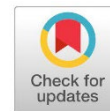


Research Article

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Prevalence of Congenital Heart Disease Among Preterm Newborns Between 28 and 35 Weeks Admitted at Al Bayda Medical Center, Libya (2021)

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Abstract

Congenital heart diseases (CHDs) are defined as structural abnormalities of the heart. CHD can be simple (isolated lesions) or complex (multiple lesions). Premature infant (newborn delivered before 37 weeks of geospatial age). This study was carried out to determine the prevalence of CHD among very preterm to moderate premature newborns and to investigate associated risk and mortality. A prospective cohort study was designed with concurrent timing of data collection and was carried out in the Department of the Neonatal Intensive Care Unit (NICU) at Al Bayda Medical Center (2021), Gestational age was calculated as postnatal assessment by the Dubowitz/Ballard method. Echocardiography was done to identify the presence and types of congenital heart defects. Out of 60 admitted preterm infants, 43 were found to have congenital heart disease. The prevalence rate was (71.67%) of admissions. Out of the total defects, Echocardiographic findings showed that atrial septal defect (ASD) was the most common structural defect no=30 (69.77%), (Patent ductus arteriosus) PDA no=12 (27.91%), and ventricular septal defect (VSD) no=10 (23.26%). Of the studied premature infants, 9 patients died during the study period. The case fatality rate (CFR) was (15%). Death rates were higher for premature neonates with CHD 7 (16.3%) than those with normal hearts, which were 2 (11.8%), but the observed difference was statistically not significant. Congenital heart anomalies are not significantly associated with birth weight and gender or maternal age, consanguinity, maternal socioeconomic state, and maternal illness. Conclusion: CHD was found to be high among preterm. The most common heart defect was ASD, followed by PDA and VSD.

Keywords: Congenital heart disease, Prevalence, Premature, Mortality, Risk factors, NICU.

INTRODUCTION

Congenital heart disease, representing structural or functional abnormalities present at birth, is a global health challenge, affecting 8 million newborns annually, available by (Mashuda et al., 2014; Shetty et al., 2023). CHDs are diagnosed according to the International Pediatric and Congenital Cardiac Code (IPCCC) (Franklin et al., 2017). CHDs usually in need of intervention



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or close follow-up the first year of life were defined as severe CHDs (Lytzen et al., 2018): [Single ventricle, hypo-plastic left heart syndrome (HLHS), transposition of the great arteries (TGA), congenitally corrected TGA (ccTGA), tetralogy of Fallot (TOF), double outlet right ventricle (DORV), truncus arteriosus, coarctation of the aorta (CoA) aortic arch hypoplasia, and interrupted aortic arch (IAA), atrioventricular septal defect (ASD, VSD), total anomalous pulmonary venous connection (TAPVC), and other complex CHD].

Preterm birth is defined as the birth of a baby less than 37 weeks of gestational age (Quinn et al., 2016). According to the World Health Organization (WHO, 2023), preterm births are those delivered before 37 weeks of pregnancy. Preterm birth is further subdivided based on gestational age: extremely preterm (less than 28 weeks), very preterm (28 to less than 32 weeks), and moderate to late preterm (32 to 37 weeks). Worldwide 5%-18% of newborns are born premature, and preterm birth is considered the leading cause of childhood mortality and morbidity (Liu et al., 2016; Saigal & Doyle, 2008). Preterm delivery remains a significant clinical problem, accounting for all neonatal morbidity and mortality. Preterm birth is a leading cause of death in children under five years of age globally (IGME, 2018).

Congenital heart diseases are major causes of morbidity and remain the leading cause of childhood mortality and morbidity (Jacobs et al., 2016; Lopes et al., 2018; Mackie et al., 2017). Preterm birth has also been associated with the risk of cardiovascular disease in adult life (Markopoulou et al., 2019; Saigal & Doyle, 2008).

The combination of CHD and preterm birth has shown higher increases in mortality and morbidity. Previous studies have shown associations between some subgroups of CHD and increased risks of preterm birth (Laas et al., 2012; van Velzen et al., 2016). The lower the gestational age, the higher the frequency of onset of PDA (Jasani et al., 2023).

Prevalence of CHDs and defect types depended upon factors like the nature of the study center (whether it is a tertiary level hospital where all critical obstetrical cases were admitted, nature of the sample, source of information, spot examination by a pediatric cardiologist, whether Eco cardiology is done for all suspected cases who are at risk of having CHD. This study aimed to determine the prevalence of congenital heart disease among very preterm to moderate premature newborns and associated risk and mortality.

MATERIALS AND METHODS

Study design and settings: A prospective cohort study design with concurrent timing of data collection was carried out to investigate the prevalence of CHD and associated risk factors among newborns delivered at Al Bayda Medical Center (secondary hospital). This study was conducted from the 1st of January to the 31st of December through the year (2021) on 60 preterm infants with and without CHDs.

Sampling method: Purposive sampling was used to target all premature newborns born through one year (2021). Inclusion criteria involve all premature infants in the study reference period and screened by echocardiogram. Exclusion criteria: extremely preterm, as their conditions are usually critical, in addition to those critically ill, were excluded, also, late preterm >36 were usually well and discharged, in addition to newborns discharged against medical advice and those referred to other centers after birth due to additional reasons.

Source of data: A questionnaire was prepared by the researcher where the study group was pre-

term infants with and without CHDs, which included detailed history regarding preterm babies, such as gestational age, birth weight, and cause of admission, which were recorded. All preterm infants were investigated by echocardiogram. The maternal history was also recorded for mothers, including age, weight, height, history of exposure to radiation, chronic maternal disease, maternal infection, vaginal bleeding, severe abdominal pain, and history of anomalies in other babies.

Data and statistical analysis: Data were fed to the computer using SPSS software package version 20.0 (Armonk, NY: IBM Corp). The chi-square test and Mann-Whitney test: were used for abnormally distributed variables to compare between two studied groups.

Limitations: The study limitations include when the mother was unhelpful in giving information about medical history, financial income, and age. Also, among the obstacles was the small sample size in addition to all data being taken from one hospital.

RESULTS

Out of 60 admitted preterm infants, 43 were found to have congenital heart disease, while 17 were normal. The prevalence rate was 71.67% (Figure 1).

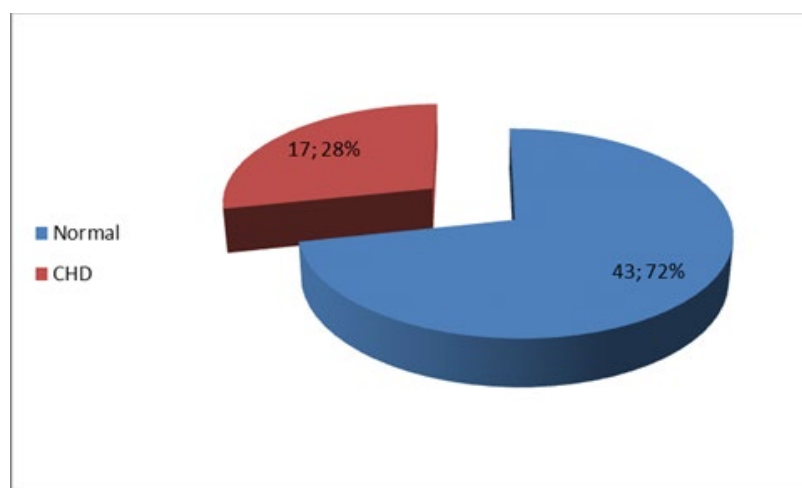


Figure (1). Distribution of the studied cases according to the prevalence of CHD in preterm infants (n = 60)

Regarding general character, the distribution of CHD in preterm by gestational age between 28-35 weeks and birth weight (0.9-2.5 grams) with a mean of (1.66 ± 0.38) was shown. The distribution by gender was: males (58.3%) and females (41.7%). Mother ages ranged from 18-42 years, with mean $\pm$ SD 31.32 ± 6.71 . Their weights ranged between 50-108 kg with means of 72 ± 14.66 (BMI =15-44, means 28.17 ± 6.06) (Table 1).

Table (1). General character for a profile of the studied sample N=60

Maternal history	Mean
Gestational age (weeks, mean $\pm$ SD)	(28.0 – 35.0 weeks, 31.85 ± 1.98)
Admission weight (grams, mean $\pm$ SD)	(0.90 – 2.50 gram, 1.66 ± 0.38)
Sex distribution	
Male	35 (58%)
Female	(25) 41.7%
Maternal ages	18-42 years, (mean $\pm$ SD 31.32 ± 6.71)

The echocardiographic findings showed: ASD was the most common structural defect (n=30) (69.77%), then PDA (n=12) (27.91%), VSD (n=10) (23.26%), and other anomalies were uncommon and findings were 1 for each (2.33%): Dilated left atrium, left ventricle thick wall (Figure 2).

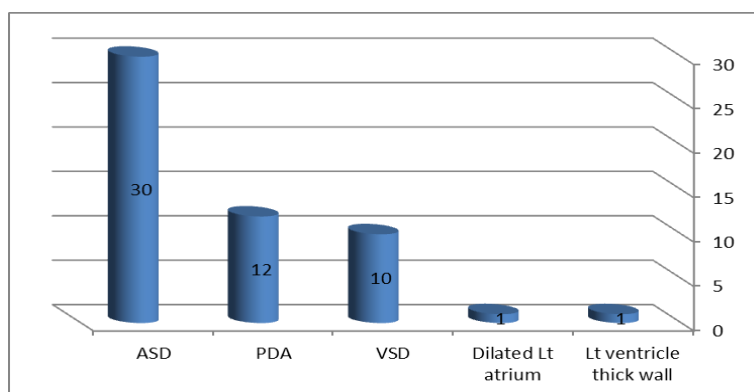


Figure (2). Distribution of the studied premature babies according to the prevalence of CHD

Associated maternal risk factors in preterm infants diagnosed with CHD: gestational diabetes was found in (6.7%), hypertension in (15%), drug intake, like antiepileptic (18.3%), and radiation exposure (1.7%), while (58.3%) of mothers did not register any disease during pregnancy (Figure 3).

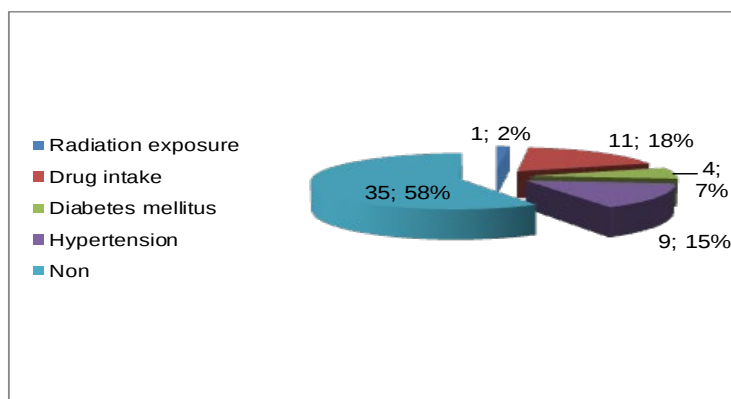


Figure (3). Distribution of diseases during pregnancy of the studied sample

Of the 60 mothers from the studied sample, 18% of them were consanguineous married and had CHD in their babies (figure 4).

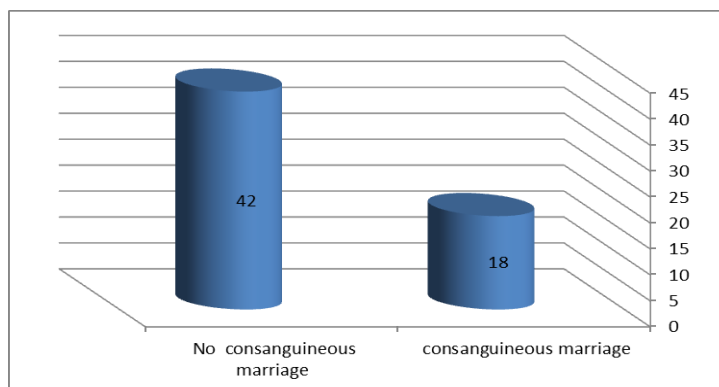


Figure (4). Relation of CHD and consanguineous marriage

Of the studied premature infants, 9 patients died during the study period, CFR (15%) (Figure 5).

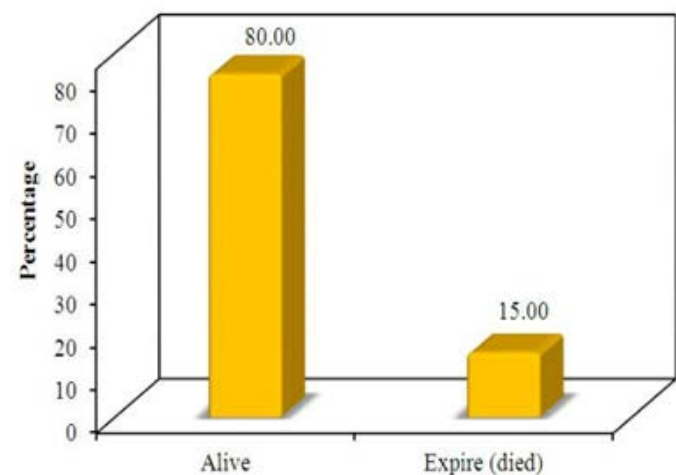


Figure (5). Distribution of the studied cases according to mortality

Out of the total deaths, the proportion of 9 premature infants with CHD (16.3%) was higher than normal (11.8%), and the observed difference was ($p > 0.05$), which was statistically not significant (Table 2).

Table (2). Distribution of the studied premature babies according to the outcome.

Outcome	Normal		CHD		χ^2	FE_p
	(n =17)		(n =43)			
	No.	%	No.	%		
Alive	15	88.2	36	83.7	115.567	0.550
Expired (died)	2	11.8	7	16.3	0.195	1.000

This study also focused on the relation between the age of mothers of premature babies, with and without CHD (Table 3).

Table (3). Relation between mothers' age and CHD babies

Age (years)	Normal (n =17)	CHD(n =43)	U	p
Min. – Max.	18.0 – 42.0	19.0 – 42.0		
Mean $\pm$ SD.	31.59 $\pm$ 6.99	31.21 $\pm$ 6.67		
			31.0*: 358.500	0.908
Median	35.0	Statistically significant at $p \leq 0.05$		

The observed differences in the risk factors concerning hypertension, smoking exposure, malnutrition, low socioeconomic state, and maternal infection between normal heart and CHD mothers were (0.255), (0.832), (0.073), (0.073), (0.440), respectively, and the difference was statistically not significant ($p > 0.05$) (Table 4).

Table (4). Distribution of maternal risk factors for the studied patients (no = 60).

Variable	normal No=17	CHD No=43	P value
High blood pressure			
Yes	79.1	94.1	0.255
No	20.9	5.9	
Smoking			
Yes	55..8	58.8	0.832
No	44.2	41.2	
Maternal nutrition			
Good	51.2	76.5	0.073
Average	48.4	23.5	
Socioeconomic state			
Good	51.2	76.5	0.073
Average	48.4	23.5	
Maternal infection			
Yes	86%	76.50%	0.448
No	14%	23.50%	

No statistical significance was observed using the Chi-square test ($P > 0.05$)

DISCUSSION

The present study described the results of the prevalence of CHD in hospital-based preterm infants. In this study, males were more common than females. This gender distribution was in accordance with observations reported by (Mollah et al., 2002). Maternal age was significantly associated with CHD in preterm babies in a study in Saudia Arabia (Hashim Jr et al., 2020). The current study found mothers who are older than 35 years are more likely to have babies with VSD and PDA. In the current study, the most common congenital heart defect was ASD (n=30, 69.77%) versus the literature. VSD was the commonest defect in contrast to other studies done by (Mollah et al., 2002; Sallout et al., 2008) which show VSD (29%) contrary to our finding VSD (n=10. 23.26%). This could be explained by the birth prevalence of CHDs, as observed differences in environmental and/or genetic risk factors that could refer to different phenotypes may also be possible for dissemination patterns. The expansion in the availability of diagnostic technologies and skills across different participating hospitals, and probably the advances in diagnostic methods, had the most impact in detecting mild CHDs. Other studies (Begum & Ahmed, 2001) support our finding that many small-sized VSDs, particularly if associated with TOF, may not manifest by neonatal time.

The overall high prevalence of CHDs in premature infants is partly driven by a high prevalence of ASDs, which are more commonly diagnosed in premature infants due to the increased likelihood of receiving an echocardiogram, which is consistent with other studies (Reller et al., 2008; Van Der Linde et al., 2011). Other defects in the current study: PDA (27.91%), complex congenital heart disease (8%), TGA (8%), and TOF (6%), were correlated with other studies (Begum & Ahmed, 2001; Rahman et al., 1992).

The presenting study also shows that there is no significant association between smoking ($p=0.832$), socioeconomic state, and maternal nutrition and development of CHD ($p=0.073$),

contrary to the results of several studies conducted in the United States followed by Europe and Asia (Kučienė & Dulskienė, 2009; Long et al., 2010; Williams et al., 2004) that examined socioeconomic variables (mother education, nutrition, income levels), in addition to CHD researchers (Loffredo et al., 2001; Vrijheid et al., 2000) who reported that low socioeconomic status increased the risk of structural heart defects. Study results by (Malik et al., 2008) showed the association between the risk of septal defects in infants and exposure to moderate and heavy smoking. Consanguineous marriage accounted for 18% of CHD in this studied sample, comparatively lower than a study reported by (Taksande et al., 2010) in central India. All these contrary findings could be explained by the small size of our study.

Regarding maternal illness, (6.7%) were diabetic, (15%) were hypertensive, and (18.3%) had a history of ingestion of drugs, as anti-epileptic drugs have been found in this study as observed in the literature. As in previous studies, maternal diabetes mellitus was observed to be a significant risk factor for CHD overall and for almost all subtypes of CHD. Numerous studies by (Lisowski et al., 2010; Nielsen et al., 2005) have shown that diabetes mellitus causes cardiovascular malformations. Congenital heart disease has already been recognized as one of the significant causes of neonatal mortality and morbidity. The overall mortality rate was 15% in the current study.

This report is lower than the 44% - 55% in-hospital mortality rates reported in two previous database studies (Archer et al., 2011; Lynema et al., 2016) that focused on very low birth weight neonates (< 1500 grams) with severe CHDs. Some differences may reflect that our study included patients with a birth weight > 1500. The other possibility to account for our mortality rates may be explained by the small size sample. Prospective researches with a large sample are highly recommended.

CONCLUSION

Our study shows a high prevalence of CHD in the studied premature infants (69.77%). The case fatality rate was (15%). Death rates were higher for premature infants with CHD (16.3%) than those with normal hearts (11.8%) with no statistical significance. There is a need for targeted prenatal care for mothers with known high-risk CHDs to delay delivery to the latest possible gestational age to avoid premature births to reduce neonatal mortality.

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CONSENT

Informed consent was obtained from the patient's parents regarding the study objectives and methods.

ETHICS

The authors assured that informed consent was obtained during admission as a teaching center for data use. The proposal was provided by the Ethical Committee of the Libyan Board of Medical Specialties.

Duality of interest: There is a conflict of interest.

Author contributions: A. developed the theoretical formalism. B supervised the project. A, C, and D performed the analytic calculations and performed the numerical simulations. All authors read, reviewed, and approved the final manuscript.

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REFERENCES

- Archer, J. M., Yeager, S. B., Kenny, M. J., Soll, R. F., & Horbar, J. D. J. P. (2011). Distribution of and mortality from serious congenital heart disease in very low birth weight infants. *127*(2), 293-299.
- Begum, N., & Ahmed, Q. J. B. J. c. h. (2001). Pattern of Heart disease among neonates and their outcome: one year experience in non-invasive cardiac laboratory of Combined Military Hospital, Dhaka. *25*, 48-52.
- Franklin, R. C., Béland, M. J., Colan, S. D., Walters, H. L., Aiello, V. D., Anderson, R. H.,...Gaynor, J. W. J. C. i. t. Y. (2017). Nomenclature for congenital and paediatric cardiac disease: the International Paediatric and Congenital Cardiac Code (IPCCC) and the Eleventh Iteration of the International Classification of Diseases (ICD-11). *27*(10), 1872-1938.
- Hashim Jr, S. T., Alamri, R. A., Bakraa, R., Rawas, R., Farahat, F., & Waggass, R. J. C. (2020). The association between maternal age and the prevalence of congenital heart disease in newborns from 2016 to 2018 in single cardiac center in Jeddah, Saudi Arabia. *12*(3).
- IGME, U. (2018). Levels & trend in child mortality: Estimates developed by the UN Inter-Agency Group for UN Inter-Agency Group for Child Mortality Estimation Child Mortality Estimation.
- Jacobs, J. P., He, X., Mayer Jr, J. E., Austin III, E. H., Quintessenza, J. A., Karl, T. R.,...Pasquali, S. K. J. T. A. o. t. s. (2016). Mortality trends in pediatric and congenital heart surgery: an analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database. *102*(4), 1345-1352.
- Jasani, B., Weisz, D. E., Reese, J., & Jain, A. (2023). Combination pharmacotherapy for patent ductus arteriosus: Rationale and evidence. *Seminars in perinatology*,
- Kučienė, R., & Dulskienė, V. J. M. (2009). Maternal socioeconomic and lifestyle factors during pregnancy and the risk of congenital heart defects. *45*(11), 904.
- Laas, E., Lelong, N., Thieulin, A.-C., Houyel, L., Bonnet, D., Ancel, P.-Y.,...Khoshnood, B. J. P. (2012). Preterm birth and congenital heart defects: a population-based study. *130*(4), e829-e837.
- Lisowski, L., Verheijen, P., Copel, J., Kleinman, C., Wassink, S., Visser, G., & Meijboom, E. J. C. p. (2010). Congenital heart disease in pregnancies complicated by maternal diabetes mellitus. An international clinical collaboration, literature review, and meta-analysis. *120*.

- Liu, L., Oza, S., Hogan, D., Chu, Y., Perin, J., Zhu, J.,...Black, R. E. J. T. L. (2016). Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals. *388*(10063), 3027-3035.
- Loffredo, C. A., Silbergeld, E. K., Ferencz, C., & Zhang, J. J. A. j. o. e. (2001). Association of transposition of the great arteries in infants with maternal exposures to herbicides and rodenticides. *153*(6), 529-536.
- Long, J., Ramadhani, T., Mitchell, L. E. J. B. D. R. P. A. C., & Teratology, M. (2010). Epidemiology of nonsyndromic conotruncal heart defects in Texas, 1999–2004. *88*(11), 971-979.
- Lopes, S. A. V. d. A., Guimarães, I. C. B., Costa, S. F. d. O., Acosta, A. X., Sandes, K. A., & Mendes, C. M. C. J. A. b. d. c. (2018). Mortality for critical congenital heart diseases and associated risk factors in newborns. A cohort study. *111*, 666-673.
- Lynema, S., Fifer, C. G., & Laventhal, N. T. J. P. C. (2016). Perinatal decision making for preterm infants with congenital heart disease: determinable risk factors for mortality. *37*, 938-945.
- Lytzen, R., Vejlstup, N., Bjerre, J., Petersen, O. B., Leenskjold, S., Dodd, J. K.,...Søndergaard, L. J. J. c. (2018). Live-born major congenital heart disease in Denmark: incidence, detection rate, and termination of pregnancy rate from 1996 to 2013. *3*(9), 829-837.
- Mackie, A. S., Tran, D. T., Marelli, A. J., & Kaul, P. J. C. J. o. C. (2017). Cost of congenital heart disease hospitalizations in Canada: a population-based study. *33*(6), 792-798.
- Malik, S., Cleves, M. A., Honein, M. A., Romitti, P. A., Botto, L. D., Yang, S.,...Pediatrics, N. B. D. P. S. J. (2008). Maternal smoking and congenital heart defects. *121*(4), e810-e816.
- Markopoulou, P., Papanikolaou, E., Analytis, A., Zoumakis, E., & Siahianidou, T. J. T. J. o. p. (2019). Preterm birth as a risk factor for metabolic syndrome and cardiovascular disease in adult life: a systematic review and meta-analysis. *210*, 69-80. e65.
- Mashuda, F., Zuechner, A., Chalya, P. L., Kidenya, B. R., & Manyama, M. J. B. r. n. (2014). Pattern and factors associated with congenital anomalies among young infants admitted at Bugando medical centre, Mwanza, Tanzania. *7*, 1-7.
- Mollah, M., Begum, N., Islam, M., Mahmud, R., Haq, M., Nahar, N., & Rashid, M. J. B. h. J. (2002). Clinical profile of congenital heart diseases (CHD): An analysis of 218 cases. *17*, 62-67.
- Nielsen, G. L., Nørgard, B., Puho, E., Rothman, K., Sørensen, H. T., & Czeizel, A. J. D. m. (2005). Risk of specific congenital abnormalities in offspring of women with diabetes. *22*(6), 693-696.
- Quinn, J.-A., Munoz, F. M., Gonik, B., Frau, L., Cutland, C., Mallett-Moore, T.,...Nunes, T. J. V. (2016). Preterm birth: Case definition & guidelines for data collection, analysis, and presentation of immunisation safety data. *34*(49), 6047-6056.

- Rahman, S., Ahmed, M., Rahmatullah, K., & Alam, M. J. D. H. (1992). The incidence of congenital heart diseases diagnosed by non-invasive technique-Ten years study in Bangladesh. 8, 5-15.
- Reller, M. D., Strickland, M. J., Riehle-Colarusso, T., Mahle, W. T., & Correa, A. J. T. J. o. p. (2008). Prevalence of congenital heart defects in metropolitan Atlanta, 1998-2005. 153(6), 807-813.
- Saigal, S., & Doyle, L. W. J. T. L. (2008). An overview of mortality and sequelae of preterm birth from infancy to adulthood. 371(9608), 261-269.
- Sallout, B. I., Al Hoshan, M. S., Attyyaa, R. A., & Al Suleimat, A. A. J. A. o. S. m. (2008). Antenatal diagnosis, prevalence and outcome of major congenital anomalies in Saudi Arabia: a hospital-based study. 28(4), 272-276.
- Shetty, N., Mantri, S., Agarwal, S., Potdukhe, A., Wanjari, M. B., Taksande, A. B., & Yelne, S. J. C. (2023). Unraveling the Challenges: A Critical Review of Congenital Malformations in Low Socioeconomic Strata of Developing Countries. 15(7).
- Taksande, A., Vilhekar, K., Chaturvedi, P., & Jain, M. J. I. j. o. h. g. (2010). Congenital malformations at birth in Central India: A rural medical college hospital based data. 16(3), 159.
- Van Der Linde, D., Konings, E. E., Slager, M. A., Witsenburg, M., Helbing, W. A., Takkenberg, J. J., & Roos-Hesselink, J. W. J. J. o. t. A. C. o. C. (2011). Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. 58(21), 2241-2247.
- van Velzen, C. L., Türkeri, F., Pajkrt, E., Clur, S. A., Rijlaarsdam, M. E., Bax, C. J.,...Haak, M. C. J. A. o. e. g. S. (2016). Pregnancy complications in singleton pregnancies with isolated fetal heart defects. 95(11), 1273-1280.
- Vrijheid, M., Dolk, H., Stone, D., Abramsky, L., Alberman, E., & Scott, J. J. A. o. D. i. C. (2000). Socioeconomic inequalities in risk of congenital anomaly. 82(5), 349-352.
- WHO, W. H. O. (2023). *WHO presence in countries, territories and areas: 2023 report*. World Health Organization.
- Williams, L. J., Correa, A., Rasmussen, S. J. B. D. R. P. A. C., & Teratology, M. (2004). Maternal lifestyle factors and risk for ventricular septal defects. 70(2), 59-64.