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Organisation of Care for Pregnancy in Patients with Congenital Heart Disease. On behalf of the ESC Working Group of Grown-Up Congenital Heart Disease, the International Federation of Gynecology and Obstetrics and European Society of Anaesthesiology

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Abstract

Improvements in surgery have resulted in more women with repaired congenital heart disease surviving to adulthood. Women with congenital heart disease, who wish to embark on pregnancy require pre-pregnancy counselling. This consultation should cover several issues such as the long-term prognosis of the mother, fertility and miscarriage rates, recurrence risk of congenital heart disease in the baby, drug therapy during pregnancy, estimated maternal risk and outcome, expected fetal outcomes, and plans for pregnancy. Prenatal genetic testing is available for those patients with an identified genetic defect using pre-gestational diagnosis or prenatal diagnosis chorionic villous sampling or amniocentesis. Centralisation of care may be needed for high-risk patients, however, this should be specified and highlighted. Finally, currently there are no recommendations addressing the issue of the delivery. It is crucial that a dedicated plan for delivery should be available for all cardiac patients. The maternal mortality in low-to-middle income countries is 14 times higher than in high-income countries and needs additional aspects and dedicated care.

Introduction

The population of adult patients with congenital heart defects continues to increase worldwide and, inevitably, as they achieve reproductive maturity, more women are contemplating pregnancy. Physicians, including non-specialists, are challenged by the questions of how to organize the optimal provision of preconception counselling and subsequent care during pregnancy for these patients. In 2011, the European Society of Cardiology (ESC) produced guidelines for pregnancy in cardiovascular disease. (14) These guidelines focused on the medical conditions to define who are at high-risk and should be counselled against pregnancy and what treatment should or should not be given. Although this document is extremely valuable, the recommendations are primarily written from the perspective of the type of anatomical defect and its haemodynamic or electrophysiological implications. As a result, the recommendations cannot be used to define who has to be treated where and do not provide in-depth information on patients with congenital heart defects. Standardized care and research evidence are both underdeveloped. In the absence of evidence from randomized-controlled-trials, there is a clear need to provide practical guidance to clinicians. The most important issue in providing preconceptional counselling is early referral, optimally long before pregnancy is considered. Patients in whom pregnancy is contraindicated should be clearly counseled and effective, safe contraceptive options discussed. In other patients, diagnostic and sometimes treatment procedures should be performed pre-pregnancy to minimize their risk of deterioration during pregnancy. In addition, although the importance of making and widely disseminating a plan for delivery is recognized, there are no recommendations addressing the mode, timing, location or necessary resources for delivery. Finally, specific issues for low resource setting should be highlighted. To meet this need, the ESC working group on Grown-up Congenital Heart Disease, together with the International Federation of Gynecology and Obstetrics, appointed a Taskforce to write this position paper; the group including cardiologists, obstetricians and anesthestists with extensive expertise in congenital heart disease and pregnancy. The paper was discussed and approved by the involved bodies.

Risk stratification

The basis of meaningful pre-conception counselling and obstetric care planning is effective risk stratification. Several risk stratification tools are available and these provide a framework on which to base more individualized counselling tailored to the particular clinical scenario. Ideally,

prior to pregnancy, a suitably trained multi-disciplinary team should perform a comprehensive risk assessment, stratifying an individual's risk and offering them appropriate counseling, including a discussion on the advisable mode and setting of delivery.

Risk Scores

Over the last decade a variety of risk scoring systems have been developed. The first important maternal cardiac study was the CARPREG (Cardiac Disease in Pregnancy) study. In the CARPREG scoring system, points were allocated for various risk factors, such as left ventricular outflow tract obstruction, diminished ventricular function, higher NYHA class and prior cardiac event. When studied prospectively the presence of these risk factors was associated with an increased risk of maternal events (1). The ZAHARA scoring system had similar predictors but also included the use of cardiac medication pre-pregnancy and the presence of severe atrioventricular valve regurgitation (2). Khairy et al identified the additional factors of smoking and the presence of significant right ventricular dysfunction or severe pulmonary regurgitation (3). More recently an alternative scoring system with a more comprehensive application - the Modified World Health Organisation (mWHO) risk score has been adopted (Table 3) (4). In the mWHO classification, patients are allocated a risk group based on their underlying cardiac condition. These risk groups are then associated with proposals regarding care. For example, a patient in risk group III, such as a patient with a mechanical valve, is said to have a "significantly increased risk of maternal mortality or severe morbidity". This then triggers the recommendations that a woman in this risk group is cared for in a "specialist multi-disciplinary cardiac obstetric unit". These risk groups have subsequently been applied to the large ESC registry studies (ROPAC) assessing actual maternal outcomes in patients with cardiac disease. This generated further useful information that can be used in risk stratification. From this registry a woman in mWHO Class III had a maternal mortality of 1.5% and a risk of heart failure of 19%. Her risk of antenatal or perinatal hospital admission due to cardiac issues was 36% (5).

Other risk stratification tools

Risk scoring systems are very informative, but are not nuanced enough to be the only basis of determining risk. Pre-conception investigations, including ECG, echocardiogram and exercise testing, are useful adjuncts. Peak heart rate and peak oxygen uptake are both known to be predictive of maternal cardiac events in pregnancy (6). The chronotropic response to exercise is also informative (7). For some patients, cardiac Magnetic Resonance (cMR) is important to assess systemic ventricular function, Fontan palliation or aortic dilatation/aortic coarctation.

More recently several groups have looked at biomarkers to further delineate risk. In women with heart disease, N-terminal pro-BNP can be predictive when measured at 20 weeks gestation (8). There are not yet enough data to be convinced that pre-conception biomarkers are equally useful, but tracking BNP in high-risk pregnancies is likely to be informative. Women with pacemakers/ICD's *in-situ* should have a device interrogation within 6 months of planned conception to define battery longevity, arrhythmia burden and device management at the time of delivery (15,16). It must, however, be borne in mind that both in pregnancy and congenital heart disease there is unpredictability, obstetric complications and unexpected cardiac complications can occur, e.g multiple pregnancy or arrhythmias, and therefore the limitations of any pre-conception risk estimation must be explained.

Fetal Risk Stratification

The major determinants of fetal outcome are prematurity and growth restriction. Recognised risk factors include reduced cardiac output, the presence of cyanosis and the use of medication such as beta-blockers (10-12). In women with severe cardiac disease, prematurity may be iatrogenic – with fears of maternal complications triggering early delivery. The mother should be counselled regarding all of these potential fetal risks.

Counselling

Women with CHD who wish to embark on pregnancy require pre-pregnancy counselling. Ideally preliminary discussions should take place during teenage years, as part of the transition process from paediatrics to the adult care environment. Initial discussions should include which contraceptive methods are safe in the context of their underlying CHD, with emphasis on the importance of pre-pregnancy planning (13-17). Patients should be advised to raise pregnancy as a specific discussion point, as and when they themselves begin to consider motherhood.

When the patient is ready to have more detailed discussions about pregnancy this should use all available data and information in conjunction with any lesion specific pregnancy outcomes reported in the medical literature. This detailed consultation should cover the following;

- Long-term prognosis – perhaps most important in CHD lesions with significantly reduced life expectancy, such as atrial switch repair of transposition of the great arteries, Fontan circulation, pulmonary hypertension, cyanotic heart disease (18). When the data to direct this conversation are absent there should be an honest discussion regarding the areas

of uncertainty. The importance of non-cardiac risk factors should not be forgotten. This includes maternal age, smoking history and body mass index and other organ dysfunction or damage, e.g. due to syndromes. The obstetric history is another key component of risk as is the risk for coagulation disorders, thrombophilia and constellations with implications and caveats in conjunction with anaesthesia care, e.g. difficult airway.

- Fertility and miscarriage rates – particularly relevant for patients with cyanotic heart disease and the Fontan circulation where sub-fertility is not uncommon and miscarriage rates are ~ 50% (19).
- CHD recurrence risk – recurrence risk is generally estimated at 3-5%, but for some this risk is much higher (10-50%) (9). Where appropriate women should be given access to prenatal diagnosis and pre-implantation genetic diagnosis.
- Drug therapy – drugs contra-indicated in pregnancy including Amiodarone, ACE inhibitors, Angiotensin receptor inhibitors, NOAC's and Spironolactone should be stopped prior to conception. Warfarin should be avoided between gestational weeks 6-12 (20). Advice with regards to medication that may need to be commenced in pregnancy tends to be lesion specific, but drugs that are commonly added include beta-blockers, furosemide and low molecular weight heparin.
- Estimated maternal risk and outcome – (assessment as above). Once the risk of pregnancy has been estimated, the discussion should turn to any known detrimental effect of pregnancy on a patient's long-term health as has been reported in patients with a systemic right ventricle, systemic ventricular dysfunction, aortic stenosis and Marfan syndrome (21,22,23,24,25).
- Expected fetal outcomes – pre-term birth, small for gestational age and growth restriction are particularly associated with cyanosis and impaired systemic ventricular function and are more common in patients with a Fontan circulation, mechanical valve or pulmonary hypertension (26).
- Plans for pregnancy care – the hospital care setting, multi-disciplinary team specialists, frequency of visits, delivery planning and general hierarchy of antenatal care is based upon the maternal risk assessment and expected maternal and fetal outcomes. Any plan must be flexible, adaptable and responsive to the circumstances of the patient bearing in mind the unpredictable nature of pregnancy and CHD (27).

When pregnancy is contra-indicated, as in women at highest risk of death or complications during pregnancy (WHO IV), other options for motherhood should be discussed, including adoption and surrogacy. Adoption is available to anyone aged 21 years or over. There is no upper age limit but there is an expectation that the adoptee must have a life expectancy that would ensure they are able to parent a child through to independent living and that the adoptees health would not cause disruption or a negative impact upon the child's education and or psychological well-being. There are 2 forms of surrogacy, which can be explored. In traditional surrogacy, the surrogate mothers egg is used making her the genetic mother, while in gestational surrogacy the egg is provided by the intended mother, or a donor. The egg is fertilised through *in vitro* fertilisation (IVF) and implanted into the surrogate mother. Surrogacy laws vary between countries. France, Germany, Italy, Spain, Portugal and Bulgaria prohibit all forms of surrogacy. The UK, Ireland, Denmark and Belgium, allow surrogacy provided the surrogate mother is not paid, other than reasonable expenses e.g. travel to antenatal visits etc. Commercial surrogacy (whereby a fee is paid to the surrogate mother) is allowed in some US states, Russia, Thailand and Ukraine. The average cost of commercial surrogacy in the US is about $100,000. Advice must therefore be individualised and based on the country of citizenship [www.hfea.gov.uk]. In practice, surrogacy often proves difficult to achieve unless a family member or close friend is willing to act as a surrogate or a patient's finances allow the option of seeking commercial surrogacy abroad.

Prenatal diagnostics

1. Timing

Currently, the underlying cause of most congenital heart disease (CHD) is unknown, despite epidemiological evidence of an inherited component in at least a subset of patients. It is important to acknowledge though that some patients may have a transmittable genetic condition for which prenatal diagnostics can and should be offered and discussed (28-31). However, laws regarding the use of prenatal and pre-implantation testing differ substantially between countries and this may contribute to the fact that despite the advances in genetic techniques and their wider availability, counseling about genetic testing is often neglected in adult congenital heart disease (ACHD) clinics. Both the Canadian and American Heart associations have put forward recommendations for genetic testing in adults with CHD (32, 33), which are summarized in table 1.

The process of genetic testing and counseling, as well as addressing the recurrence risk in all boys and girls with CHD, needs to take place once the mutation is identified and the counseling should be repeated during the transition process and thereafter at regular intervals. Patients with negative genetic test results in childhood may need retesting in the future as more sensitive genetic tests are developed. (32)

2. Modalities for prenatal testing

In brief, 2 options for prenatal genetic testing are available for those patients with an identified genetic defect (either chromosomal defects such as insertions/deletions/translocations or single gene defects), (i) pre-gestational diagnosis or (ii) prenatal diagnosis, chorionic villous sampling or amniocentesis. In the first option, pre-gestational diagnosis, embryos are made using *in vitro* fertilization (IVF) followed by an embryo biopsy performed typically on day 3 and genetic testing carried out on the early embryonal cell. (35,36) Non-affected embryos are used for subsequent transfer. The availability of both techniques is not universal and important differences in ethical considerations exist between countries. A survey performed in a large Dutch center in 2010 revealed that almost 50% of patients with various established genetic disorders were unaware of the option of pre-gestational diagnosis, indicating the need to make information more widely available. (37) The second option, prenatal diagnosis, consists of screening for the familial mutation in fetal cells obtained at the time of chorionic villous sampling or amniocentesis, performed at 12 and 15 weeks of gestation respectively. (34) In case of an abnormal test result, the pregnancy can be terminated. In this case, the risk of having anaesthesia should be considered.
Main characteristics of both techniques are explained in table 2.

Generally speaking, pre-gestational diagnosis may be perceived to be an ethically more acceptable choice than prenatal diagnosis followed by abortion (17). However, the restricted availability of pre-gestational diagnosis and the need for IVF may limit the uptake of this approach. (37)

It goes without saying prenatal options should be carefully discussed with the couple – their final decision should be a well-informed one and this requires a multidisciplinary approach. The couple should be informed about the transmission risk (50% in case of monogenetic Mendelian disorders) and the unpredictability of the clinical expression of some diseases such as Marfan syndrome. The evolving treatment opportunities for CHD should be discussed – which may be

very different from the situation when they were born, justifying natural pregnancy in some cases. Other reproductive options including remaining childless, having no genetic testing on any pregnancy (reproductive chance), gamete donation, surrogacy and adoption should be addressed. Psychological support is an absolute prerequisite and aspects related to guilt (in the parents) and reproach (in the offspring) need careful attention.

Future developments will definitely increase the possibilities for prenatal testing. A promising technique is the Non Invasive Prenatal Testing method, where testing is performed on a venous blood sample of the pregnant woman – this method is already widely applied for aneuploidy testing but is rapidly evolving and testing for monogenetic diseases such as Wilson disease have already been set up with success. (38,39)

Organization of facilities for prenatal testing requires a multidisciplinary approach and interdisciplinary consultations with geneticists, obstetricians and cardiologists; psychologists need to be available.

Care during pregnancy

There are currently no clear recommendations about the *location* of care management of pregnant women with heart disease. However, maternal and offspring risk assessment might help to determine the location of follow-up. The higher the risk, the more intensive and specialized follow-up is indicated. Ideally, the location of follow-up will have been discussed during pre-pregnancy counselling. (14) The mWHO classification is currently the best tool to estimate maternal outcome. (14,40) Follow-up of pregnant women with a mWHO class I risk can be organized in a local care centre, as long as the team responsible for the patient management has basic knowledge about potential complications related to the underlying heart disease. However, when complications occur, transfer to a specialised care centre with sufficient expertise in the patient's heart problem, is recommended. Women with a mWHO class III or IV risk must be followed primarily in a highly expertized tertiary care centre. Although little data are available in literature (41), a multidisciplinary approach, which is in general the rule for an experienced centre, will probably result in a better maternal and fetal outcome. Patients with a maternal mWHO class II risk have a small increase in their risk of maternal mortality or moderate increase in morbidity and follow-up is better in an experienced tertiary care centre.

(13,14) In high risk-women, mWHO class III or IV, follow-up is best in a centre with tertiary level neonatal care management. If fetal heart disease (e.g. congenital heart disease) is discovered, not only fetal, but also maternal follow-up must be scheduled in a tertiary care centre.

Frequency of follow-up is determined by the severity of the maternal risk. During pregnancy, the expansion in the plasma volume (50%) and of the red blood cell mass (20–30%) peaks at the end of the second or beginning of the third trimester. Therefore, even in patients with WHO class I, a single check-up around 20-24 weeks is advised. Indeed, the results of the risk assessment might change during pregnancy. If complications occur, more frequent follow-up is needed. For patients with a mWHO class II risk assessment, a check-up in each trimester of the pregnancy is recommended. For the high-risk patients (mWHO class III – IV) a more frequent assessment is necessary, a minimum of a monthly review is mandatory and this is often increased to weekly. (42)

The *nature and extent of investigations* during follow-up depends on the underlying heart disease. In addition to asking focussed questions and performing a physical examination, a resting electrocardiogram and a transthoracic echocardiography should be carried out at intervals. (43) Holter monitoring is indicated in women with palpitations and mandatory in the presence of a previously documented arrhythmia. Ionizing radiation should be avoided if possible, but can be considered if it is critical to management and the information cannot be otherwise obtained. (44) Cardiac MR might be indicated in complex heart disease and aortic pathology (43) and is considered to be safe from 12 weeks of gestation; however, gadolinium contrast should be avoided, unless critical. (45, 46) In diseases involving a high likelihood for vascular malformations located in the lumbar spine, it could be advisable to assess the lumbar spine in view of the need for central neuraxial analgesia / anaesthesia (via MRI). Routine laboratory testing specifically for the underlying heart defect is not indicated, however, myocardial ischemia or heart failure might be ruled out by elevated serum troponin I or BNP levels, respectively. In patients with associated haematological disorders, or in patients treated with oral anticoagulants, regular blood sampling is indicated. (47,48) Exercise testing can be recommended for further patient management during pregnancy, but is not part of the routine follow-up.

Hospital admission during pregnancy is not uncommon and indicated when maternal, obstetric, or fetal complications occur. Indeed hospital admission with bedrest is advised to reduce the hemodynamic load in a woman with heart failure. In the large prospective ROPAC registry, which included pregnant women with cardiac disease, 26% of patients were admitted during pregnancy in the majority of cases, for cardiac reasons. (14) In pregnant women with a

mechanical valve, the incidence of hospital admission reached 36.7%. (49) Heart failure was the most common cause of hospitalization, while thrombotic and haemorrhagic complications occurred most frequently in patients with a mechanical valve. (14,49) Admission for myocardial ischaemia, arrhythmia and endocarditis are less common. There are no clear recommendations regarding when hospital admission is necessary for cardiac reasons, but it is obvious in those who need close monitoring, intravenous drug therapy or mechanical support.

Pregnant patients with heart failure are advised to reduce their physical activity and to limit their fluid intake. More frequent clinical follow-up and a low threshold for hospital admission are indicated. In the case of a marked deterioration, decisions for mechanical support, device therapy and urgent transplantation may need to be taken, all of which carry a substantially higher risk of an adverse fetal outcome.

Indeed, several heart conditions have a greater risk of arrhythmia, not only during, but also outside pregnancy. When supraventricular arrhythmia occurs and triggers hemodynamic instability, direct current (DC) cardioversion should be applied. (50). Although the DC current exposure to the fetus is minimal, fetal monitoring during the procedure is recommended. Both cardiac or non-cardiac *surgical interventions may* occasionally be necessary during pregnancy. It is better to postpone elective surgery until after delivery, semi-urgent or urgent interventions have to take place during pregnancy. Non-cardiac surgery in pregnant women with a WHO class I risk can probably be safely performed in a secondary centre. However, when there is a potential risk for fetal distress during surgery requiring urgent delivery, then the patient is better transferred to a tertiary centre with experienced interdisciplinary (obstetric, neonatal, anaesthesia) staff. Non-cardiac surgery, in pregnant women with WHO class II-IV risk, is preferable performed in a tertiary centre with sufficient expertise in the relevant cardiac condition and in neonatal care. Surgery in the first - and in the third trimester of the pregnancy carries a higher risk of fetal malformations and pre-term delivery, respectively. (14) Therefore, surgery is best performed between the 13th and 28th week.

Cardiac surgery requiring cardiopulmonary bypass after 26 weeks has a fetal survival rate of 80%, but with 20% having serious neurological impairment. For this reason, Caesarean delivery may be considered first if gestational age is more than 26 weeks. However, before surgery, antenatal corticosteroids, to mature the fetal lungs, should be administered. If cardiopulmonary bypass is needed in a pregnant patient, then normothermic perfusion is advised and hypocapnia, responsible for utero-placental vasoconstriction, and fetal hypoxia have to be avoided. The duration of the cardiopulmonary bypass should be minimized. (51)

Delivery

All women with heart disease should be delivered in an obstetric-led setting, most commonly in the labour ward, but occasionally in a cardiac theatre if close cardiac monitoring, with transoesophageal echo for example, is required or the need for acute cardiac intervention, including extracorporeal circulation, is anticipated. An experienced multidisciplinary team should be available to provide care. Lower risk cases, mWHO class I, can be managed in secondary centres, but high-risk cases, mWHO class II-IV, should be cared for in a tertiary centre with access to cardiac surgery. The plan of care during delivery should be determined in the antenatal period, preferably around 25 weeks of pregnancy.

Mode of delivery: The data from ROPAC show that vaginal delivery is associated with a better birthweight (52). Vaginal delivery is associated with smaller blood volume changes and is less often complicated by haemorrhage, thrombosis and infection. However, a Caesarean section (CS) should be planned for the usual obstetric indications and in cases with an aortic root diameter of >4.5cm, acute heart failure or severe pulmonary hypertension. Similarly, an emergency CS should be performed for the usual obstetric indications and if a case presents in preterm labour while taking oral anticoagulants (14). In this situation, the CS should be performed under general anaesthesia with Fresh Frozen Plasma cover and with prothrombin complex concentrate available. Haemostasis must be meticulous to avoid haematoma formation and the risk of infection. In order to avoid emergency CS and to ensure optimal logistics and risk-minimization, planned CS seems also be a viable option in situations where CS per se may not have an absolute indication. This is especially true in view of the anticoagulation management and the appropriate termination to prevent complications in conjunction with central neuraxial anaesthesia.

Induction of labour should be performed for the usual obstetric indications. At the dose used for induction of labour, both PGE_2 and oxytocin are safe with no reported adverse cardiovascular effects. Induction may be indicated when a patient is taking anticoagulants to better time the cessation of therapy, allowing epidural analgesia to be used for vaginal delivery and to avoid intra or post partum haemorrhage.

Labour: Women should be transferred to the delivery room early in labour to facilitate siting of the epidural and initiation of maternal and fetal monitoring, including blood pressure, heart rhythm and saturation monitoring. Haemodynamic stability is essential and facilitated by early epidural insertion and careful fluid balance management avoiding dehydration and fluid

overload. The initial epidural doses should be low and gradually increased to achieve effective pain relief. Continuous electronic fetal monitoring should be used throughout labour. Infective endocarditis in pregnancy is rare and at present antibiotic prophylaxis is not routinely recommended during CS or vaginal delivery although this is disputed. (53) When the cervix is fully dilated, 2 hours of passive descent should be allowed. The duration of the active phase of the second stage should be limited in some cases; however, in all cases, if there is poor maternal effort or no progress during the second stage, then assisted delivery should be performed early using either ventouse or forceps.

Current recommendations are to manage the third stage with a low dose oxytocin infusion (14) because of concern about hypotension, tachycardia and myocardial ischaemia, due to vasodilatation of subcutaneous vessels, vasoconstriction of the coronary arteries and a chronotropic effect (54-56). However if this proves inadequate, prompt management of uterine atony with physical methods, bimanual compression, intrauterine balloon or uterine brace sutures, and pharmacological agents including slow administration of bolus oxytocin (5iu) and an oxytocin infusion (40iu over 4 hours) is required. Misoprostol is effective at a dose of 400µg, but may cause hypotension and hyperthermia (57). Care should be taken in the use of prostaglandin $F_{2\alpha}$ analogues, which can cause severe vasoconstriction. Ergometrine, which can cause hypertension and coronary artery spasm, should be avoided where possible, but can be considered if uterine atony is hard to control in those who do not have aortopathy or pre-eclampsia. Sulprostone for treatment of postpartum haemorrhage should not be delayed, but rather carefully titrated with appropriate monitoring.

In the early post-natal period up to 48 hours, high-risk cases should be kept under close observation, particularly those with heart failure or aortopathy; imaging of the aortic root should be performed as indicated. Some patients, especially those with pulmonary hypertension may require inpatient monitoring for up to 1 or 2 weeks. The process of uterine contraction/involution produces an auto-transfusion of about 500mls of blood into the circulation, which may precipitate cardiac failure. However, most hemodynamic changes are reversed within two weeks with further normalization towards preconception values after 2 months. Some pregnancy changes may take longer to resolve or indeed never completely resolve.

Breast-feeding is rarely a problem and should be encouraged except in those with severe heart failure, where the extra energy expenditure may be detrimental. Some cardiac medications have been suggested to cause neonatal problems, amiodarone should be avoided if possible. ACE inhibitors are linked to neonatal hypotension and infant blood pressure should be monitored carefully, and beta blockers may cause bradycardia, hypoglycaemia and failure to thrive, but the

amount in breast milk is generally too little to affect infants. Mastitis should be treated aggressively with intravenous antibiotics.

Specific issues for low resource setting

The maternal mortality in low-to-middle income countries (LMIC) is 14 times higher than in high-income countries (HIC) (58) and recognising this, the reduction of maternal mortality was the first target for the new Sustainable Development Goal (SDG) for health (59). While direct causes of maternal death such as obstetric haemorrhage, sepsis and hypertensive disease remain the largest contributors, heart disease in pregnancy is a common problem in all countries (60-62) with a disease profile that includes poverty-related conditions such as rheumatic heart disease, peripartum and other cardiomyopathies as well as un-operated congenital heart disease. Risk-factors contributing to the morbidity and mortality of pre-existing heart disease in pregnant women such as hypertension, obesity and diabetes are increasingly important, occurring in high numbers in some countries, urban settings and specific sub-populations in Asia, Latin-America and sub-Saharan Africa.

To improve pregnancy outcomes through the identification and referral of patients requiring specialist care, the basic elements of clinical assessment need to be in place reliably and consistently. Efforts to develop sustainable specialist services should be built on a health systems strengthening approach and supported by the appropriate resourcing plans, in particular the Global Financing Facility (63). As we move to the era of the SDGs the needs of 'very sick obstetric patients' are starting to be more clearly articulated (64).

Recommendations for the organisation of care for pregnancy in patients with heart disease in LMICs are presented in table 3 (65). Following delivery, appropriate postnatal family planning needs to be offered using an effective method and, where patients are being managed with anticoagulation, taking into account the adverse impact of some hormonal-based methods. Finally, support from cognate clinical services especially anaesthesiology during clinical care especially around the time of delivery is essential. Active strategies for suspected and previously known cardiac disease in pregnancy are expected to avoid a substantial portion of maternal morbidity and mortality.

Conclusion

This paper complements the existing guidelines, giving practical advice about setting up a clinic for pregnant women with heart disease in both high and low income countries. It focuses on the

importance of the pre-conception appointment, when key decisions will be made about operative corrections or changes in therapy to optimize maternal health prior to conception, describes the essential components for the care during and after pregnancy in cardiac patients, while establishing the principle that the higher the risk then the greater the level and intensity of follow up is needed.

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Table 1. Recommendations for genetic testing and counseling in ACHD patients

1. A detailed family history for CHD and other birth defects spanning at least 3 generations should be taken to identify familial inheritance. *(AHA Class I; Level of Evidence C)*.
2. As some CHD defects such as BAV or ASD may go unnoticed into adulthood, additional clinical evaluation in family members with echocardiography is reasonable *(AHA Class IIa; Level of Evidence C)*.
3. Detailed history and physical examination should be performed to detect dysmorphic features, extracardiac malformations, and other organ system involvement *(AHA Class I; Level of Evidence C)*.

Table 2: Main characteristics of Prenatal chorionic villous sampling or amniocentesis (PND) and Pre-gestational diagnostics (PGD)

PND:

- No artificial pregnancy
- No need for hormonal stimulation
- Risk of fetal loss
- Emotional burden of terminating pregnancy

PGD:

- No emotional and moral issues related to terminating pregnancy
- Technically complex procedure – hormonal stimulation
- No anaesthesia needed
- Long waiting lists

Table 3. Recommendations for the organisation of care (66))

Context	Recommendation
Routine ANC	All pregnant women should be screened at antenatal booking for underlying medical or surgical conditions
Known disease	Women with known or recently detected cardiovascular disease should undergo risk assessment based on a published algorithm (Sliwa et al. 2014)
Unstable clinical state	Women presenting with difficulty in breathing, systolic blood pressure of <100mmHg, heart rate > 120 beats per minute or appearing cyanotic need to be transferred by ambulance to a tertiary centre within 12 hours; those presenting with signs of fluid overload should receive a bolus of furosemide 40mg IV and oxygen per face mask prior to transfer
Pregnancy and Postnatal surveillance	Clinicians should have a low threshold for investigating pregnant or recently delivered women (up to 6 months post-partum), especially those with cardiovascular risk factors (hypertension, diabetes), suspected rheumatic heart disease or with symptoms such as shortness of breath, a respiratory rate exceeding 20 breaths/min. or chest pain. Appropriate investigations include ECG, chest x-ray, echocardiogram and CT pulmonary angiography will aid decision making about the mode and timing of delivery and postpartum management.
Extended follow up for High Risk patients	Certain patients with high-risk cardiovascular disease might need careful monitoring for up to 1 year post-partum owing to a high risk of developing heart failure, serious arrhythmia and embolic events.

Table 4 Organisation of care for women with congenital heart disease concerning pregnancy

	mWHO1	mWHO2	mWHO2-3	mWHO3	mWHO4
Diagnosis	*Uncomplicated small or mild -PS, -PDA, -MVP *Successfully repaired simple lesions (ASD, VSD, PDA,anomalous PVD)	If otherwise well and uncomplicated: *Unoperated ASD, VSD *repaired ToF *most arrhythmias	Depending on individual: *mild LV impairment *HCM *native or tissue valve disease not considered WHO 1 or 4 *Marfan without aortic dilatation *repaired coarctation	*mechanical valve *systemic RV *Fontan *unrepaired cyanotic heart disease *other complex heart disease * mild aortic dilatation (Marfan 40-45mm; BAV 45-50mm)	*Pulmonary arterial hypertension *severe systemic ventricular dysfunction (EF <30%) *previous PPCM with any residual LV impairment *severe MS *severe symptomatic AS Severe aortic dilatation (Marfan >45mm, BAV >50mm)
Risk	No detectable increased risk of maternal mortality and no/mild increased risk in morbidity	Small increased risk of maternal mortality ot moderate increase in morbidity	Intermediate increased risk of maternal mortality or moderate to severe increase in morbidity	Significantly increased risk of maternal mortality or severe morbidity	Extremely high risk of maternal mortality or severe morbidity
Counselling	yes	yes	yes	Expert counselling required	Pregnancy contraindicated. If pregnancy occurs termination should be discussed
Care during pregnancy	Local hospital	Local hospital	Referral hospital	Expert center for Pregnancy and Cardiac disease	Expert center for Pregnancy and Cardiac disease
Location of delivery	Local hospital	Local hospital	Referral hospital	Expert center for Pregnancy and Cardiac disease	Expert center for Pregnancy and Cardiac disease