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CURRENT UPDATE ON CONGENITAL HEART DISEASE SCREENING IN PREGNANCY

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ABSTRACT

Congenital Heart Disease (CHD) affects 8 births per 1,000 live births; equivalent to 1.35 million children born with CHD each year. Based on global incidence rate, Atrial Septal Defect (ASD), Ventricular Septal Defect (VSD), and Atrioventricular Septal Defect (AVSD) are found on 54.5% of CHD cases. Genetic factors are known to involve in CHD. Moreover, it can also be caused by environmental and infectious factors. Ultrasonography has been widely utilized to screen CHD at 18–22 weeks gestational age. Screening aims to measure heart rate, heart size, heart position, four chamber of the heart, pericardium, atrium, ventricles, atrioventricular junctions, and ventriculoatrial junctions. Doppler echocardiography becomes primary diagnostic tools in CHD patients because of its high sensitivity and specificity, safety, and noninvasiveness. Follow-up examination is indicated on a few conditions. Maternal indications include autoimmune antibody, family history of defects, in vitro fertilization, maternal metabolic disease, or teratogenic exposure. Fetal indications include abnormal screening result, family history of CHD, abnormal heart rhythm, chromosomal abnormalities, extracardiac abnormalities, hydrops, or monochorionic twin pregnancy. With increased rate of CHD, better screening and follow-up should be conducted to achieve acceptable detection rate.

Keywords: Congenital heart disease, Ultrasonography, Embryology

I. INTRODUCTION

Globally, Congenital Heart Disease (CHD) affects 8 births per 1,000 live births; equivalent to 1.35 million children born with CHD each year.[1,2] Meanwhile, CHD incidence rate is higher in Asia; involving 9.3 cases per 1,000 live birth.[2] Based on global incidence rate, Atrial Septal Defect (ASD), Ventricular Septal Defect (VSD), and Atrioventricular Septal Defect (AVSD) are found on 54.5% of CHD cases.[3] CHD incidence rate increases approximately 10% each 5 years.[2–5]

Atrial Septal Defect, VSD, and AVSD incidence increased from 1970–1974 (49.2%) to 2010–2017 (65.3%).[3] CHD showed regional variability; Asian population study showed higher incidence of pulmonal outflow obstruction and lower incidence of left ventricle outflow obstruction and Transposition of Great Arteries (TGA).[2]

Preliminary screening is able to detect up to 40% of CHD before 22 weeks gestational age, and additional screening is able to detect up to 80% cases of CHD.[1] Prenatal screening for congenital malformations, including CHD, gained traction from 1980s and usually conducted at 18–22 weeks gestational age.[1,6,7]

Atrial Septal Defect, VSD, and AVSD are usually shown as right-to-left shunt in imaging studies; and depending on location, is categorized based on anatomical location of defects.[1,7] Majority of fetus with CHD showed no heart failure

symptoms *in utero* because of placental circulation that provides oxygen and nutrition. After birth, with closure of fetal shunt, symptoms of heart failure may presents clearly.[6]

Left side obstruction may present as systemic hypoperfusion accompanied by acidosis, especially in ductus-dependent circulation, such as in Hypoplastic Left Heart Syndrome (HLHS), aortic stenosis, and Coarctation of Aorta (CoA). During antenatal care, these CHD may be detected using three-vessel and tracheal view (3VT). Right-sided obstruction may present as significant cyanosis in case of ductus-dependent pulmonal circulation, such as in pulmonal atresia.[6]

Four-chamber view with outflow tracts allows *in utero* screening of otherwise normal four-chamber view, such as in Tetralogy of Fallot (ToF) and Transposition of Great Arteries (TGA).[6] Closure or restriction of foramen ovale may result in severe cyanosis and circulatory collapse in TGA where systemic and pulmonal circulation work in parallel and mixing of oxygenated and non-oxygenated blood.[6]

Currently, intrauterine CHD detection is problematic because of gestational age, complex heart structure in imaging studies, training and experience needed, fetal and maternal movement, maternal obesity, amniotic fluids amount, fetal position, and maternal tissues. Intrauterine screening is usually done using ultrasonography and conducted by GP or OBGYN involves preliminary screening at 18–22 weeks of gestation and follow-up screening to increase the accuracy (up to 80% in CHD-focused screening).[7]

Preliminary screening increases chance of detection and intervention; with ultimate goal of reducing morbidity and mortality of CHD. Even with trainings, some CHD, including Total Anomalous Pulmonary Venous Drainage (TAPVD), CoA, and progressive valvular abnormalities are still becoming challenge to detect.[6] Therefore, this literature review aims to review the prevalence, anatomy, embryology, and ultrasonographic findings of CHD.

II. DEFINITION

Congenital heart diseases are structural abnormalities in heart or major vessels that present during birth. Top eight congenital heart diseases are Ventricular Septal Defect (VSD), Atrial Septal Defect (ASD), Patent Ductus Arteriosus (PDA), Pulmonary Stenosis, Tetralogy of Fallot (ToF), Transposition of Great Arteries (TGA), Atrioventricular Septal Defect (AVSD), dan Coarctation of Aorta (CoA).[3,8] Congenital heart diseases are found globally and become major health issues in millions of babies each year. It affects one-third of congenital anomalies found each year.[2]

III. EPIDEMIOLOGY

Prevalence of CHD varies in time. Congenital heart disease was found on 0.6 births per 1,000 live births on 1930 and increasing to 9.1 births per 1,000 live births after 1995. The incidence increased markedly in 1930–1960, followed with a plateau of around 5.3 births per 1,000 live births during 1961–1975, and increased sharply once more in 1975–1995.[2,3]

Ventricular Septal Defect, ASD, and PDA become three major CHD cases globally. These 3 lesions affect 57.9% of CHD cases globally and increased from 49.2% in 1970–1974 to 65.3% in 2010–2017.[3] Regional variability exists; where in Asia, pulmonal outflow obstruction is more commonly found than left ventricle outflow obstruction. Transposition of Great Arteries is also rarer in Asia than in Europe, North and South America, and Oceania.[2]

Table 1. Global Prevalence of Congenital Heart Disease

Subtypes of CHD	Prevalence per 1,000 live births (95% CI)	Percentage of subtype (95% CI)
Ventricular Septal Defect	3.071 (2.845–3.305)	35.568 (33.876–37.278)
Atrial Septal Defect	1.441 (1.215–1.687)	15.378 (13.492–17.363)
Patent Ductus Arteriosus	1.004 (0.803–1.228)	10.172 (8.519–11.954)
Pulmonary Stenosis	0.546 (0.485–0.611)	6.233 (5.703–6.784)
Tetralogy of Fallot	0.356 (0.326–0.387)	4.422 (4.064–4.794)
Transposition of Great Arteries	0.295 (0.269–0.322)	3.819 (3.446–4.210)
Atrioventricular Septal Defect	0.290 (0.265–0.316)	3.595 (3.302–3.900)
Coarctation of Aorta	0.287 (0.261–0.314)	3.570 (3.273–3.879)

Cited from: Liu et al., 2019.[3]

IV. RISK FACTORS

CHD involves many risk factors. In a study conducted in Pakistan, major risk factors included consanguineous marriage (OR 2.34; 95% CI 1.61–3.38), family history of CHD (OR 9.43; 95% CI 3.30–27.02), maternal comorbidities (OR3.9; 95% CI 1.2–5.6), and low birth weight (OR 3.11; 95% CI 1.84–5.29).[9]

Meanwhile, based on a study in India, CHD risk factors included paternal age above 25 years old (OR 1.943; 95% CI 1.421–2.658), no multivitamin consumption during pregnancy (OR 2.853; 95% CI 2.089–3.895), history of fever in first trimester (OR 3.717; 95% CI 1.625–8.501), history of obstetric issues (OR 2.454; 95% CI 1.565–3.848), and maternal age above 30 years old (OR 2.868; 95% CI 1.255–6.555).[10]

A study conducted in Shaanxi, China, showed similar results. Congenital heart disease risk factors found in Shaanxi included multiple pregnancy, family history of CHD, old maternal age, and parity.[11] Genetic factors, including chromosomal and syndrome, are known to involve in CHD. The genetic factors are elaborated in Table 2.

Table 2. Genetic Factors of Congenital Heart Disease

Syndrome	Chromosomal/genetic abnormalities	Common lesions	Proportions
Down	Trisomy 21	AVSD, ASD, VSD, TOF	40–50%
Edwards	Trisomy 18	VSD, ASD, DORV, TOF, CoA, HLHS	90–100%

Patau	Trisomy 13	ASD, VSD, DORV, HLHS, L-TGA, AVSD, TAPVR, dextrocardia, PDA	80%
Turner	Monosomy X	CoA, AS, HLHS, PAPVR	25–35%
Klinefelter	47, XXY	ASD, PDA, MVP	50%
Cat eye	Tetrasomy 22p	TAPVR, PAPVR	50%
Pallister-Kilian	Tetrasomy 12p	VSD, CoA, PDA, ASD, AS	25%
Velocardiofacial	Del 22q11.2	IAA(B), TA, TOF, aortic arch anomalies	75–85%
Williams	Del 7q11.23	SVAS±PVS, PS, PPS	50–80%
Alagille	*JAG1, NOTCH1* (del 20p12)	PPS, TOF, ASD, PS	85–95%
Noonan	*PTPN11, SOS1, KRAS, RAF1*	PVS, ASD, CoA, HCM	80–90%
Holt-Oram	*TBX5*	ASD, VSD, AVSD, TOF	80%
Char	*TFAP2B*	PDA	60%
Ellis-van Creveld	*EVC, EVC2*	Primum ASD, common atrium, AVSD	60%
Smith-Lemli-Opitz	*DHCR7*	AVSD, primum ASD, VSD, PAPVR	45%
CHARGE	*CHD7, SEMA3E*	ASD, VSD, valvular abnormalities	50–80%
Kabuki	*MLL2*	CoA, ASD, VSD	40%
Heterotaxy	*ZIC3*	Dextrocardia, L-TGA, AVSD, TAPVR	90–100%

ASD: atrial septal defect; AS: aortic stenosis; AVSD: atrioventricular septal defect; CoA: coarctation of aorta; DORV: double outlet right ventricle; HCM: hypertrophic cardiomyopathy; HLHS: hypoplastic left heart syndrome; IAA(B): interrupted aortic arch (type B); L-TGA: congenitally corrected transposition of great arteries; MVP: mitral valve prolapse; PAPVR: partial anomalous pulmonary venous return; PDA: patent ductus arteriosus; PPS: peripheral pulmonary stenosis; PS: pulomary stenosis; PVS: pulmonary valve stenosis; SVAS: supravalvular aortic stenosis; TA: truncus arteriosus; TAPVR: total anomalous pulmonary venous return; TOF: tetralogy of Fallot; VSD: ventricular septal defect
Cited from: Blue, et al. 2012.[12]

Besides syndromic factors, nonsyndromic genetic mutations also play parts in congenital heart diseases; as shown on Table 3.

Table 3. Nonsyndromic Genetic Factors in Congenital Heart Disease

Gene	Function	Lesions
NKX2-5	Transcription factor	ASD-AV block, TF, HLHS, TGA, DORV, Ebstein anomaly, VSD
NKX2-6	Transcription factor	TA
GATA4	Transcription factor	ASD±PS, TOF, VSD, DORV
GATA6	Transcription factor	TA, TOF, AVSD
TBX1	Transcription factor	IAA, aortic arch anomalies, VSD

TBX5	Transcription factor	ASD, VSD, AVSD, conduction anomalies
TBX20	Transcription factor	ASD, VSD, valvular disease, LVOTO
CITED2	Transcription factor	ASD, VSD, TOF, TGA
ZIC3	Transcription factor	Heterotaxy, ASD, AVSD, TGA, VSD, TAPVR, PS
ZFPM2	Transcription factor	TOF
FOXH1	Transcription factor	TOF, VSD
HAND1	Transcription factor	HLHS (somatic mutation)
TFAP2B	Transcription factor	PDA
NOTCH1	Membrane-ligand receptor	AS, BAV
NODAL	Membrane-ligand receptor	Heterotaxy, TGA
JAG1	Membrane-ligand receptor	PS, TOF
CFC1	Membrane-ligand receptor	Heterotaxy, TGA, DORV, TOF
MYH6	Sarcomere protein	ASD
MYH7	Sarcomere protein	ASD, Ebstein anomaly
MYH11	Sarcomere protein	PDA
ACTC1	Sarcomere protein	ASD, VSD
GJA1	Gap junction protein	HLHS (somatic mutation)
GJA5	Gap junction protein	TOF
CRELD1	Cellular matrix protein	AVSD, dextrocardia
ELN	Structural protein	SVAS
VEGFA	Mitogen	TOF

ASD: *atrial septal defect*; AS: *aortic stenosis*; AV: *atrioventricular*; AVSD: *atrioventricular septal defect*; BAV: *bicuspid aortic valve*; DORV: *double outlet right ventricle*; HLHS: *hypoplastic left heart syndrome*; IAA: *interrupted aortic arch*; LVOTO: *left ventricular outflow tract obstruction*; PDA: *patent ductus arteriosus*; PS: *pulmonary stenosis*; SVAS: *supravalvular aortic stenosis*; TA: *truncus arteriosus*; TAPVR: *total anomalous pulmonary venous return*; TGA: *transposition of great arteries*; TOF: *tetralogy of Fallot*; VSD: *ventricular septal defect*. Cited from: Blue et al., 2012.[12]

Moreover, congenital heart disease can also be caused by environmental and infectious factors, as shown on Table 4 below.

Table 4. Environmental and Infectious Factors of Congenital Heart Diseases

Teratogen	Commonly found lesions	Risks
Maternal diabetes	VSD, ASD, L-TGA, AVSD, TAPVR, CoA, TOF, TGA	5%
Maternal rubella	PDA, VSD, ASD, PS, TOF	30–60%

Maternal phenylketonuria	TOF, VSD, PDA, left heart lesions	15–50%
Systemic lupus erythematosus	Complete heart block	Unknown
Fever in pregnancy	PS, left-sided and right-sided obstruction defects, tricuspid atresia, VSD	Unknown
Thalidomide	TOF, ASD, VSD, TA	Up to 30%
Retinoic acids	TA, TOF, IAA, DORV	25%
Anticonvulsants	All common defects	Unknown
Lithium	Ebstein anomaly, tricuspid atresia	Unknown
Selective serotonin reuptake inhibitors	VSD, ASD, TOF	Unknown
Alcohol	VSD, ASD, TOF	Unknown
Marijuana	VSD, Ebstein anomaly	Unknown

ASD: *atrial septal defect*; AS: *aortic stenosis*; AV: *atrioventricular*; AVSD: *atrioventricular septal defect*; BAV: *bicuspid aortic valve*; CoA: *coarcation of aorta*; DORV: *double outlet right ventricle*; HLHS: *hypoplastic left heart syndrome*; IAA: *interrupted aortic arch*; LVOTO: *left ventricular outflow tract obstruction*; PDA: *patent ductus arteriosus*; PS: *pulmonary stenosis*; SVAS: *supravalvular aortic stenosis*; TA: *truncus arteriosus*; TAPVR: *total anomalous pulmonary venous return*; TGA: *transposition of great arteries*; TOF: *tetralogy of Fallot*; VSD: *ventricular septal defect*.
Cited from: Blue et al., 2012.[12]

V. EMBRYOLOGY OF HEART

Formation of heart starts at third week of gestation. Cardiac cells arise from mesodermal layers in cranial area that migrate to primary heart field (cranial of neural folds) and start forming parts of atria and whole left ventricle. Right ventricle and outflow tracts arise from secondary heart field from visceral side of mesoderm.[13,14]

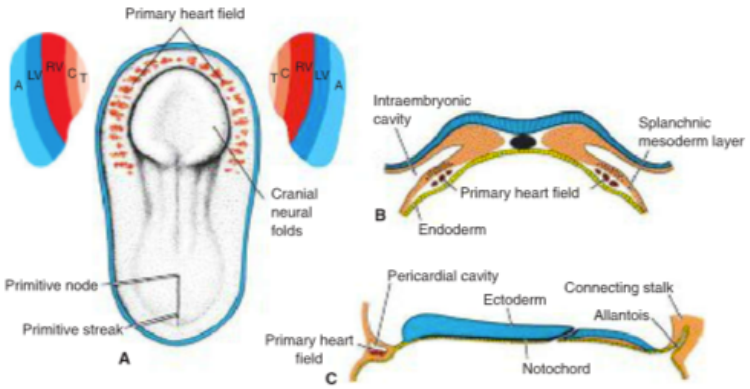

Figure 1. Heart embryology. (A) Dorsal view of 18-days old embryo. Progenitor cells of hear migrate and form horseshoe-shaped primary heart field. Primary heart field forms right- and left-side of heart, including both atrium and whole left ventricle. Right ventricle, outflow tract, and truncus arteriosus arise from secondary heart field; (B) transverse view showing primary heart field in visceral mesoderm; (C) lateral cut on embryo showing primary heart field. Cited from: Sadler, 2019.[14]

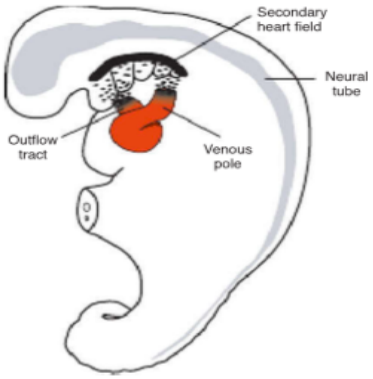

Figure 2. Secondary heart field in visceral mesoderm. Secondary heart field creates elongation on artery and vein poles, that encompass right ventricle and outflow tract (conus cordis and truncus arteriosus), atrium, and sinus venosus. Secondary heart field defect creates shortening and outflow defect.
Cited from: Sadler, 2019.[14]

In the beginning, central part of cardiogenic area is located on the anterior of oropharyngeal membrane and neural plate. During closure of neural tube and formation of brain, oropharyngeal membrane pulled anteriorly and heart moves cervically before migrating to thorax.[13,14] In time of cephalocaudal embryo development, embryo also folds laterally and creates outflow and heart ventricles. During embryo development, heart becomes whole tube consisting of endothelial and myocardium cells. With continuing development, middle section of mesocardium disappears, creating transverse pericardial sinus that connects both sides of pericardial cavity.[14]

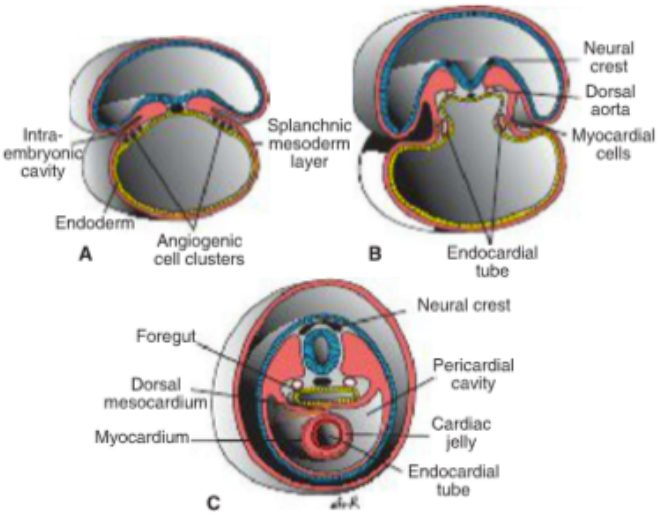

Figure 3. Cross-section of embryo in heart development; (A) 17-days old embryo; (B) 18-days old embryo; (C) 22-days old embryo. Fusion froms on caudal area of tube. Outflow and majority of ventricles arise from growth of horseshoe-shaped area before.
Cited from: Sadler, 2019.[14]

Heart undergoes elongation from cells arising from secondary heart field to create right ventricle and outflow tracts. This is an important stage for outflow defects, including VSD, ToF, pulmonary atresia, and pulmonary stenosis.[14] During outflow elongation, cardiac tube starts folding in 23rd day to create cardiac loop, finishing on 28th day.[13,14]

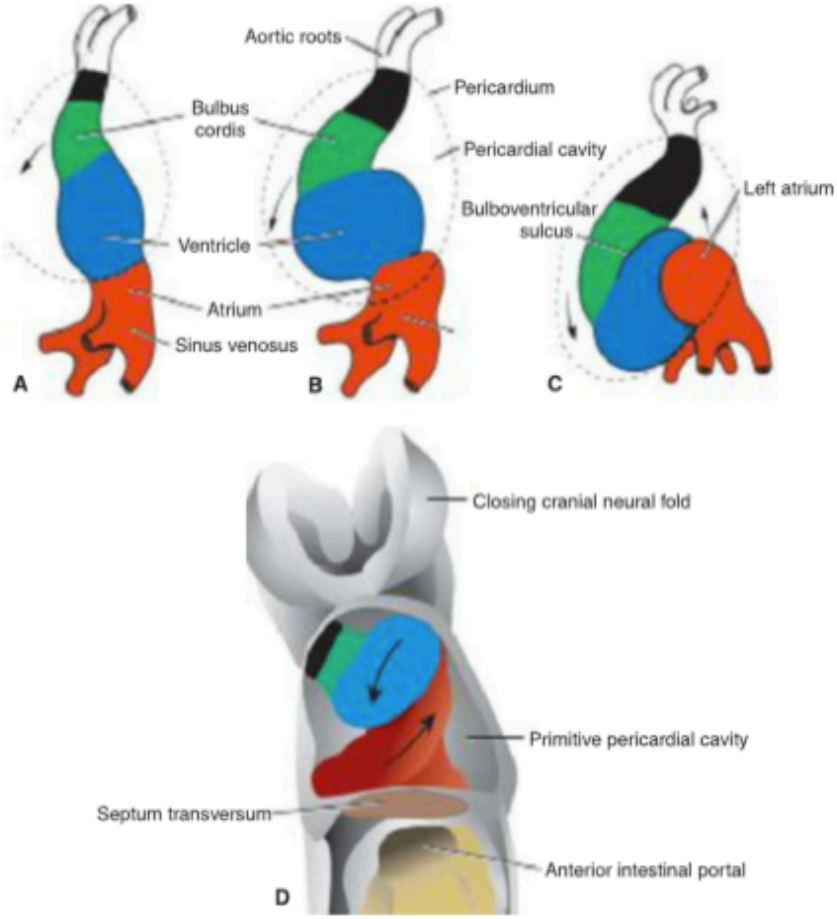

Figure 4. Formation of cardiac loop; (A) 22 days; (B) 23 days; (C) 24 days; (D) frontal view of looping heart tube. Primitive ventricles move ventrally and to the right, while atria move dorsally and to the left.
Cited from: Sadler, 2019.[14]

Cardiac septum is formed on 27th day until 37th day. Development of tissues create endocardial cushions that develop around atrioventricular and conotruncal area to form septum of atrium and ventricles. The same process also forms canals and valves of atrioventricular area. Disruption of development in this stage creates ASD, VSD, TGA, and ToF.[13,14]

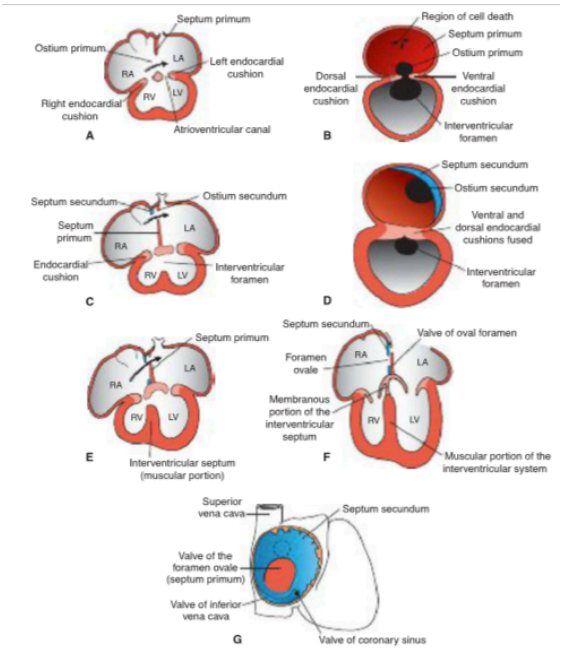

Figure 5. Septum on different development stages. (A, B) 30 days; (C, D) 33 days; (E) 37 days; (F, G) neonates. Cited from: Sadler, 2019.[14]

Table 5. Developmental Stages and Associated Lesions

Tissue	Cellular process	Normal effects	Abnormalities
Primary heart field (16th day until 18th day)	Laterality and patterning	Formation of four heart chambers	DORV, TGA, ASD, VSD, atrial isomerism, ventricular inversion, dextrocardia
Heart tube (22nd day until 28th day)	Genetic signal to create normal loop	Cardiac loop	Dextrocardia
Atrioventricular canal, endocardial cushions (26th day until 35th day)	Formation of endocardial cushions, proliferation and cellular migration	Division of atrioventricular canal to right and left canal, formation of mitral and tricuspid valve, formation of interventricular septum	VSD, mitral and tricuspid defect
Secondary heart field (22nd day until 28th day)	Visceral mesoderm from ventral pharynx and signals from neural crest cells	Elongation and separation of outflow into aortic and pulmonary canal	ToF, TGA, pulmonary atresia, pulmonary stenosis
Outflow tract (36th day until 49th day)	Migration of neural crest cell, proliferation	Formation of conotruncal cushions and division of outflow tract	Common truncus arteriosus, outflow defect
Aortic arch (22nd day until 42nd day)	Migration of neural crest cell, proliferation	Formation of aortic arch	Anomalous right pulmonary artery

Cited from: Sadler, et al.[14]

VI. ULTRASONOGRAPHY FINDINGS

Ultrasonography has been widely utilized to screen CHD at 18–22 weeks gestational age.[15,16] In Great Britain, detection rate of CHD was 35%. In United Kingdom, 35% of CHD was able to be prenatally detected, while in Northern Ireland the detection rate was 32%. In Scotland, the detection rate was 36%, while in Wales the detection rate was 52%. In Great Britain, the number is lower than the target of 60% detection rate.[16]

In a national study in Czech, around one-third of CHD could be screened prenatally. The detection rate was 77.3% for double outlet right ventricle, 50.6% for left heart hypoplasia, 50% for Ebstein anomaly, 42.9% for AVSD, and 42.5% for single ventricle. However, ASD, VSD, and pulmonary stenosis rate was low; 0.8%, 2.4%, and 3.2%, respectively.[15]

In a study in Brazil, detection rate of CHD is only 9.96%. From this number, 48.1% were complex cases (left heart hypoplasia, tricuspid atresia, Ebstein anomaly, truncus arteriosus), 18.5% were significant cases (ToF, large VSD, tricuspid dysplasia, large pulmonary stenosis), 7.4% were minor cases (small VSD), and 26% were not categorized (cardiomyopathy, dysrhythmia, and others).[17]

Congenital heart diseases screening can be done starting from 11 weeks gestational age using four-chamber view. After that, screening can be conducted from second trimester to follow-up any septal or developmental defects. Sensitivity of CHD may approach 92% in 13th week of gestation.[7]

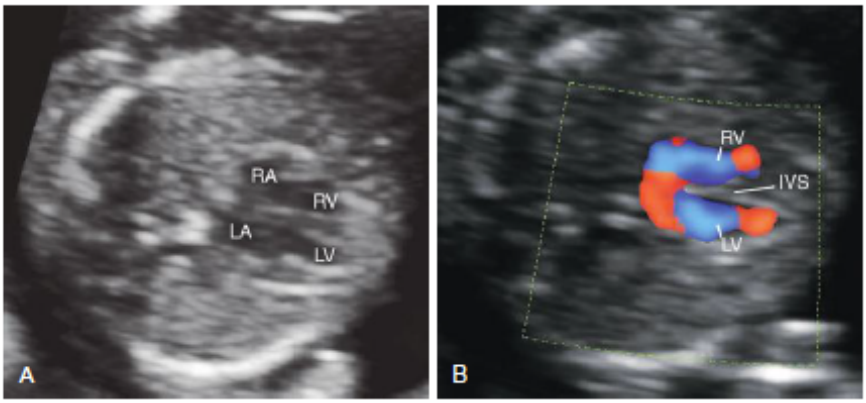

Figure 6. Four-chamber view in early gestation. (A) Four-chamber view in 13th week; (B) Four-chamber view with Doppler in 13th week.
Cited from: Norton *et al.*[7]

Second trimester screening aims to detect CHD. Screenings are usually done at week 18–22 gestational age. Screening aims to measure heart rate, heart size, heart position, four chamber of the heart, pericardium, atrium, ventricles, atrioventricular junctions, and ventriculoatrial junctions.[7] Early detection of CHD is paramount because of clinical complications that may arise shortly after birth.

Doppler echocardiography becomes primary diagnostic tools in CHD patients because of its high sensitivity and specificity, safety, and noninvasiveness.[6,18] Echocardiography starts from determination of heart location, followed by four-chamber view, left ventricular outflow tract view, right ventricular outflow tract view, and three-vessel view or three-vessel tracheal view.[6] Goals of these examinations are to measure heart shape and abnormalities.[19]

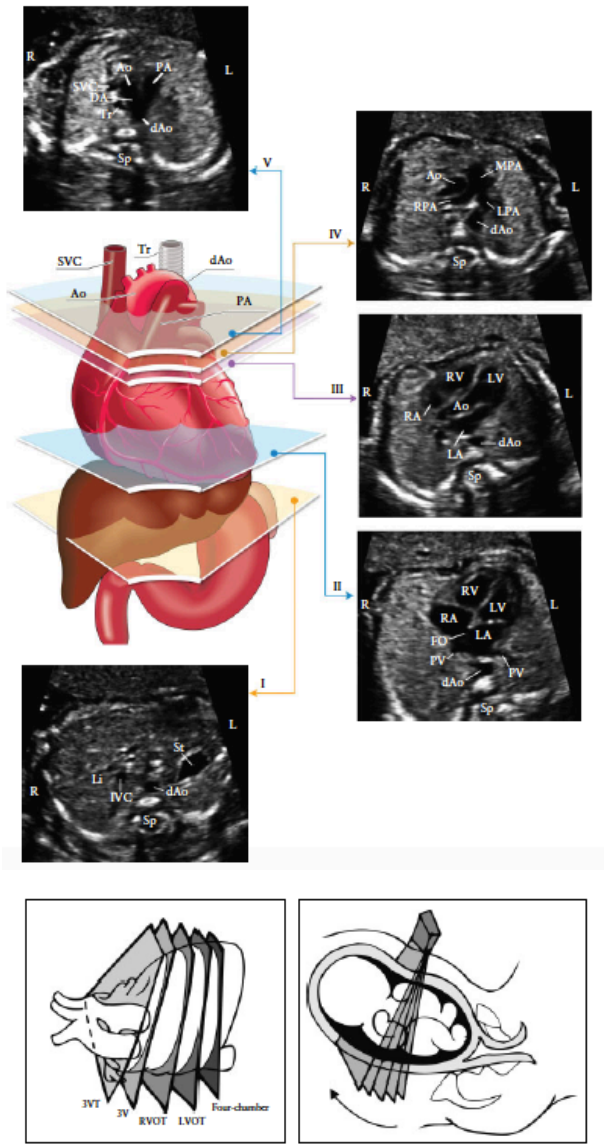

Figure 7. Main axis of fetal heart screening. I: most caudal plane, showing fetal stomach (St), descending aorta cross section (dAo), spine (Sp), and fetal liver (Li). II: four-chamber view of fetal heart, showing right and left ventricle (RV, LV), atria (RA, LA), foramen ovale (FO), and pulmonary veins beside descending aorta. III: left ventricular outflow tract view, showing aorta (Ao), LV, RV, LA, and RA with descending aorta cross section (dAo). IV: most cephalad position (right ventricular outflow tract view) showing pulmonary artery (MPA) and its branches (RPA dan LPA), ascending aorta (Ao), and descending aorta (dAo). V: three vessels tracheal view show superior vena cava (SVC), pulmonary artery (PA), ductus arteriosus (DA), aortic arch (Ao-dAo), and trachea (Tr). Cited from: The International Society of Ultrasound in Obstetrics, 2013.[19]

Heart location screening is essential to measure heart orientation. In situs inversus, other lesions can sometimes be found; therefore, more detailed screening is warranted. Four-chamber view is used to measure heart location and anomalies, surrounding tissue lesion, ToF, cardiomegaly, and septal or valvular defects. [6,20] Four-chamber view is also utilized to measure fetal heart rhythm and fetal heart rate. Persistent bradycardia may arise from heart block. Abnormal heart location may also come from abnormalities in thorax cavity, such as diaphragmatic hernia or pulmonary hypoplasia.[19]

Left ventricular outflow tract view is utilized to detect valvular defect, aortal defect, and ventricular septal defect. Right

ventricular outflow tract view is used to measure right heart outflow, including pulmonary valve, pulmonary stenosis, and TGA.[6,18–20]

Three-vessels view and three-vessel tracheal view is used to locate any congenital heart defects and to confirm defects shown in four-chamber view. Three-vessels view is also used to aid diagnosis in syndromic chromosomal abnormalities.[6,18,20]

Follow-up examination is indicated on a few conditions. Maternal indications include autoimmune antibody, family history of defects, *in vitro* fertilization, maternal metabolic disease, or teratogenic exposure. Fetal indications include abnormal screening result, family history of CHD, abnormal heart rhythm, chromosomal abnormalities, extracardiac abnormalities, hydrops, or monochorionic twin pregnancy.[21]

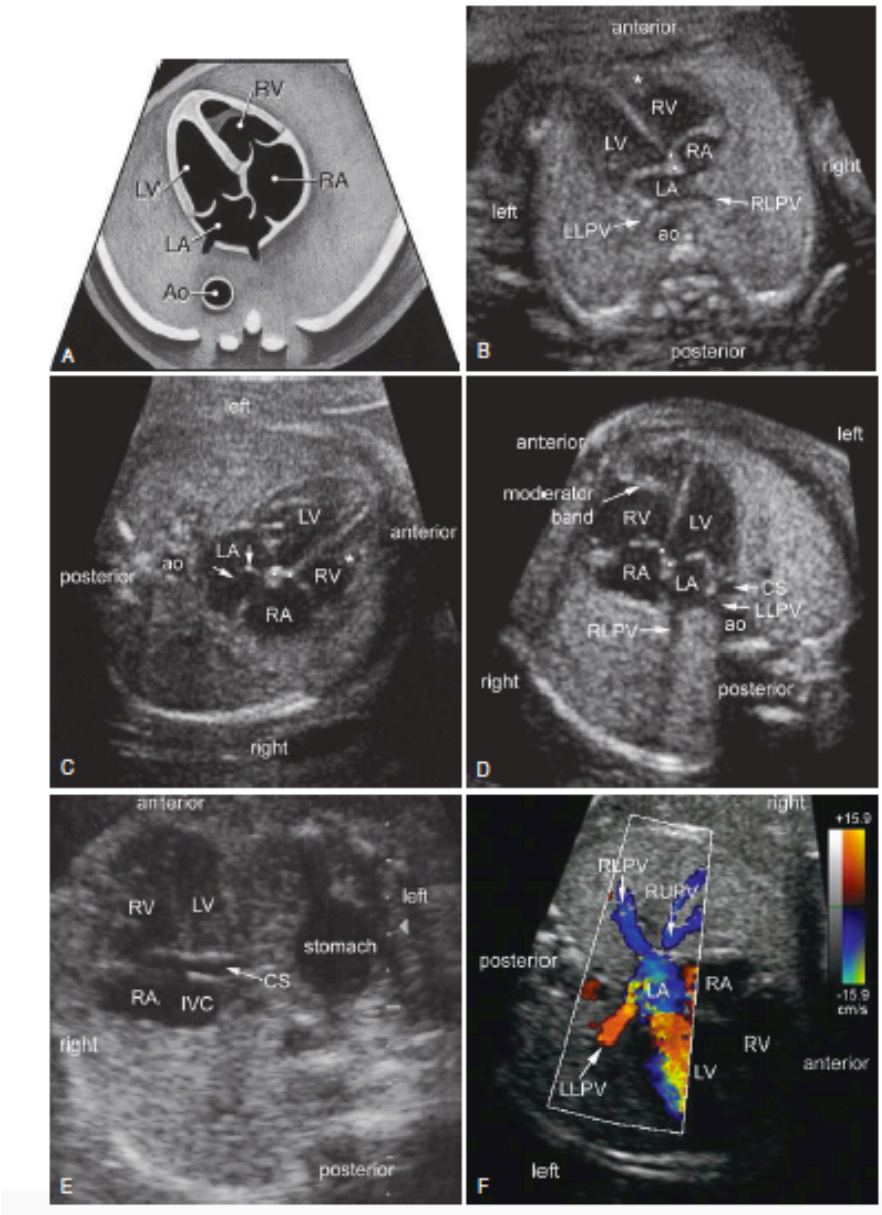

Figure 8. Four-chamber view on second trimester. (A) Diagram; (**B-F**) Ultrasonographic findings. Cited from: Norton, 2008.[7]

Table 6. Congenital Heart Lesions and Clinical Symptoms

Lesions	Prevalence per 10,000 live births	Hypoxemia	Ductus arteriosus dependent
Tetralogy of Fallot	5.1	Majority	Rare
Transposition of great arteries	4.0	All	Rare
Double-outlet right ventricle	1.7	Some	Not
Truncus arteriosus	1.0	All	Not
Total anomalous pulmonary venous connection	1.2	All	Not
Ebstein anomaly	0.6	Some	Sone
Tricuspid atresia	0.5	All	Some
Pulmonary atresia, intact septum	0.8	All	All
Pulmonary stenosis/atresia	6.3	Some	Some
Right heart hypoplasia	3.3	all	All
Coarctation of aorta	4.7	Some	Some
Aortic arch atresia/hypoplasia	1.0	Some	All
Aortic valve stenosis	1.6	Rare	Some
Other defects	12.4	Some	Some

Cited from: Norton, 2008.[7]

VII. CONCLUSION

Congenital heart disease is a major health concern, affecting 1.35 million children born every year. With increased rate of CHD, better screening and follow-up should be conducted to achieve acceptable detection rate. Ventricular septal defect, ASD, and AVSD are found in 57.9% cases of CHD globally and increasing. Their risk factors include consanguineous marriage, family history of CHD, old maternal and paternal age, and exposure to teratogens. Genetic factors, including chromosomal or syndromic conditions, are known to manifest as CHD.

Missteps in cardiac development are the main pathophysiology of CHD. Ultrasonography screening in 18–22 weeks gestational age can be utilized to screen developmental issues. Follow-up screening can be conducted to increase detection rate to 80% or even better.

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