Chapter One: Introduction

1-1 Epidemiology :

Congenital heart disease (CHD) is one of the most common congenital defects and accounts for nearly one-third of all major congenital anomalies [(1)]. Some population-based epidemiological studies on CHD have indicated a prevalence ranging from 4 to 50 per 1,000 live births [(2–3)] and the incidence is even higher in cases of premature children, stillbirth or spontaneous abortion [(4)]. CHD in children continues to be an important cause of death [(5)],and constitutes a potential risk of sudden cardiac death in adulthood even with mild cardiac lesion [(6)].With the development of diagnostics and cardiothoracic surgery and the introduction of intracardiac interventional techniques, survival of affected children has markedly improved, which have continuously influenced the size of the population of patients with CHD [(5)].

1-2 Evaluation and Screening of the Neonate with C.H.D. :

The initial evaluation for suspected congenital heart disease involves a systematic approach with 3 major components. First, congenital cardiac defects can be divided into 2 major groups based on the presence or absence of cyanosis, which can be determined by physical examination aided by pulse oximetry. Second, these 2 groups can usually be further subdivided according to whether the chest radiograph shows evidence of increased, normal, or decreased pulmonary vascular markings. Finally, the electrocardiogram can be used to determine whether right, left, or biventricular hypertrophy exists. The character of the heart sounds and the presence and character of any murmurs further narrow the differential diagnosis. The final diagnosis is then confirmed by echocardiography, CT or MRI, or cardiac cathetrization[(7)] .

Screening is performed between 24 and 48 hr of life and before discharge in asymptomatic newborns. A pulse oximetry saturation <90% in the right hand or either foot requires urgent echocardiography. A pulse oximetry saturation <95% in either location or a saturation difference >3% between the right hand and eithe9r foot is considered a positive test and should be repeated in an hour; if positive again, it should be repeated in another hour. If it remains positive, echocardiography is indicated. In addition, a careful reexamination of the pulses and blood pressure in the upper and lower extremity as well as a cardiac exam are indicated in children with an initial positive exam[(7)] .

1-3 Classification of CHD :

Congenital heart defects can be divided into three pathophysiologic groups (Table 1).

1. Left-to-right shunts
2. Right-to-left shunts
3. Obstructive, stenotic lesions [8] .

Table 1 : Classification of Congenital Cardiac Defects [8]

STENOTIC	RIGHT →LEFT	LEFT →RIGHT	MIXING
Aortic stenosis	Tetralogy	Patent ductus arteriosus	Truncus
Pulmonary Stenosis	Transposition	Ventricular septal defect	TAPVR
Coarctation of the aorta	Tricuspid Atresia	Atrial septal defect	HLH

Acyanotic congenital heart disease includes left-to-right shunts resulting in an increase in pulmonary blood flow (patent ductus arteriosus [PDA], ventricular septal defect [VSD], atrial septal defect [ASD]) and obstructive lesions (aortic stenosis, pulmonary stenosis, coarctation of the aorta), which usually have normal pulmonary blood flow [8] .

Cyanotic congenital heart disease occurs when some of the systemic venous return crosses from the right side of the heart to the left and returns to the body without going through the lungs (**right-to-left shunt**). **Cyanosis**, the visible sign of this shunt, occurs when approximately 5 g/100 mL of reduced hemoglobin is present in systemic blood. Thus, a polycythemic patient appears cyanotic with a lower percentage of reduced hemoglobin. A patient with anemia requires a higher percentage of reduced hemoglobin for the recognition of cyanosis. The most common cyanotic congenital heart defects are the five *Ts*:

Tetralogy of Fallot
Transposition of the great arteries
Tricuspid atresia
Truncus arteriosus
Total anomalous pulmonary venous return [8] .

Other congenital heart defects that allow complete mixing of systemic and pulmonary venous return can present with cyanosis depending on the amount of pulmonary blood flow that is present [8] .

1-4 Signs and symptoms of CHD :

There are many different types of congenital heart defects. How someone might feel will depend on the type of congenital heart disease. Some congenital heart defects are so mild that you or your child may not have any symptoms until later in life. More severe types of congenital heart problems are often detected while the baby is still in the womb or within the first few weeks of life [9] . Some signs and symptoms may include:

- Low levels of oxygen in the blood (nurses test for this within the first 24 hours of a baby's life)
- Bluish color to the skin, lips or nail beds (called cyanosis)
- Heart murmur
- Palpitations (when your heart feels like it's skipping beats)
- Rapid breathing or difficulty breathing
- Tiring very easily (for babies, even when feeding difficulty)
- Poor weight gain
- Poor blood circulation
- Fewer wet diapers
- Babies or kids with congenital heart disease may not get as big or gain weight as they should [9] .

Table 2 :signs and symptoms of CHD [8] .

SYMPTOM/SIGN	PHYSIOLOGIC CATEGORY	ANATOMIC CAUSE	LESION
Cyanosis with respiratory distress	Increased pulmonary blood flow	Transposition	d-Transposition with or without associated lesions
Cyanosis without respiratory distress	Decreased pulmonary blood flow	Right heart obstruction	Tricuspid atresia Ebstein anomaly Pulmonary atresia Pulmonary stenosis Tetralogy of Fallot
Hypoperfusion	Poor cardiac output Poor cardiac function	Left heart obstruction Normal anatomy	Total anomalous pulmonary venous return with obstruction Aortic stenosis Hypoplastic left heart syndrome Cardiomyopathy Myocarditis
Respiratory distress with desaturation (not visible cyanosis)	Bidirectional shunting	Complete mixing	Truncus arteriosus AV canal Complex single ventricle (including heterotaxias) without pulmonary stenosis
Respiratory distress with normal saturation	Left-to-right shunting	Simple intracardiac shunt	ASD VSD PDA Aortopulmonary window AVM

1-5 Diagnosis of CHD :

Several tests can be used to help determine whether a baby or child has a congenital heart disease. These may include: .

Fetal echocardiogram (during pregnancy): This test shows moving pictures of a baby's heart and how it is working as early as 16-18 weeks into pregnancy. It is usually used if congenital heart disease runs in family, or if there are other factors that make a heart problem more likely. .

Pulse oximetry: This simple and painless test measures how much oxygen is in the baby's blood. In many states, it is a standard screening test for newborns to helpdetect possible problems.

After a full physical exam and if a heart issue is suspected, **other tests may be ordered for the baby or child** and may include:

- Echocardiogram : provides assessment of the site of stenosis, degree of hypertrophy, and valve morphology, as well as an estimate of the pressure gradient.
- ECG : findings reflect the **increased blood flow** through the right atrium, right ventricle, pulmonary arteries, and lungs. The ECG may show **right axis deviation** and **right ventricular enlargement.**
- Chest X-ray : may show cardiomegaly, right atrial enlargement, and a prominent pulmonary artery.
- Cardiac catheterization
- Cardiac stress test [(9)] .

1-6 Treatment of CHD

What treatment your child might receive depends on several factors. For example:

- type of heart defect
- how severe it is
- your child's age
- his or her general health

Your child's heart team should talk with you about treatment options and what to expect. Always share any concerns and what matters most to you [10] .
Treatment may include a combination of [(10)] :

- **Medications** to help the heart work better, lower blood pressure or cholesterol and manage symptoms until the heart defect is repaired.
- **Cardiac catheterization** to look for or fix the problem (for example, to repair a hole or place a new valve). In this procedure, a long, thin, flexible tube is threaded through a blood vessel into the heart and gives doctors access to the heart.
- **Devices that are placed or implanted in the heart** to control heart rate or address life-threatening heart rhythms.
- **Open heart surgery** to repair the heart or help improve blood flow by widening arteries or closing blood vessels.
- **Heart transplant**, in rare cases.
- **Self-care at home** and **ongoing follow-up** for the condition [(10)] .

Remember, even if your child has a surgery to fix a heart defect, he or she may need more procedures down the line.

Having congenital heart disease also means you are more likely to develop other heart issues later in life. That's why you or your child needs ongoing care by a doctor who has special training in congenital heart disease. For example, they can help you and your child navigate issues such as:

- Understanding, preventing and monitoring heart problems that can develop as you age — issues with how your heart beats (arrhythmia), an enlarged heart, leaky or narrowing heart valves, heart failure, heart infections, pulmonary hypertension
- Pregnancy/birth control/sexuality
- Stress and coping
- Psychosocial issues [(10)] .

Chapter Two : The Study

2.1 Aim of study:

To study the frequency of conginital heart disease in premature neonates.

2.2 Patients And Methods:

250 neonates were randomly enrolled in the study who admitted to the pediatric ward in AL-Emamain AL-Khadhumain Medical city.

The neonates were examined at our hospital during the period from 15th of November, 2018 to 7th of January, 2019 if they have congenital heart disease or not.

The neonates with suspesion of congenital heart disease were sent for Echocardiography,and looking for presence or absence of the disease. After completing data collection, data (name, gender, the age at delivery, presence and type of C.H.D., maternal exposure to drugs , if they are dead or alive) were allocated regarding the questionnaire form , and packed into groups to simplify their insertion and calculation regarding the type of C.H.D.

2.3 Results :

From the total 250 patients that have been admitted to the Pediatric ward during the mentioned period, of those neonates define as having cardiac defect 11 (4.4%). As seen in **Figure 1**.

Table 1 : The percentage of cardiac defect among the neonates.

The neonates statstics		
Cases	Frequency	Percetage %
Having cardiac defect	11/250	4.4%
Without cardiac defect	239/250	95.6%
Total	250	100%

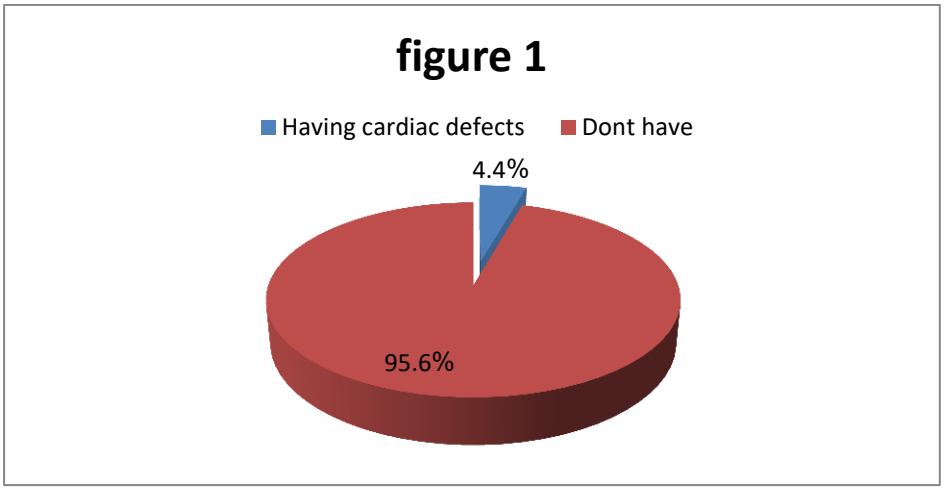

Figure (1): : The percentage of cardiac defect among the neonates.

We found among the neonates who have cardiac defect that 8 (72.7%) of them have ASD, 2 (18.2%) of them have VSD,and 1 (9.1%) of them have TOF ,as seen in **Figure 2**.

Table 2 : The percentage of cardiac defect among the neonates.

The neonates statstics		
Cases	Frequency	Percetage %
Having ASD	8/11	72.7%
Having VSD	2/11	18.2%
Having TOF	1/11	9.1%
Total	11	100%

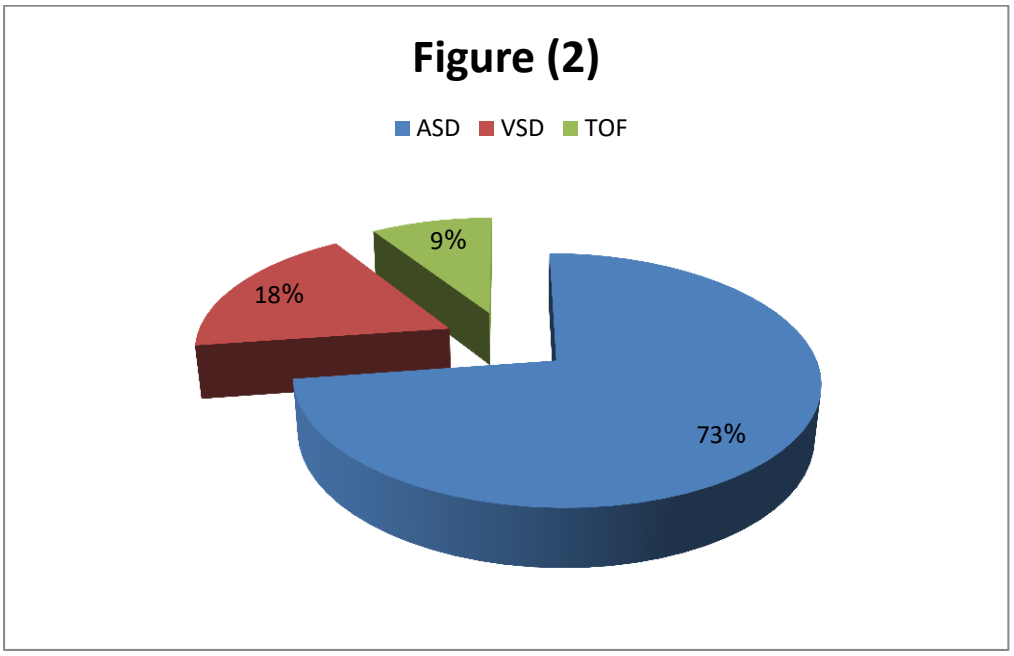

Figure (2): : The percentage of cardiac ASD & VSD among the neonates who have cardiac defect.

In general, the percentage of cardiac defect related to the gestational age of those neonates was (28.5%) between 25-28 week GA and about (28.5%) between 29-30 week GA and (43%) between 31-32 week GA , as in **figure 3**.

Table 3 : The percentage of cardiac defect -related to neontal GA.

The neonates statstics		
Cases	**Frequency**	**Percetage %**
Between 25-28 week	3/11	27.2%
Between 29-30 week	3/11	27.2%
Between 31-32 week	5/11	45.6%
Total	11	100%

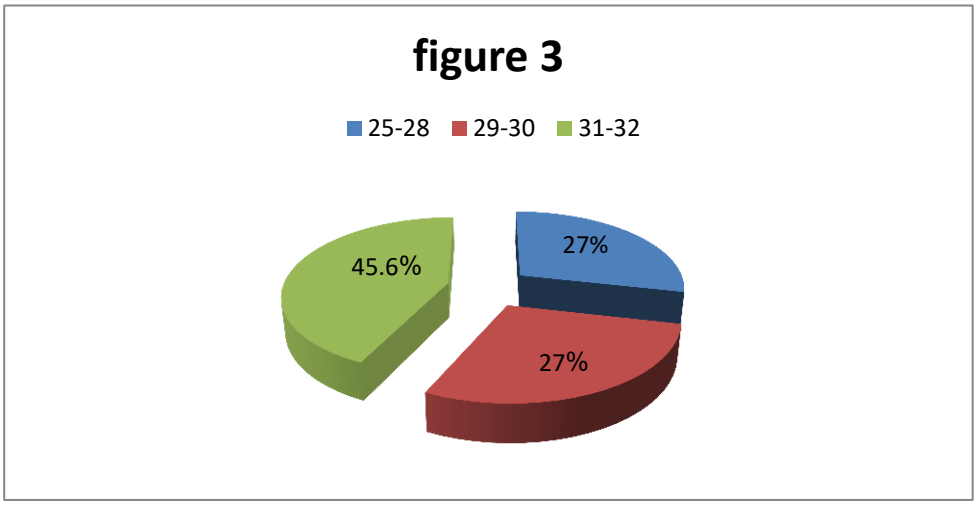

Figure 3 : The percentage of cardiac defect -related to neontal GA.

This table below show the relationship between the type of CHD and the gender of the premature neonate,and the P value (0.94)and it was not significant .

Table 4: Type Of CHD (acyanotic or cyanotic) According To The Gender

Type of CHD		Gender		Total
		male	female	
acyanotic	ASD	5	3	8
	VSD	1	1	2
cyanotic	TOF	1	0	1
Total		7	4	11

This table below show the relation between the Precense of CHD and it's relation to mother 's drugs taken ,and we found that P value was (1) and it was not significant.

Table 5: Precense of CHD and it 's relation to mother 's drugs take.

Precense of CHD	Drugs		Total
	take drugs	Don' t take drugs	
Have CHD	6	5	11
Don 't Have CHD	26	211	237
Total	32	216	250

The table below shows the relation between the mother drug exposure and the type of CHD and as it show that acyanotic CHD are more common than cyanotic

Table 6: type of CHD according to exposure to drugs

Type of CHD	drugs		Total (%)
	yes	no	
Cyanotic	1	0	1 (9%)
Acyanotic	5	5	10 (91%)
Total	6	5	11

Table 7:type of CHD and it 's relation to the mortalityrate

Type of CHD	Mortality	Total
	alive	
Cyanotic	1	1
Acyanotic	10	10
Total	11	11

2.4 Discussion :

In this analysis of very and extremely premature infants born 25 to 32 weeks GA, the overall birth prevalence of CHDs 4.4% (11 /250 births of similar GA) was significantly higher than the reported birth prevalence of CHDs in term neonates 0.6 – 1 % (6-10/1000 births) [11-12] . Importantly, the subset of severe CHDs were almost five-fold more likely in very/extremely premature neonates when compared with term neonates, and very/extremely premature neonates with severe CHDs had a more than seven-fold increased odds of mortality when compared with very/extremely premature neonates without CHD [13].

The overall high prevalence of CHDs in very/extremely premature infants is partly driven by a high prevalence of ASDs which are undoubtedly more commonly diagnosed in premature infants due to the increased likelihood of receiving an echocardiogram [13] . However, echocardiography utilization practices should minimally impact the prevalence of severe CHDs as these defects would be expected to be almost universally diagnosed during the neonatal period. In our Cross section, the birth prevalence of severe defects in very/extremely premature infants was (4.4%) 11/250 birth hospitalizations compared with 7.4/1000 birth hospitalizations in pre term infants in other study [14] . Other epidemiological studies of severe CHDs in term infants have reported slightly higher prevalence than our analysis . It is possible that we underestimated the true birth prevalence of severe CHDs in term infants as we restricted the analysis to birth hospitalizations [14].

In the study we also found that the most frequent cardiac defect is ASD 72.2 % and least frequent is TOF 9.1% and this correlate with the other studies [14]. And this indicate that acyanotic CHD are more common that the cyanotic .

When evaluating the frequency of CHD according to the GA , greater prematurity was associated with markedly higher frequency (45.6% at 31-32 weeks GA vs 27.2% at 25 to 28 weeks GA and 27.2% at 29 to 30 weeks GA ,). These data highlight the substantial differences that small increments of prematurity can have on outcomes in neonates with CHD, and may influence future decisions surrounding surgical interventions, medical management, and palliative care.

It was also studied the relationship between the type of CHD and the gender of the premature neonate,and it was that the male with CHD was more than female,

Which was the same results as in the other studies [14]. Also we try if a specific gender is related to a specific type of CHD and it was not signficant (p-value = 0.914).

In the study we also study The effect of embryonic exposure to maternal drugs during cardiogenesis , and the evidence suggests that maternal use of ethanol, anticonvulsants, lithium, and exogeneous female hormones may increase the risk of congenital heart disease. An antiemetic agent containing doxylamine has been implicated in the courts. This review offers an analysis of the epidemiologic evidence of the occurrence of congenital heart disease in relation to maternal drug use during pregnancy. The evidence indicates that the vast majority of heart malformations cannot be attributed to these pharmacologic agents ,and this result was the same result that obtained by another research [15] .

and about the mortality rate of our study ,we found that all the cases alife without any dead neonates ,without any significant, and it was the same result to the research [14] , that having a diagnosed ASD or pulmonary stenosis was associated with improved survival. This finding requires further study. Plausibly one could speculate that ASDs might offer a survival benefit in very/extremely premature infants with pulmonary hypertension. However this hypothesis is contrary to several prior reports suggesting that larger ASDs actually exacerbate underlying chronic lung disease of prematurity [16,17] .

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2.5 Conclusion :

In the research we found that the acyanotic congential heart disease were more common than cyanotic congential heart disease and the embryonic exposure to maternal drugs during cardiogenesis can be a risk factor to CHD in a premature neonates and also the incidance of congential heart disease were higher in males than female .

2.6 Recomendations :

It is recomended to expand the study to involve more cases .

it is reccommend that every premature neonate sholud undergone investigation for CHD beacuse the clinical features of some CHD are often started to present after childhood , and this will give us a real estimation of the incidence of these disease .

We also recommend that there are more studies to study the drug effect on the fetus during the cardiogenesis .

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Incedence of Congenital Heart Disease in Premature Newborn

Patient s" name:_____
Gender: male female
the age at delivery : (28_32)weeks
(32_36) weeks
(36_38)
presence of C.H.D: Yes No
Type of C.H.D.: Cyanotic Acyanotic _____
presence of another anomaly: Yes No ( )
Mode of Delivery: C\S Vaginal
Small for gestational age: Yes No
Mother s" age: ↑35 ↓35
presence of congenital infections for the mother:
Yes No
radiation exposure: Yes No
Drugs: Yes No ( )
Hormones: Yes No
Mortality: Alive Dead