Pattern, rate, and Gender Correlation of Diagnosed Congenital Heart Defects in Neonates: A Retrospective Study at Prince Zeid Ben Al-Hussein Military Hospital

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ABSTRACT

Objective: To detect the pattern, frequency, and gender correlation of diagnosed congenital heart defects (CHD) among neonatal evaluation during the first week of life in Prince Zeid Ben Al-Hussein Military Hospital.
Methods: An observational retrospective study was conducted at Prince Zeid Ben Al-Hussein Military Hospital from October 1, 2009, to May 31, 2010. We included all neonates who were referred for cardiology evaluation during the first week of life and had 2-dimensional echocardiography reports.
Results: A total of 424 neonates were referred for cardiology evaluation and had 2-dimentional echocardiology in the first week of life during the study period. The sample included 214 (50.5%) males and 210 (49.5%) females. Murmur and cyanosis were the most frequent indications for cardiology evaluation. CHD was diagnosed in 64.85% of the study population. Patent ductus arteriosus (PDA) was the most frequent diagnosis, which accounted for 43.4%, followed by atrial septal defect (ASD) at 17.2% and ventricular septal defect (VSD) at 4.3%. The incidence rate of CHD was 70% among female neonates and 59.81% among males. A notable female predilection was observed in the distribution of total diagnosed CHD based on gender.
Conclusion: PDA was the most frequently diagnosed CHD, followed by ASD and VSD. Notable differences in the prevalence of total diagnosed CHD and sub-phenotype of lesions based on gender were observed with a female predilection.
Keywords: Congenital heart defect (CHD), Atrial septal defect (ASD), Ventricular septal defect (VSD), Patent ductus arteriosus (PDA), Pattern of CHD.
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INTRODUCTION

Congenital heart defect (CHD) is considered as the most common of all birth defects and accounts for around 28% of all congenital anomalies [1]. Significantly, CHD is the major cause of mortality and morbidity in the first year of neonatal life compared with other types of birth defects [2, 3].

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Despite recent development and improvement in healthcare services, including diagnosis, interventional, surgical techniques, and management, CHD continues to be a serious health problem worldwide [4, 5]. In 2017, the Global Burden of Disease (GBD) reported that more than 260,000 deaths were associated with CHD globally [6]. Several international studies and reports showed that the incidence rate and prevalence of CHD vary widely from 2 to 13 per 1000 live births [7, 8].

Despite the etiology of most CHD being unknown, numerous studies have reported that CHD has a multifactorial origin and is associated with predisposing risk factors [9, 10]. A review of the literature showed that around 10% of CHDs were linked to genetic abnormality [11], and environmental conditions were associated with 3% [12]. Furthermore, maternal ailments and conditions were reported as significant predisposing risk factors [13, 14]. Younger or advanced maternal age was reported to increase the risk of CHD [15]. Diabetes mellitus is consistently associated with CHD, and it is widely believed that hyperglycemia plays a significant role in inducing malformation during the critical period of organogenesis and embryogenesis [16-18].

Hypertension is a common problem during pregnancy, and untreated hypertension was reported in many studies to increase the risk of CHD by twofold [19, 20]. Obesity and excess weight among potential mothers are strongly associated with higher risk of having an infant with CHD [21, 22]. According to the Baltimore-Washington Infant Study (BWIS) and California Birth Defects Monitoring Program, maternal use of therapeutic drugs such as antidepressant, antihypertensive, and anti-infection medications is associated with increased risk of CHD [23, 24].

According to the Centers for Disease Control and Prevention (CDC) and the National Health Service (NHS), CHD is categorized based on pathophysiology and affected heart structure as acyanotic and cyanotic. Acyanotic lesions include obstructive heart defects (OHD), which are characterized by abnormal narrowing or blocking of heart valves, arteries, or veins [25]. Pulmonary stenosis (PS) is a common example of obstructive heart defects and accounts for 8% of CHDs. Compared to sub-phenotypes of OHD, coarctation of the aorta and aortic stenosis account for 5% and 4%, respectively [26].

Septal heart defects allow blood to flow through the septum between the right and left chambers. They are subdivided into atrial septal defect (ASD) and ventricular septal defect (VSD), which is considered as the most frequent phenotype of all CHDs and cardiac anomalies [27]. While Patent foramen ovale (PFO) is as a result of an incompetent fossa ovalis valve with up to 25% prevalence in the general population [28]. Blood with less than a normal percentage of oxygen can result from cyanotic heart defects such as tetralogy of Fallott, tricuspid atresia, transposition of great arteries, patent ductus arteriosus (PDA), hypoplastic left heart syndrome, truncus arteriosus, and tricuspid atresia [29].

In the Middle East and North Africa, limited reports from government or healthcare providers have been issued about the prevalence of CHD. In Jordan, research and documented data are limited in regard to the pattern and incidence rate of CHDs among the population. Thus, the aim of this study was to assess the pattern, incidence, and gender correlation of detected CHDs in neonatal evaluation during the first week of life at Prince Zeid Ben Al-Hussein Military Hospital in Tafilah. Geographically, Tafilah located in the southern of Jordan at around 180 km southwest of Amman with estimated population of 120,000. Prince Zeid Ben Al-Hussein Military Hospital is the major hospital in Tafilah governate offering medical and clinical services for the population residing in the region.

METHODS

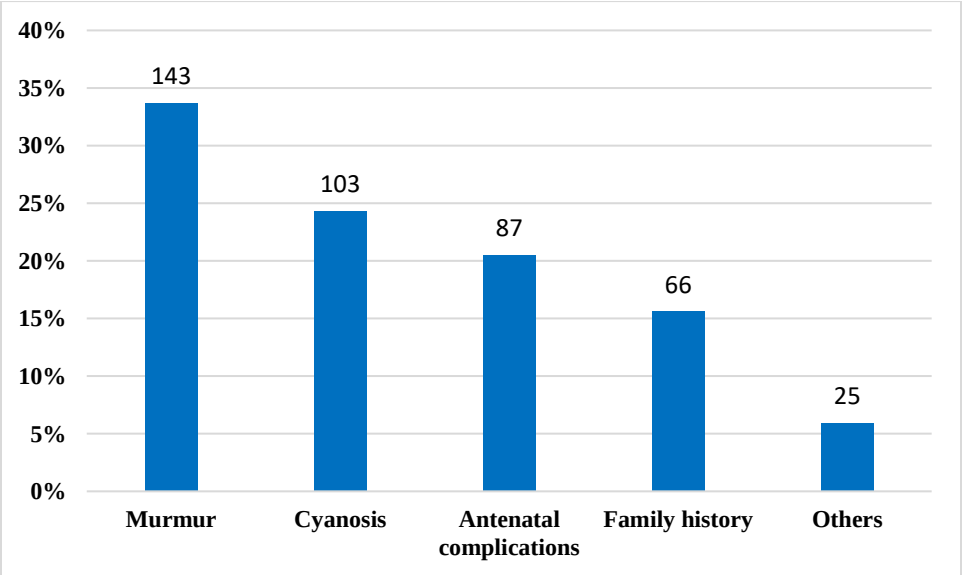
An observational retrospective study was conducted at Prince Zeid Ben Al-Hussein Military Hospital from October 1, 2009, to May 31, 2010. We included all neonates who had 2-dimensional echocardiography reports from neonatal evaluation during the first week of life. The primary variable of interest was the type of diagnosed CHD. 2-dimensional echocardiography was the definitive tool for diagnosis of CHD. The collected data included gender, indications for echocardiography, and types of diagnosed CHD.

All collected data were entered into Microsoft Excel sheets and analyzed by IBM (SPSS) Statistics version 26. The analyzed data were presented as frequency distributions and percentages for categorical variables. A chi-squared test was used to estimate the risk of CHD based on gender, p-value < 0.05 was considered as significant.

RESULTS

A total of 424 neonates were referred for cardiology evaluation and had 2-dimensional echocardiology in the first week of life during the study period. There were 214 (50.5%) males and 210 (49.5%) females. The indications for echocardiology referral are summarized in figure 1. During neonatal evaluation, murmur (33.7%), bluish color of the skin (24.3%), antenatal complications (20.5%), and family history (15.6%) were the leading indications for echocardiology.

Figure 1: Indications for echocardiology referral



Among the total study population referred to echocardiology, CHD was encountered in 275 (64.85%) neonates. The findings of 2-dimensional echocardiography showed that acyanotic CHD lesions were the predominant diagnosis. We found that PDA was the most frequent diagnosis during neonatal evaluation, accounting for 43.4%, followed by ASD at 17.2% and VSD at 4.3%, as shown in figure 2.

Figure 2: Prevalence of diagnosed CHD based total study population (n=424).

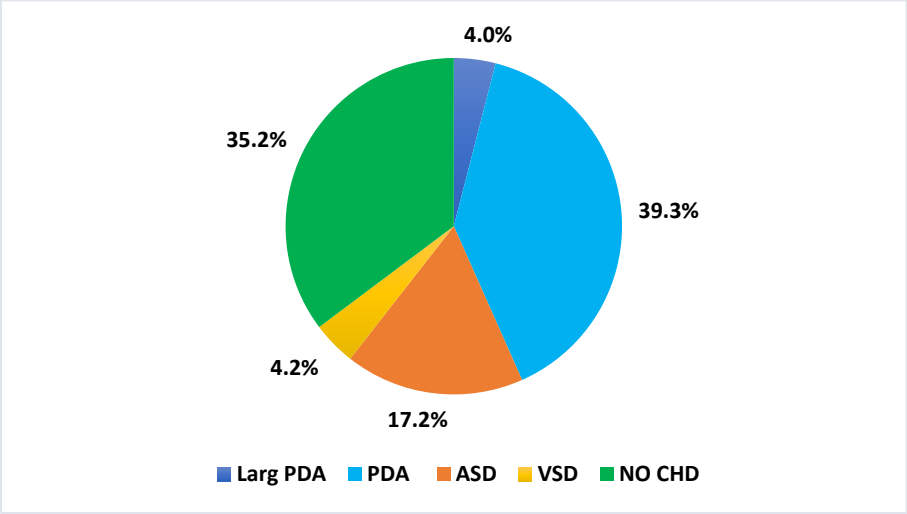


Table 1: Crosstabulation of diagnosed cardiac defects vs gender

Table 1.a: Crosstabulation of PDA vs gender

Diagnosis	Gender		Chi-Square	*P*-Value
	Female n (%)	Male n (%)		
PDA	84 (40%)	83 (38.78%)	0.316	0.574
Large PDA	10 (4.76%)	7 (3.27%)		
NO PDA	116 (55.23%)	124 (57.4%)		

Diagnosis	Gender		Chi-Square	*P*-Value
	Female n (%)	Male n (%)		
ASD	42 (20%)	31 (14.48%)	2.261	0.133
NO ASD	168 (80%)	183 (85.51%)		

Table 1.c: Crosstabulation of VSD vs gender

Diagnosis	Gender		Chi-Square	*P*-Value
	Female n (%)	Male n (%)		
VSD	11 (5.23%)	7 (3.27%)	1.109	0.315
NO VSD	199 (94.76%)	207 (96.72%)		

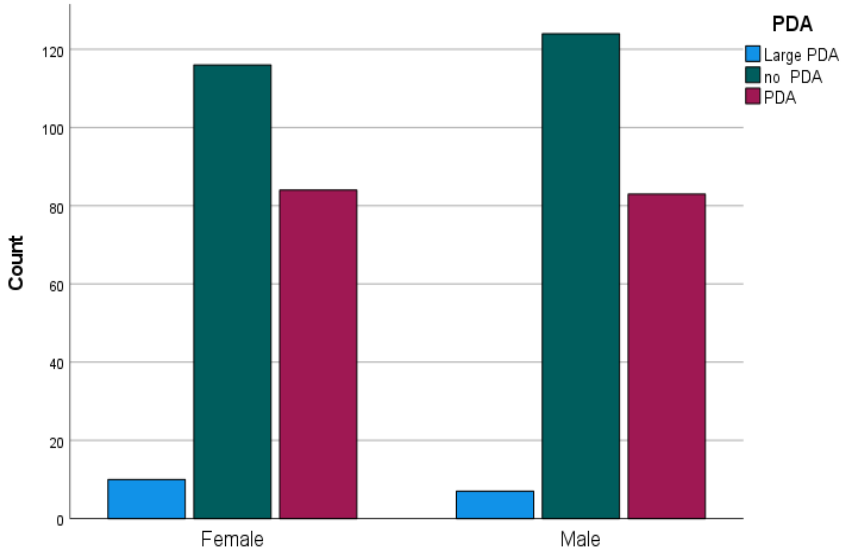
Table 1.d: Crosstabulation of CHD vs gender

Diagnosis	Gender		Chi-Square	*P*-Value
	Female n (%)	Male n (%)		
CHD	147 (70%)	128 (59.82%)	1.201	0.273
NO CHD	63 (30%)	86 (40.18%)		

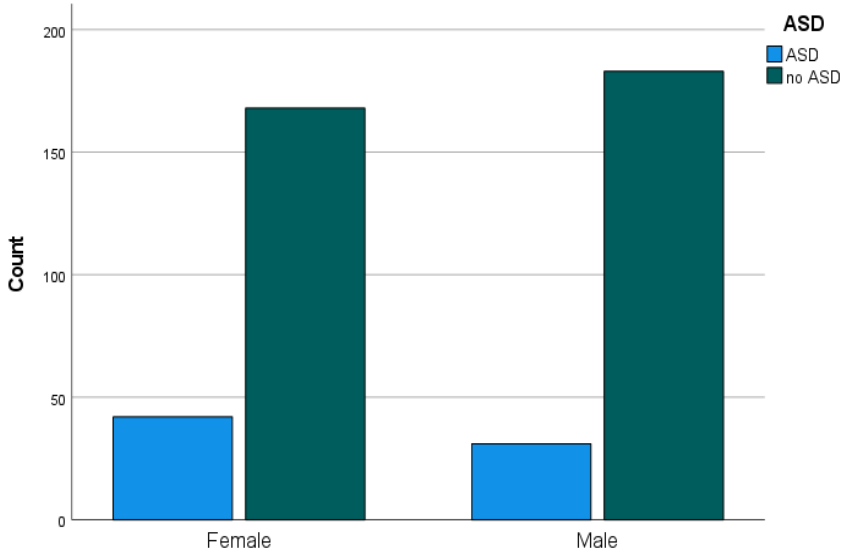
Among all diagnosed neonates with CHD (n=275), the findings shown in figure 2 and table 1 offer important new information about the rates and gender distribution of neonatal cardiac defects.

According to Table 1.a, 40% of newborn females and 38.78% of newborn males had Patent Ductus Arteriosus (PDA) diagnoses. The percentage difference between the gender is not statistically significant (p-value = 0.574), indicating that PDA occurs at about the same rates in both groups. Atrial septal defect (ASD) was identified in 20% of newborn females and 14.48% of newborn males, according to Table 1.b. It is true that females have a higher incidence of ASD, however the difference is not statistically significant (p-value = 0.133). Similarly, Table 1.c shows that Ventricular Septal Defect (VSD) was diagnosed in 5.23% of female neonates and 3.27% of male neonates. With a p-value of 0.315, the incidence rate difference is not statistically significant. The crosstabulation of Congenital Heart Defects (CHD) and gender is shown in Table 1.d. It shows that 59.82% of male neonates and 70% of female neonates had CHD diagnoses. Females are more likely to be diagnosed with CHDs than males are, however this difference is not statistically significant (p-value = 0.273). The incidence rates of each category of diagnosed CHD based on gender are shown graphically in Figure 2. It highlights the relative distribution of CHD among male and female neonates and supports the findings in Table 1 regarding the observations made. The findings as a whole point to a possible gender difference in the incidence of diagnosed CHDs, with females showing a marginally higher frequency. To verify the significance of these results, additional research and larger sample sizes would be required.

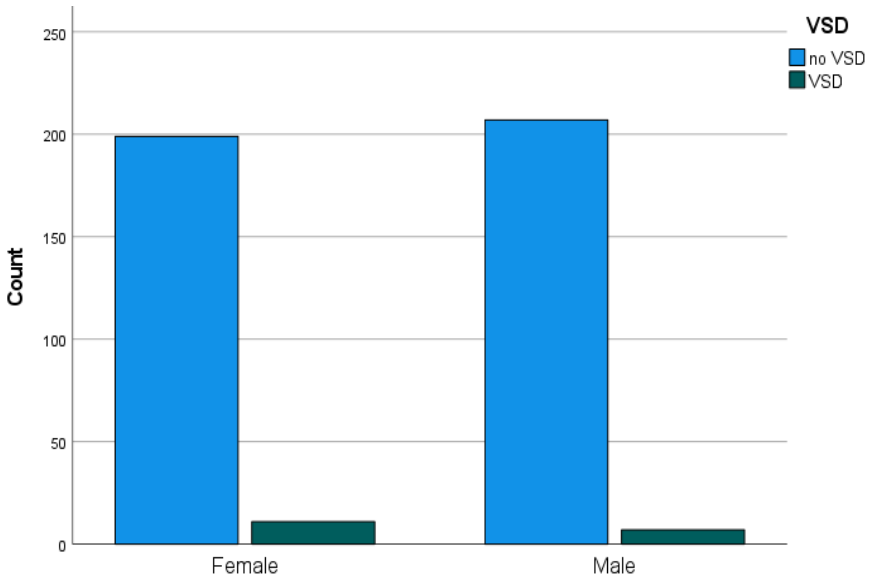
Figure 2: Diagnosed CHD according to gender.



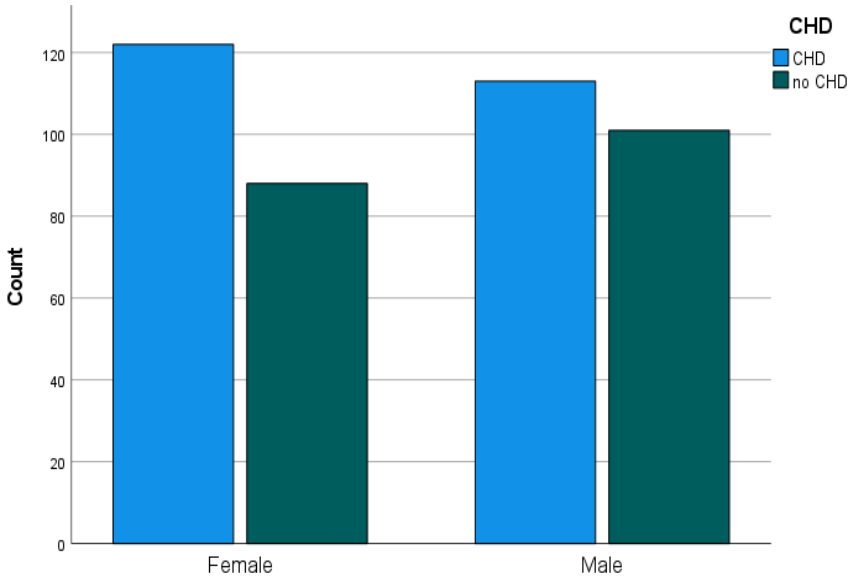
a: PDA diagnosis according to gender.



b: ASD diagnosis according to gender.



c: VSD diagnosis according to gender.



d: Total diagnosis of CHD according to gender.

DISCUSSION

CHDs are a significant global health problem and remain the most frequent cause of neonatal mortality and morbidity with congenital birth defects [2]. We analyzed the prevalence and frequency of diagnosed CHD among neonates referred for echocardiology evaluation during the first week of life. Our results showed that the prevalence of detected CHD was 64.85% among all neonates referred for echocardiology evaluation during the study period. PDA was the most commonly diagnosed CHD and accounted for 43.4% of the study population, compared with ASD at 17.2% and VSD at 4.3%. Our findings are compatible with the results obtained by Khasawneh et al., who reported that 84% of evaluated infants had abnormal echo results, and PDA was the most common diagnosis, accounting for 43%, followed by VSD and ASD with rates of 25% for each [30].

Al-Ammouri et al. reported that PDA was more common when echocardiographic evaluation was performed on the first day of life and accounted for 35% of CHD [31]. On the other hand, Amro et al. found that 43% of confirmed diagnoses of CHD were VSD. ASD and PDA accounted for 13.6% and 8.3%, respectively [32]. In another regional study from the Arab world and developing countries, Saidan et al. reported that CHD was associated with 40% of infants in a control group in Saudi Arabia. The prevalence of ASD and VSD was found to be 40.3% and 23.1% of detected CHDs, respectively [33].

Among diagnosed CHD cases in the Gaza Strip, Zaqout et al. reported that the prevalence of VSD and PDA was 28% and 9%, respectively [34]. In Egypt, Al-Fahham et al. showed that CHD was confirmed in 79% of all patients who were registered in the pediatric cardiology clinic at a children's university hospital. The most common detected CHD was VSD and accounted for 19.8%, followed by ASD at 15.2% [35]. Kulaet al. reported that the incidence rate of diagnosed CHD among neonates referred for echocardiographic and catheter angiography in Turkey was 39.3%. VSD was the most frequent diagnosis at 22.2%, while ASD and PDA accounted for 11% and 9.2%, respectively [36].

In developed countries, Samáneket al. observed that VSD was the most frequent CHD with a rate of 31.41%, followed by ASD at 11.3%. Their study that included 91,823 live-born children [37]. In the United Kingdom, a population-based study performed by Tanner et al. investigated cardiovascular malformations among infants and found that the prevalence of CHD was 5.7 per 1000 live births. The rates of diagnosed CHDs were presented as 30% for VSD, 22% for ASD, and 9% for PDA [38].

Wren et al. investigated the diagnosis of CHD among neonates in a population study over 20 years. The study reported that 62% of cardiovascular malformations were diagnosed by echocardiography during neonatal screening in the first week, which is similar to our result of 64.85% [39]. Another study from the United States of America was based on the Nationwide Inpatient Sample (NIS) database between 1998 and 2008. The study showed that VSD was the most common diagnosed CHD and accounted for 31.4%, followed by PDA and ASD with prevalence rates of 26.5% and 15.6%, respectively [40].

Our findings indicated a notable difference in the prevalence of CHD between females and males. We found a marked higher percentage of female gender among total diagnosed CHD and sub-phenotype lesions. The calculated chi-square and *p*-value showed that females had higher percentages of total diagnosed CHD (70%, $x^2 = 1.201$, $p = 0.273$) as shown in table 1. The distribution of diagnosed CHD including PDA, VSD and ASD were higher but non-significant in females than males as shown in table 1 and figure 2. Consistently, our findings agreed with international studies that indicated a predominance difference in the prevalence of CHD between female and male newborns, with females showing a higher prevalence of CHD [41, 42]. In addition, specific CHD lesions such as ASD, VSD, and PDA were associated with gender and found to be more common in females [43, 44].

In general, the prevalence and the incidence of CHD have plateaued after increasing during the last two decades due to improvement of diagnosis tools and technology [26]. The prevalence of certain subcategories of CHD, like PDA and VSD, has increased compared to other types of CHD according to the CDC, but antenatal diagnosis has improved significantly [1]. However, differences in the incidence rate of diagnosed CHD have been observed between different studies and different populations, which may be associated with the study design and inclusion criteria, such as age, selection of the study population, categories of studied CHDs, and diagnostic tools [29, 45].

Among studies in Jordan, only three hospital-based studies were published (by Khasawneh et al. [30], Al-Ammouri et al. [31], and Amro et al. [32]). To the best of our knowledge, our study is the first one to attempt to determine the prevalence and pattern of diagnosed CHD among neonates who had 2-dimensional echocardiography reports from neonatal evaluation during the first week of life. Despite this, no national studies have reported the incidence and pattern of diagnosed CHD based on the total Jordan population. This may be explained by a lack of registration and medical records for congenital heart diseases at the national level. In addition, there is an unequal distribution of diagnostics tools, medical equipment, and specialists between urban, cities, and rural areas.

The obtained pattern and distribution of diagnosed CHD in our study have some variation from other studies worldwide. We found that PDA was the most common diagnosis in our study population, followed by VSD and ASD. On the other hand, most international reports found that the most common diagnosis was VSD [36, 40, 46-48]. The high prevalence of PDA in our results may explained by the age of included neonates and the study design, which included all neonates diagnosed with CHD and referred to echocardiology during neonatal evaluation in the first week of life. Similar findings were reported by Khasawneh et al., who assessed the pattern and distribution of CHD among infants before the age of 30 days who were referred for echocardiology at King Abdullah University Hospital in Irbid [30].

Nationwide, developing national databases and medical records for congenital anomalies could play a significant role in establishing a national registry to monitor and record CHD. This could enable healthcare providers and decision makers to implement national guidelines for evaluating the incidence rate and pattern of CHDs in Jordan. Future multicenter studies including hospital and cardiac surgical centers are required for better evaluation and assessment of the incidence and pattern of CHD.

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Vol. 31 No. 1 April 2024

(Table1) Demographic distribution of the study population

Factor	Categories	Number	Percentage %
Age group n=189	20-40 years	55	29
	41-60 years	75	40
	61-80 years	59	31
Gender n=189	Male	109	58
	female	80	42

Table 2) the prevalence of anterior loop of the mandibular nerve according to the side of the mouth and the gender of the patient

Group (n)	**Total**	**Absence of anterior loop n (%)**	**Presence of anterior loop n (%)**	**p-value**
Gender				0.13
Male (109)	218	81 (37.2)	137 (62.8)	
Female (80)	160	72 (45)	88 (55)	
Hemimandibles				0,021
Right	189	65 (34.4)	124 (65.6)	
Left	189	88 (46.6)	101 (53.4)	

(Table 3) prevalence of anterior loop in 189 mandible CBCTs

Anterior loop prevalence	**n (%)**
Absent	39 (20.63%)
Bilateral	76 (40.21%)
Right only	49 (25.93%)

(Table 3) prevalence of anterior loop in 189 mandible CBCTs

Anterior loop prevalence	**n (%)**
Absent	39 (20.63%)
Bilateral	76 (40.21%)
Right only	49 (25.93%)
Left only	25 (13.23%)
Total	189 (100%)

(Table 4) Mean values of anterior loop length according to gender and side of the face

Factor	**Mean length mm (±SD)**	***P*-value (Student's t-test)**
Side of the mandible		
Right	1.69 (±0.76)	0.603 (221)
Left	1.76 (±0.93)	
Gender		
Male	1.76 (±0.88)	0.344 (0.947)
Female	1.65 (±0.88)	

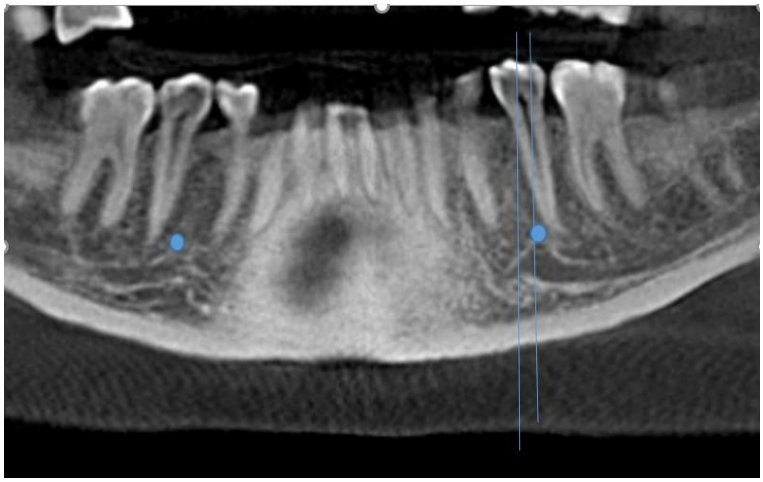

Figure 1: Anterior loop shows as radiolucency anterior to the mesial end of the mental foramen.

Left hemimandible shows an anterior loop (between the two blue lines). While the **right** hemimandible shows no anterior loop.

Figure 2: Rotating the volume to position the long axis of the mandibular canal parallel to sagittal plane (purple line).

The coronal section (green line) passes through the anterior end of the mental foramen; we started looking for the radiolucencies anterior to this section.

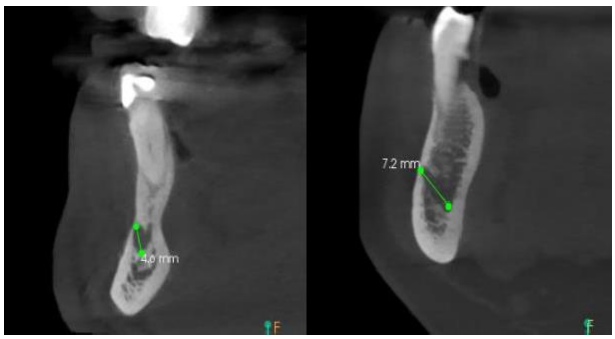

Figure 3: Two examples of anterior loops showing as single radiolucency greater than 3mm anterior to the mental foramina.

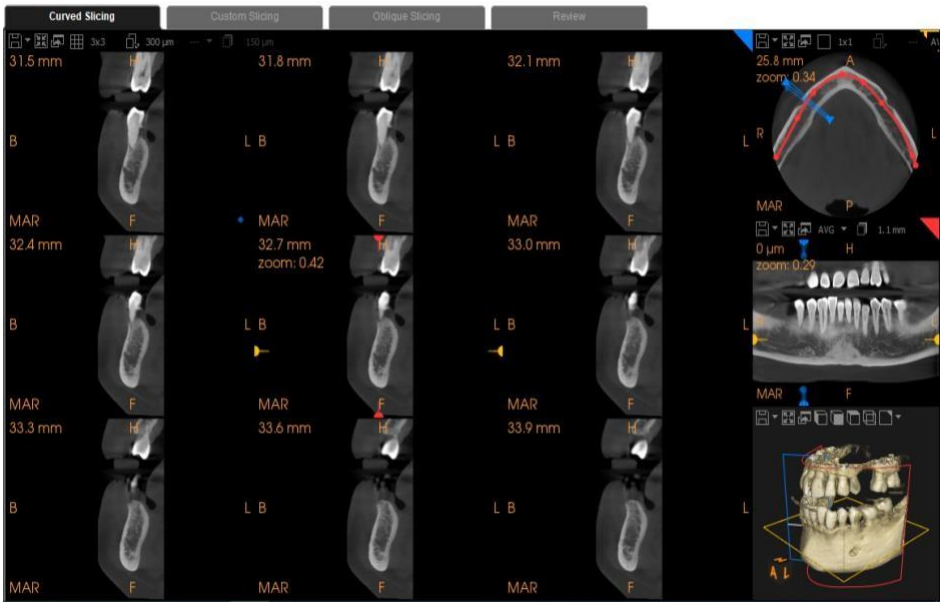

Figure4: An example of measuring the anterior loop length; eight coronal sections (from section 2 to 9) in this case are showing an anterior loop. So as each section thickness is 0.3, and 0.3*8 equals 2.4, the length of the anterior loop is then considered to be 2.4mm.

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cardiac surgery Yousef Jamal zraigat MD This single-center study has reported on the pattern and incidence of diagnosed CHD among neonates who were referred for cardiology evaluation and had 2-dimentional echocardiology in the first week of life. Our findings showed that PDA was the most commonly diagnosed CHD, followed by ASD and VSD. The obtained pattern and incidence of CHD varied in comparison with other international reports due to the age of included neonates and the study design. Notable differences in the prevalence of total diagnosed CHDs and sub-phenotype lesions based on gender were observed with a female predilection. Multicenter studies based on a national medical registry are suggested, which could play a significant role in evaluating the incidence rate and pattern of CHD in Jordan.

ETHICS APPROVAL

Institutional Review Board (IRB) approval was obtained from the ethics committee at Royal Medical Services. Patients' data privacy and confidentiality were maintained as this study was conducted in compliance with the ethical standards outlined in the Declaration of Helsinki.

LIMITATIONS

The main limitation of our study is the retrospective nature of single center study in the south of Jordan making it difficult to infer our results at a national level. Multi-centric similar studies are required to be performed in different geographical area of Jordan. In addition, the primary variable of interest was the type of diagnosed CHD by 2-dimensional echocardiography as the definitive tool for diagnosis of CHD. However, no verification mechanism for diagnosis was used.

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