Ebstein anomaly in the adult: focus on pregnancy

Paraskevi Koutrolou-Sotiropoulou, Fabio V. Lima, Anjali Kapur and Kathleen Stergiopoulos*

*Correspondence: Kathleen.Stergiopoulos@stonybrookmedicine.edu

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Department of Medicine, Division of Cardiovascular Medicine, State University of New York, Stony Brook, New York.

Abstract

Ebstein anomaly (EA) is a rare cardiac congenital abnormality characterized by downward displacement of the posterior and septal leaflets of the tricuspid valve which results in atrialization of the right ventricle, enlargement of the right atrium and tricuspid regurgitation. Affected individuals experience a wide spectrum of clinical severity, ranging from heart failure in infants to asymptomatic adults and identification of the disease later in life. Other clinical presentations include cyanosis, arrhythmias and paradoxical emboli through atrial level shunts. Imaging modalities such as echocardiography and cardiac magnetic resonance are used for diagnosis. Appropriate surgical and medical management tailored to each patient's anatomy and hemodynamic status is necessary in order to ensure acceptable patient outcomes. Since most patients survive to childbearing age, understanding of the hemodynamic changes during pregnancy and careful planning of labor and delivery are paramount. The purpose of this review is to focus on Ebstein anomaly in the adult patient tailored for the adult cardiologist and to provide a systematic review of pregnancy outcomes in women with Ebstein anomaly.

Keywords: Ebstein anomaly, congenital heart disease, right heart dysfunction, cardiac magnetic resonance imaging, echocardiography, pregnancy, systematic review

Introduction

In 1866, Dr Wilhelm Ebstein first described the clinical and anatomical features of the congenital anomaly of the tricuspid valve [1]. He described the case of a man who died of cyanotic heart disease secondary to a malformation of the tricuspid valve, which ultimately became known as Ebstein anomaly (EA). Since that time, advances in the diagnosis and management of this disease have been made, many of which will be described herein.

Review

Epidemiology and genetics

Ebstein anomaly (EA) is a rare cardiac congenital defect which accounts for less than 1% of congenital heart disease (CHD) [2]. The prevalence of Ebstein anomaly is estimated at 1 in 200,000 live births [3]. Several genetic and environmental risk factors have been identified, including exposure to benzodiazepines, lithium, cocaine and marijuana [2]. Most cases of Ebstein anomaly are sporadic, although familial cases have been described in the literature [4]. Mutations in several genes encoding sarcomeric proteins have been identified in association with Ebstein anomaly, including cardiac myosin-binding protein C, alpha-cardiac actin, cardiac troponin T and I, and

alpha-tropomyosin. The genetic association with sarcomeric proteins allows for plausibility that Ebstein anomaly is a disease of the myocardium as well as valve tissue [5]. Specifically, an association between Ebstein anomaly and mutation in *MYH7*. *MYH7* mutations are predominantly found in Ebstein anomaly associated with left ventricular noncompaction [6].

Anatomy

Anatomically Ebstein anomaly is characterized by a functionally and morphologically abnormal tricuspid valve (TV) and right ventricle (RV). Embryologically, the leaflets of the TV develop from the endocardial cushion tissue and the myocardium of the RV via delamination which is characterized by separation of the tissue from the underlying myocardium during weeks 8 through 12 [7]. In Ebstein anomaly, failure of delamination results in a large anterior tricuspid leaflet, which is usually attached to the tricuspid valve annulus and can be redundant and fenestrated (Figure 1). In normal individuals, displacement of the posterior and septal leaflets of the TV in comparison with the mitral valve leaflet is 8 millimeter per square surface body area or less. In Ebstein anomaly, the posterior and septal leaflets are displaced posteriorly and downward towards the RV. This accounts for

the “atrialization” of the RV (aRV) and dilation of the tricuspid annulus with resultant tricuspid regurgitation and enlargement of the right atrium (RA). Patients with untreated Ebstein anomaly have large functional right ventricles, as shown in an elegant magnetic resonance imaging (MRI) study [8]. In this study, the size of the enlarged functional right ventricle seemed to depend on the degree of tricuspid regurgitation and not the size of the atrialized right ventricle or the age of the patient. The functional RV consists mostly of the right ventricular outflow tract and RV apex. The rest of the RV combines with the RA and serves as a passive conduit of blood. Majority of the Ebstein anomaly cases have a dilated RV and RA, with varying degrees of tricuspid annular dilatation. The extent of the TV displacement, RV dilation and TV regurgitation vary from patient to patient, accounting for diversity in the clinical presentation of this anomaly. The dictum “every single heart in Ebstein anomaly is different” [9] has been professed. **Table 1** notes the most commonly used classification [10]. Elevated atrial pressures increase the possibility

of a right to left shunt in cases that have a coexistent patent foramen ovale (PFO) or atrial septal defect (ASD). Dilation of the RV may lead to abnormal right ventricular systolic function and clinical heart failure. Concomitant lesions in patients with Ebstein anomaly have been reported [11]. Other cardiac lesions and associations include ventricular septal defect, coarctation of the aorta, pulmonary outflow obstruction and mitral valve prolapse, among others [12] (**Table 2**).

Clinical presentation and physical examination

Physical examination

In an adult patient with Ebstein anomaly, clinical features that may be present on physical exam include edema and cyanosis [13,14]. An Ebstein patient may have a holosystolic murmur associated with tricuspid regurgitation. A widely split S1 heart sound can be heard with a loud tricuspid component resulting from delayed closure of the tricuspid valve due to an enlarged anterior leaflet and tricuspid annular dilatation [15]. In cases of severe right ventricular atrialization and right atrial enlargement, jugular venous distension and hepatosplenomegaly may be present, suggestive of right heart failure [13].

Ebstein anomaly and cyanosis

Eighty percent of patients with Ebstein anomaly have atrial

Table 1. Anatomic classification of Ebstein anomaly [10].

Anatomic type	Characterization
Type I	<ul style="list-style-type: none"> Minimal displacement of the tricuspid valve with an adequate size right ventricle Patients often remain asymptomatic until adulthood
Type II	<ul style="list-style-type: none"> Marked displacement of the tricuspid valve and the functional right ventricle is small Anterior leaflet is mobile
Type III	<ul style="list-style-type: none"> Anterior leaflet is restricted
Type IV	<ul style="list-style-type: none"> Displacement of the tricuspid valve is so severe that the right ventricle is absent and the patients present in neonatal life with cyanosis

Table 2. Associated anatomical abnormalities in Ebstein anomaly patients.

<ul style="list-style-type: none"> Varying degrees of tricuspid regurgitation Atrial level communication (patent foramen ovale or atrial septal defect) Ventricular septal defect Tricuspid stenosis Right ventricular outflow tract obstruction Mitral valve prolapse Bicuspid aortic valve Left ventricular abnormalities: Noncompaction cardiomyopathy, systolic and diastolic dysfunction Partially anomalous pulmonary venous drainage Congenitally corrected transposition of the great arteries (ccTGA)
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Figure 1. Pathologic specimen from a patient with Ebstein anomaly.

Tricuspid valve is displaced markedly inferiorly and the right ventricular wall is thin. With permission from [59]. Severe right atrial (RA) enlargement, the atrialized right ventricle (ARV), small RV, and the apically displaced tricuspid valve (white arrow, TV) consistent with Ebstein anomaly. A secundum atrial septal defect (ASD) is also present.

septal defect or patent foramen ovale [16,17]. Depending on the severity of tricuspid valve regurgitation and elevation of right heart pressure, the degree of right to left shunt may vary and lead to cyanosis. The clinical spectrum of cyanosis extends from cyanosis present in the neonate, to the presence of cyanosis later in adult life. Potential causes of increases in right to left shunting can be related to exercise or pregnancy. The right to left shunt may result in hypoxemia which does not respond to supplemental oxygen. Erythrocytosis may develop secondary to hypoxia, accounting for a high hematocrit and possibly hyperviscosity syndrome, which can include thrombosis and/or bleeding [18]. However, erythrocytosis may not only develop due to secondary hypoxemia related to shunt lesions, but also due to impaired pulmonary perfusion due to TR and RV dysfunction. Erythrocytosis correlates with EA disease severity [18].

Ebstein anomaly and paradoxical emboli

The presence of interatrial communication in Ebstein anomaly patients poses an increased risk of paradoxical emboli including transient ischemic attack/stroke, brain abscess or myocardial infarction [19]. Percutaneous closure of atrial septal defects or surgical closure may prevent paradoxical emboli [20].

Electrocardiography in ebstein anomaly

A twelve-lead electrocardiogram (ECG) may demonstrate evidence of right bundle block, right atrial and right ventricular hypertrophy, accessory pathways, “Himalayan” p waves, referring to giant p waves [21] (Figure 2). Atrial arrhythmias including atrial fibrillation, atrial flutter or atrial tachycardia may be present. Fragmented QRS complex (Figure 2, Arrow) on 12-lead ECG, a marker of myocardial scar, has been associated with larger atrialized RV area and an increased risk of arrhythmic events in adult patients with EA [22].

Ebstein anomaly and arrhythmias

Patients with EA have the substrate for the development of arrhythmias given the abnormal tricuspid valve, tricuspid valve annulus, and dilatation of the right heart. The presence of pre-excitation accessory pathways including Wolf Parkinson White syndrome, atrial fibrillation, atrial flutter, atrial ectopic tachycardia as well as ventricular tachycardia are common [23]. Rhythm disturbances can be refractory to medical management and radiofrequency ablation may offer better long term durability. However, catheter ablation of accessory pathways remains challenging in this patient population since 50% of patients have multiple accessory pathways.

Ebstein anomaly and heart failure

Given the heterogeneity of anatomic variants in Ebstein anomaly, the severity of the valvular and right ventricular dysfunction itself dictates the severity of the clinical presentation. In the adult, worsening tricuspid regurgitation, right and possibly left ventricular dysfunction may lead to worsening right to left shunt and reduced cardiac output. Patients may present with dyspnea, diminished

Figure 2. Electrocardiogram (ECG) of a patient with Ebstein anomaly.

Findings include sinus rhythm, right bundle block, right ventricular hypertrophy and right atrial enlargement. There is no accessory pathway noted. Red arrows demonstrate the fragmented QRS complex noted in Ebstein anomaly.

exercise tolerance and fatigue. Patients who have only mild disease may survive until adulthood without having any symptoms [24].

Imaging in ebstein anomaly

Echocardiography

Echocardiography remains the modality of choice for establishing the diagnosis of Ebstein anomaly. Evaluation of the tricuspid valve anatomy is performed from the apical four chamber view from which all four chambers, both atrioventricular valves and interventricular and interatrial septa are visualized (Figure 3). The ratio of the area of the right atrium and atrialized right ventricle to the area of the functional right ventricle and left atrium and left ventricle described by Celermajer has been used to predict prognosis in neonates with a ratio <0.5 indicative of grade I and 0% of death and ratio >1.5 grade IV and 100% of death [25]. The measured distance between the insertion sites of the mitral and tricuspid valve of more than 8 millimeter per square root body surface area is essential for diagnosis. The anterior leaflet can be redundant and elongated and lead to right ventricular outflow tract obstruction. It may have fenestrations and prolapse may be present. Tethering of the leaflets may be present and lead to decreased leaflet mobility. In 2007, Castellanos et al., meticulously described the degrees of leaflet tethering [26]. Increases in right heart volume and dimensions may be present with possible interventricular septum displacement to the left heart a result of right ventricular overload [27]. The left ventricle may be altered as well, with a decrease in left end diastolic volume. Aneurysmal dilation of the right ventricle, defined as an RV diameter twice the aortic root diameter, may be present due to a thinner and less fibrous right ventricular free wall. Color Doppler demonstrates tricuspid regurgitation which is usually moderate or severe.

Cardiac magnetic resonance (CMR)

The complexity of the right ventricle does not always allow accurate assessment of the anatomy by echocardiography,

Figure 3. Cardiac imaging of a pregnant woman with ebstein anomaly.

A 36 year old woman, without prior pregnancies, originally from Ecuador, presented for evaluation of a cardiac murmur and palpitations in pregnancy. She complained of NYHA Class II symptoms at prior to pregnancy, worsening to class III during pregnancy. She had no clinical evidence of cyanosis and no pre-excitation on electrocardiography.

Panel A: Apical four chamber view demonstrates severe right atrial (RA) enlargement and severe right ventricular (RV) enlargement, the atrialized right ventricle (ARV), and the apically displaced tricuspid valve (white arrow) consistent with Ebstein anomaly.

Panel B: Demonstrates severe tricuspid regurgitation (TR).

Panel C: Demonstrates a triangular contour of the spectral Doppler of the tricuspid regurgitation, consistent with severe tricuspid regurgitation. The right ventricular systolic pressure, as estimated using the tricuspid regurgitation velocity of 2.27 m/s and with an assumed right atrial pressure of 15 mmHg, was normal at 35.6 mmHg. Color Doppler seen along the interatrial septum was consistent with the presence of a patent foramen ovale or small atrial septal defect(not shown). Fetal cardiac ultrasound performed at 22 weeks was normal (not shown). She was noted to have fetal growth restriction at 37 weeks and was admitted for induction of labor; she was delivered vaginally with an assisted second stage of labor and an epidural without clinical event.

Panel D: Cardiac magnetic resonance imaging (SSFP sequence) performed postpartum demonstrates severely enlarged right ventricular size and severely reduced right ventricular systolic function with a right ventricular ejection fraction of 27 %, as well as findings consistent with Ebstein anomaly and severe tricuspid regurgitation. At this time, she was admitted 8 days postpartum for heart failure symptoms. After medical stabilization, she underwent an uncomplicated tricuspid valve replacement with a bioprosthesis.

particularly in the setting of poor acoustic windows. Cardiac magnetic resonance (CMR) has emerged as an imaging modality for patients with Ebstein anomaly [28,29]. In 2011, Yalonetsky et al., demonstrated the reproducibility of right heart measurements [30]. Accurate measurement of right ventricular systolic function (with a right ventricular ejection fraction) is reliable since accurate delineation of right ventricular walls is possible. More recently,

Hösch et al., [31] demonstrate using the easily acquired index of right sided to left sided heart volumes from CMR correlated well with established heart failure markers. CMR, in combination with echocardiography, can provide important complementary information since it can better define the posterior tricuspid leaflet and the presence of fenestrations. Echocardiography is more sensitive for small atrial or ventricular septal defects [32].

In addition, MRI is more sensitive for identification of adhesions of the anterior valve and for the assessment of RV function, an important feature in the decision making for surgery as well as for surgical planning [32] (**Figure 3**).

Exercise stress testing and physical activity recommendations

Heart failure symptoms and deterioration of exercise capacity dictate the timing and necessity of surgical intervention in Ebstein patients. Ebstein patients may complain of minimal symptoms; however, they may limit themselves secondary to unrecognized significant functional decline. Exercise stress testing (serially) has been proposed by the 2008 American College of Cardiology/American Heart Association (ACC/AHA) guidelines for the management of adults with congenital heart disease to be included in the assessment of that patient population [33]. Exercise treadmill protocols which include electrocardiographic monitoring as well as the measurement of peak oxygen consumption (peak VO₂), carbon dioxide production, slope of minute ventilation in relation to the carbon dioxide, forced vital capacity and forced expiratory volume in one second have been studied in Ebstein patients [34-36]. Peak VO₂ is depressed in the Ebstein population particularly in those with higher "Ebstein Severity Grade" (defined as the ratio of the area of the right atrium and atrialized right ventricle to the area of the functional right ventricle and left atrium and left ventricle [34]) has been identified as a significant predictor of outcome. A level of less than 60% is associated with higher risk of death, non-elective hospitalization and surgical repair [36]. In the adult Ebstein population, the decline of peak VO₂ on follow up cardiopulmonary tests was gradual over the years and the deterioration is attributed to the progressive chronotropic insufficiency and the gradual failure of the right ventricle secondary to chronic volume overload in combination with the worsening tricuspid valve insufficiency [34]. More recently however, Hösch et al., [31] have shown that the Total right/left volume index should be used as a new and simplified CMR measure, allowing more accurate assessment of disease severity than previously described.

Surgical treatment options

Based on the 2008 ACC/AHA adult congenital heart disease guidelines [33] surgical repair of Ebstein anomaly is indicated in a symptomatic patient, the presence of right ventricular dilation or reduction of systolic function, presence of cyanosis, paradoxical emboli and progressive cardiomegaly on chest X-ray (**Figure 4**). Repair of the tricuspid valve is preferred over replacement since has been shown to have excellent outcomes in appropriately selected patients, although it remains technically challenging [37]. Surgeons with training and expertise in congenital heart disease should be chosen to operate on patients with Ebstein anomaly. The goal of surgical intervention is to improve functional status and reduce the risk of further right heart enlargement, heart failure and arrhythmias. When

replacement is necessary, a bioprosthetic valve is preferred over mechanical valve [38]. Mechanical valve at the tricuspid position in the setting of annular dilation and RV dysfunction predisposes to thrombosis. In choosing a bioprosthetic valve, a porcine valve is often favored over pericardial valve, though reasonable outcomes have been described with the later [39]. The diversity of anatomical variation and age of diagnosis dictate the surgical options. In the adult population, surgery usually involves tricuspid valve repair or replacement, closure of any interatrial communication, arrhythmia treatment, plication of right ventricle and atrial reduction [10,40,41]. Furthermore, early repair before signs of cardiomegaly or right heart failure is associated with better outcomes [42].

Adolescent and adult patients with EA undergoing tricuspid valve replacement or repair and concomitant cavopulmonary shunt, created to reduce the preload on the right ventricle, are at risk for early and mid-term complications [43]. However, Ebstein surgery along with cavopulmonary shunt appears to be a reasonable surgical strategy in patients not thought to be suitable for tricuspid valve surgery alone. Quinonez et al., [44] report that a 1.5-ventricle repair can be utilized in patients with severe Ebstein anomaly and impaired right ventricular function who are at risk for surgical treatment. Moreover, Raju et al., [45] contend that concomitant bidirectional cavopulmonary shunt can be a useful adjunct in repair of advanced EA with severe RV dilatation and dysfunction.

Management and medical therapy

A summary of the major points in management and medical therapy are summarized on **Table 3**.

Figure 4. Chest X-ray of a patient with Ebstein anomaly.
Findings demonstrating enlargement of the cardiac silhouette.

Table 3. Management in adult Ebstein anomaly patients.

- Diuretics for treatment of peripheral edema and right heart failure
- Consider surgical intervention
- Monitor for arrhythmias
- Anticoagulation with warfarin for paradoxical embolus or atrial arrhythmias
- Antibiotic prophylaxis before dental procedures is reasonable in cyanotic patients and postoperative patients with a prosthetic valve*
- Routine follow up with a specialist in adult congenital heart disease
- Counseling in women of childbearing potential regarding risks of pregnancy

*Antibiotic prophylaxis is usually not necessary in the unoperated, acyanotic patient.

Prognosis

Patients with Ebstein anomaly may present with initial symptoms at different stages of life. Generally, those that present later often have more positive outcomes than those presenting in early life. Patients presenting during fetal development, neonates, and infants frequently have severe tricuspid valve distortions with right ventricular deformities causing serious hemodynamic compromises and a negative prognosis. Often these patients encounter complications of heart failure and intrauterine cardiomegaly that causes under development of the lung tissue, repeatedly resulting in fetal demise or sudden infant death [24]. Whereas those patients presenting later in childhood, adolescents, or as adults often have complications of arrhythmias associated with pre-excitation or atrial dilation [24].

Patients undergoing surgical intervention frequently have significant improvements in outcomes. This is noted especially with those undergoing primary tricuspid bioprosthesis, with ten year survival rates over 90%, a good quality of life with 92% New York Heart Association class I or II and 94% not receiving anticoagulation [46].

A risk stratification scoring system for patients with adult congenital heart disease has been considered as a means to predict prognosis among patients with Ebstein anomaly. The Seattle Heart Failure Model which was trialed by Stefanescu et al., [47] as a means to differentiate those at high vs. low risk for cardiac complication and death, and has shown evidence of predicting complications. Among patients marked as high risk based on their Seattle Heart Failure Model score, Kaplan-Meier survival analysis has shown greater probability of cardiovascular death [47].

Special issues: pregnancy

Most patients with Ebstein anomaly will survive until reproductive age and often desire pregnancy. During pregnancy, increased metabolic needs driven by the need of adequate blood supply to the mother and the fetus, lead to dramatic physiologic changes of the maternal cardiovascular system. Marked increases in blood

volume, of approximately 50% compared with the pre-gestation period [48], result in marked hypervolemia. Coincident with that, heart rate and stroke volume increase, accounting for a marked increase in cardiac output. Pregnancy exacerbates baseline abnormalities in RV dilatation and function, which can have deleterious effects on their ability to accommodate the increased blood volume. Careful planning of labor and delivery and avoidance of massive fluid overload can often prevent the consequences of hemodynamic stress. Patients with Ebstein anomaly during labor are at increased risk of developing atrial arrhythmias in the setting of increased catecholamine levels secondary to stress, pain and anxiety. The decrease of peripheral vascular resistance and the increase in pulmonary vascular resistance may increase a right-to-left shunt if present. Fluid shifts may not be well tolerated especially in women with compromised right ventricular systolic function and severe tricuspid regurgitation. The main principles of successful delivery in patients with Ebstein anomaly are to avoid cyanosis, heart failure and arrhythmias. Vaginal delivery is often preferred since has been shown to be safe [49-51].

Pre-conception counseling

As with other cardiac lesions, patients with Ebstein anomaly require a thorough pre-conception evaluation and counseling in order identify those women at the highest risk. Assessment of New York Heart Association functional class is necessary and physical examination focused on the possible presence of cyanosis, right heart dysfunction, jugular venous distention, parasternal impulse or systolic thrill at the tricuspid valve area, presence of systolic murmur from tricuspid regurgitation and hepatomegaly are essential. Eliciting a history of paradoxical emboli, arrhythmia or heart failure prior to pregnancy are essential for risk stratification. A pre-pregnancy twelve-lead electrocardiogram and echocardiography are essential components of decision-making prior to the initiation of pregnancy.

Systematic review of pregnancy outcomes in Ebstein anomaly

A systematic review of the literature was performed using the PubMed, Medline and Science Direct databases. Advanced search was used with the words: *Ebstein anomaly* and *pregnancy*. Predefined limits were 1) publication after January 1, 1985 for reasons of contemporary applicability; 2) the main body of the text in English, in order to avoid misinterpretation; 3) reviews and case reports (≤ 2 pregnancies) were excluded; and 4) number of pregnancies completed; 5) complications included adverse maternal cardiovascular and fetal outcomes (mandatory were number of pregnancies, maternal death, heart failure and arrhythmia), and if available embolic event and pre-eclampsia/eclampsia; and 6) neonatal adverse events recorded included preterm labor, preterm delivery, death, respiratory failure and intracranial hemorrhage (were recorded if available, but not mandatory for inclusion). The search was completed independently by two separate authors (KS and PKS).

The literature search was performed between December 1, 2014 and January 30, 2015. Systematic literature retrieved a total of 146 publications. Of these, 7 different, retrospective publications were available for review (Table 4). A total of 208 pregnancies were recorded. There were no maternal deaths reported. The number of miscarriages and live births was less well documented. Fetal events were also less well documented. Heart failure complicated 10 pregnancies (4.8%), while arrhythmia complicated 15 pregnancies (7.2%). Preterm labor and delivery were common (15.8% of pregnancies). There were 5 reported cases of neonatal death, 2 fetal intracranial bleeds, and 12 fetuses with low birth weight.

Pregnancy outcomes in Ebstein anomaly

Sparse literature data exists on pregnancy outcomes in women with Ebstein anomaly. In one of the largest series to date, Donnelly et al., studied forty two pregnancies in twelve women with Ebstein anomaly [50]; the majority were uneventful pregnancies with 36 live births. Most of them underwent vaginal delivery; only two of had complications including significant arrhythmias, cyanosis, and heart failure. In the largest study to date, Connolly et al., studied 44 women, with 111 pregnancies [49]. There were no serious pregnancy-related maternal complications including death, stroke, heart failure or arrhythmias. The majority delivered vaginally (89% versus 11% who delivered via Cesarean section). A retrospective study studied pregnancy outcomes in cyanotic congenital heart disease patient, including some with Ebstein anomaly [52]. Women with cyanotic congenital heart disease have higher incidence of miscarriage premature births and low birth weights [52]. Overall, pregnancy appears to be well tolerated in most women; however, there was an increased

risk of prematurity, fetal loss and fetal congenital heart disease.

Guidelines for pregnancy and Ebstein anomaly

The American College of Cardiology/American Heart Association Guidelines for Adults with Congenital Heart Disease (CHD) recommends that women with Ebstein anomaly should undertake pre-pregnancy counseling with a physician expert in adult CHD [33]. Most women have a successful pregnancy with appropriate care but there is a risk of low birth weight and fetal loss if significant cyanosis is present. Similarly, the Canadian Cardiovascular Society consensus on the management of adults with CHD suggests in the absence of cyanosis, right heart failure or arrhythmias, pregnancy is well tolerated [53]. To this end, close follow up is warranted during pregnancy, at least once a trimester. Repeat echocardiogram may be necessary to evaluate right ventricular function, as well as possible increase of right to left shunt and severity of tricuspid regurgitation. Medical management may include gentle diuresis if heart failure develops, management of arrhythmias and anticoagulation if indicated such as in patients with atrial fibrillation or history of paradoxical emboli.

Conclusions

Ebstein anomaly is a rare cardiac congenital disease which is mainly characterized by diversity in the anatomy and the clinical presentation. Diagnosis is made based on the history, clinical findings, electrocardiogram and imaging including echocardiogram and a cardiac MRI. Treatment depends on the age of patient at the time of presentation, the severity of the symptoms and the degree of right ventricular distortion. It ranges from medical management to surgical procedures including tricuspid

Table 4. Systematic literature of the review. Pregnancy outcomes and Ebstein anomaly.

Article	Women	Pregnancies	Live Births	Miscarriages	Maternal Death	Heart Failure	Arrhythmia	Preterm Labor & Delivery	Neonatal Death	Intracranial Hemorrhage	Low Birth Weight
Donnelly et al., [50]	12	42	36	5	0	1	2	5	1	0	6
Connolly et al., [49]	44	111	85	16	0	0	0	23	2	0	NR
Siu et al., [54]	NR	4	NR	NR	0	1	2	NR	NR	NR	1
Siu et al., [55]	NR	12	NR	NR	0	1	2	NR	NR	0	NR
Chopra et al., [56]	4	8	8	0	0	1	2	2	1	0	2
Zhao et al., [57]	4	4	4	0	0	0	2	1	0	1	0
Katsuragi et al., [58]	13	27	21	6	0	6	5	2	1	1	3
Total	77	208	154	27	0	10	15	33	5	2	12

NR: Not reported

repair or replacement, and possibly plication of the right ventricle. Appropriate management and follow up of this patient population is mandatory in order to achieve excellent patient outcomes. Even though pregnancy is generally well tolerated in the absence of right heart failure, cyanosis and significant arrhythmias, an individualized approach to the care of pregnant women is essential with follow up with a multidisciplinary team.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Paraskevi Koutrolou-Sotiropoulou: Data acquisition, data analysis, interpretation of data, drafting of the manuscript, revision of the manuscript Fabio V. Lima: Data acquisition, data analysis, interpretation of data, drafting of the manuscript, revision of the manuscript Anjali Kapur: Drafting of the manuscript, revision of the manuscript Kathleen Stergiopoulos: Data acquisition, data analysis, interpretation of data, drafting of the manuscript, revision of the manuscript.

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