonates suffered from PDA, 10 with Persistent pulmonary hypertension of the newborn (PPHN), 2 with ASD and 33 were free of CHD. No case of CCHD was detected among the screened newborns in this study. In a systematic review study by Liu et al.[20], shown that the CHD prevalence was 9.41 in 1000 live birth. Similar to the present study, it seems that in the majority of studies, SPO2 screening performed in two phases. And after the second phase, if the SPO2 was lower than 95% referred to cardiologist. The present study resulted that after the second phase SPO2 screening, the number of neonates with CHD were 22 that shows a prevalence of 6.98 In 1000 live births and the number of neonates with CCHD were 11 with the prevalence of 2.86 in 1000 live births. The difference between the mentioned above literatures and the present study probably is due to the time duration between the first and the second phase of the SPO2 measuring. Gopalakrishnan et al.[21], studied SPO2 to detect critical CHD in asymptomatic newborns. They considered echocardiography as a gold standard in competition with SPO2 screening.

They found that the sensitivity, specificity of pulse oximetry screening to detect CHD was 75% and 99.29% respectively. From the late study that mentioned here, a fact confirmed about the ability of SPO2 to detect heart diseases. In the other side, CCHD may not be apparent at the time of early discharge examination, post-ductal arterial pulse oximetry screening during the first 24 hours of life has been put forth as the most useful strategy to prevent circulatory collapse or death.[16] Most of the mentioned studies have suggested that performing pulse oximetry on all neonates before hospital discharge is an effective screening tool for detection of CHD. Mostly in medical care centers, SPO2 not performed routinely prior to discharge and it is a reason for rising prevalence of CHD in infancy. Taksande et al.[16], found that based on SPO2≥90% and SPO2<90% mean gestation age was 38.6 and 38.2 weeks, mean weight at birth was 2700 and 2300 gram, respectively. Purkey et al.[22], study noted maternal age had a significant association with CHD such that, the majority of mothers with age >35 at delivery time had neonates with CHD. Neonates birth weight was associated with CCHD such that the percentages of low birth weight(<2500g) neonates were significantly more in CCHD neonates compared with those who neonates were free of CCHD. In addition, they found a significant association between gestational age and CHD. They also found that most of the neonates with CCHD had lower gestational age compared to healthy children and preterm neonates were more at risk of CHD compared to term neonates. Steurer et al.[23], in the study resulted that male neonates were more at CHD risk that issued due to SPO2 in the second phase. They also did not find any risk of CHD due to differences in weight and height at birth. They also found that maternal age at childbirth >34 was a cause of an increase in CHD risk in neonates. Maternal diseases such as diabetes mellitus and systemic hypertension showed to have a positive effect of CCHD in neonates. In this regards, the results from the mentation study are similar to our findings. Despite the ability of SPO2 to detect most cases of CCHD, it is not without limitation. The commonest lesions missed by pulse oximetry are those causing obstruction to the aorta. they are even frequently missed by prenatal ultrasound and routine physical examination. Therefore, pulse oximetry may be used as an adjunct to other screening methods rather than as a substitute.

An important limitation in the present study was long time interval between the first and the second phase of SPO2 measuring (12 hours).

CONCLUSION

From the present study concluded that a high and acceptable diagnostic value of 85% found for SPO2 to detect CHD in neonates in the first 24 hours of life. The factors of maternal diseases and weight at birth had a significant effect in this issue. It is suggested that to early CCHD identification in neonates, SPO2 screening is a toll with high sensitivity and is necessary to be performed before health care centre discharge after delivery.

AUTHORS' CONTRIBUTION:

AD: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. AD, NMN, TB, AT, FD: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

Conflict of interest: Authors declared no conflict of interest.

REFERENCES

1. Desai K, Rabinowitz EJ, Epstein S. Physiologic diagnosis of congenital heart disease in cyanotic neonates. Curr Opin Pediatr. 2019;31(2):274-83.
2. Segura T, Gatzoulis MA. Where are we with coronary artery disease for the cyanotic patient with congenital heart disease? Int J Cardiol. 2019;277:108-9.
3. Mohammad Nijres B, Samuel BP, Vettukattil JJ. Subclinical atherosclerosis in patients with cyanotic congenital heart disease. Int J Cardiol. 2019;282:44.
4. Schaan CW, Feltez G, Schaan BD, Pellanda LC. Functional capacity in children and adolescents with congenital heart disease. Rev Paul Pediatr. 2019;37(1):65-72.
5. Tekgündüz KŞ, Bilen M, Kara M, Laloğlu F, Ceviz N. Oxygen saturation and perfusion index screening in neonates at high altitudes: can PDA be predicted?. Eur J Pediatr. 2021;180:31-8.
6. Campbell MJ, Quarshie WO, Faerber J, Goldberg DJ, Mascio CE, Blinder JJ. Pulse Oximetry Screening Has Not Changed Timing of Diagnosis or Mortality of Critical Congenital Heart Disease. Pediatr Cardiol. 2020:1-6.
7. Bravo-Valenzuela NJ, Peixoto AB, Júnior EA. Prenatal diagnosis of congenital heart disease: A review of current knowledge. Indian Heart J. 2018;70(1):150-64.
8. Khalil M, Jux C, Rueblinger L, Behrje J, Esmaeili A, Schranz D. Acute therapy of newborns with critical congenital heart disease. Transl Pediatr. 2019;8(2):114.
9. Yun SW. Congenital heart disease in the newborn requiring early intervention. Korean J Pediatr. 2011;54(5):183.
10. Movahedian AH, Mosayebi Z, Sagheb S. Evaluation of pulse oximetry in the early detection of cyanotic congenital heart disease in newborns. J Tehran Univ Heart Cent. 2016;11(2):73.
11. Thangaratinam S, Brown K, Zamora J, Khan KS, Ewer AK. Pulse oximetry screening for critical congenital heart defects in asymptomatic newborn babies: a systematic review and meta-analysis. Lancet. 2012 ;379(9835):2459-64.
12. Mahle W, Koppel R. Screening with pulse oximetry for congenital heart disease. Lancet. 2011;378:749-50.
13. Ewer AK, Furmston AT, Middleton LJ, Deeks JJ, Daniels JP, Pattison HM, et al. Pulse oximetry as a screening test for congenital heart defects in newborn infants: a test accuracy study with evaluation of acceptability and cost-effectiveness. Health Technol Assess. 2012;16(2):1-84.
14. Ewer AK. Review of pulse oximetry screening for critical congenital heart defects in newborn infants. Curr Opin Cardiol. 2013;28:92-6.

15. Powell R, Pattison HM, Bhoyar A, Furmston AT, Middleton LJ, Daniels JP, et al. Pulse oximetry screening for congenital heart defects in newborn infants: an evaluation of acceptability to mothers. Arch Dis Child Fetal Neonatal Ed. 2013;98(1):F59-63.
16. Taksande AM, Lakhkar B, Gadekar A, Suwarnakar K, Japzape T. Accuracy of pulse oximetry screening for detecting critical congenital heart disease in the newborns in rural hospital of Central India. Images in Paediatr Cardiol. 2013;15(4):5.
17. Kumar P. Universal pulse oximetry screening for early detection of critical congenital heart disease. Clinical Medicine Insights: Pediatrics. 2016 ;10:CMPed-S33086.
18. El IdrissiSlitine N, Bennaoui F, Sable CA, Martin GR, Hom LA, FadelA, et al. Pulse oximetry and congenital heart disease screening: Results of the first pilot study in Morocco. Int J Neonatal Screen. 2020;6(3):53.
19. Tekleab AM, Sewnet YC. Role of pulse oximetry in detecting critical congenital heart disease among newborns delivered at a high altitude setting in Ethiopia. Pediatric Health M Ther. 2019;10:83.
20. Liu Y, Chen S, Zühlke L, Black GC, Choy MK, Li N, et al. Global birth prevalence of congenital heart defects 1970–2017: updated systematic review and meta-analysis of 260 studies. Int J Epidemiol. 2019;48(2):455-63.
21. Gopalakrishnan S, Karmani S, Pandey A, Singh N, Kumar JR, Praveen R, et al. Pulse oximetry screening to detect critical congenital heart diseases in asymptomatic neonates. Med J Armed Forces India. 2021;77(2):214-9.
22. Purkey NJ, Axelrod DM, McElhinney DB, Rigdon J, Qin F, Desai M, et al. Birth location of infants with critical congenital heart disease in California. Pediatr Cardiol. 2019;40(2):310-8.
23. Steurer MA, Baer RJ, Keller RL, Oltman S, Chambers CD, Norton ME, et al. Gestational age and outcomes in critical congenital heart disease. Pediatrics. 2017;140(4).

Address for Correspondence:

Dr. Alireza Teimouri, Children and Adolescents Health research Center, Research Institute of Cellular and Molecular Science in Infectious Diseases, Zahedan University of Medical Science's, Zahedan, Iran.
Email: alirezateimouri260@gmail.com