Risk assessment for pregnancy with cardiac disease—a global perspective

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Cardiac disease is emerging as the most important indirect cause if maternal death globally.1 Cardiac conditions can be pre-existing (e.g. rheumatic or congenital heart disease) and unmasked by increased volume load in pregnancy, or can be caused by pregnancy [e.g. hypertensive disorders or peripartum cardiomyopathy (PPCM)].2,3 Physicians are therefore increasingly faced with providing adequate counselling on pregnancy risk to women wishing to conceive who are known to have cardiac disease (e.g. operated congenital heart disease or previous valve replacement because of rheumatic heart disease), or present in the advanced stage of pregnancy (>20 weeks) having heart failure because of pre-existing or newly acquired cardiac disease. The strength of epidemiological data used as a basis for counselling is a function of sample size and, although cardiac disease may be globally prevalent, single centres have too few patients to create meaningful datasets for analysis. Internationally constructed databases provide a bigger dataset from which inferences can be drawn.

Iris van Hagen and colleagues4 validated the modified World Health Organization (mWHO) risk classification in advanced and emerging countries and identified additional risk factors for cardiac events during pregnancy using data from the Registry of Pregnancy and Cardiac disease (ROPAC), which includes more than 2500 pregnant women. The spectrum of cardiac disease differed in advanced vs. emerging countries with congenital heart disease being the most prevalent diagnosis in advanced countries, and valvular heart disease and cardiomyopathies being the most common diagnoses in emerging countries. There was a substantial difference in cardiac events between regions, occurring in 12.8% of patients in advanced countries vs. 36.3% in emerging countries.

The mWHO classification showed only a moderate performance in predicting risk between women with or without cardiac events [c-statistic 0.711, 95% confidence interval (CI) 0.686–0.735] with a better performance in advanced countries compared with emerging countries. Novel findings were that pre-pregnancy signs of heart failure and atrial fibrillation added prognostic value in advanced countries. However, follow-up was only available for all patients up to 1 week after delivery, probably missing a number of events such as additional heart failure, prosthetic valve complications, or sudden death.2 The authors provided a very useful colour-coded risk chart, which determines <35%, 35–65%, and more than 65% risk in emerging and advanced countries according to pre-pregnancy mWHO class. Is this chart based on the mWHO comprehensive enough? Probably not.

Mortality data contextualize the risk of cardiac disease in pregnancy with case fatality rates approaching 1 in 200.5 This has reference to other obstetric complications that are viewed as high-risk; for example pre-eclampsia has a cited case fatality rate of 1 in 1500 and eclampsia leads to mortality in 1 in 50 cases.6,7 The maternal mortality ratio in low-to-middle income countries (LMICs) is 14 times higher than in high-income countries (HICs).8 A number of deficiencies, including lack of ante-natal care, late booking, lack of appropriate referral systems to higher level of care, no family planning, overall poor education, and low rates of birth managed by skilled health-care attendants contribute to the high maternal death rates in LMICs. Direct causes of maternal death such as obstetric haemorrhage and sepsis, as well as complications of hypertensive disorders of pregnancy remain the biggest numerical contributors. These direct causes can also occur in women with cardiac disease; for example, obstetric haemorrhage can complicate delivery in women with a prosthetic heart valve needing anti-coagulation. In LMICs, searches for heart disease in pregnant women is not performed routinely, and peripartum cardiomyopathy, Chagas disease, human immunodeficiency virus (HIV) cardiomyopathy, and endomyocardial fibrosis present specific challenges because of their

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poor prognosis and high prevalence in some geographical areas.\(^9\) Anaemia caused by a number of conditions such as poor nutrition, helminthic infections, and malaria are common among pregnant women in LMICs, contributing to heart failure in women with cardiac disease. In the global prospective registry of rheumatic heart disease (REMEDY), which enrolled 3343 patients, 1825 were women of child-bearing age (12–51 years) and only 65 (3.6%) were using contraception, reflecting the poor provision of family planning and pre-pregnancy advice for a condition that occurs in many regions of the world.\(^10\)

Data from the current publication\(^4\) also outline the general risk of adverse events taking place during pregnancy; it is unsurprising but useful to know that mWHO 4 category patients have a one in two risk of such an event and that the percentage of patients falling into this category is far greater in emerging countries than in developed nations. It is also notable that valvular heart disease is more likely to fall into mWHO category 3 and category 4 than other cardiac diseases.

The data presented bear further consideration insofar as the risk of adverse events between mWHO category 1 and category 2 show a similar incidence, possibly indicating that patients previously assigned to low-risk categories merit multidisciplinary assessment both at the beginning of pregnancy and again immediately before delivery.

The analysis of parity also provokes speculation because increasingly severe disease is associated with a falling prevalence of nulliparity despite little difference in maternal age. This may point to the cumulative effects of successive pregnancies on cardiac function and merits further investigation.

The influence of cardiac intervention in decreasing the risk of adverse events is also notable in both emerging and advanced country datasets. In advanced countries, with a higher proportion of congenital disease, this is likely to reflect the occurrence of surgical intervention, whereas in emerging countries both medical and surgical intervention related to congenital and valvular heart disease is likely to play a role. The data serve to underscore the value of treatment before pregnancy. ‘The mWHO, even if factors such as AF [atrial fibrillation] and pre-existing heart failure are included, still has a number of deficiencies as a comprehensive risk prediction score, even if factors such as atrial fibrillation and pre-existing heart failure are included. Firstly, it includes only risks for the women with cardiac disease and fails to highlight the effects on the fetus in advanced cardiac disease (e.g. which can be intrauterine death, low birth weight, and preterm birth with long-term consequences). Many conditions common in LMICs and elsewhere are also not included in the mWHO, including for example: Chagas’ disease, HIV CMO, cardiac sarcoidosis amongst others.’\(^7\)

Other cofactors increasing the risk of morbidity such as low or high maternal age, anaemia, poor nutrition, and being underweight or severely overweight are also not included. Most importantly socioeconomic factors such as low education of the mother and unskilled health-care workers, lack of appropriate tools to make an early diagnosis, or detection of heart failure, and long distances to tertiary care need to be part of the overall risk assessment.

Figure 1 highlights the factors that are likely to contribute to increased maternal and fetal risk in pregnant women with cardiac disease which could be used in conjunction with the risk chart for cardiac events by Hagen et al.\(^4\) Specific guidelines on management of women with un-operated or operated rheumatic heart disease in LMICs were also recently published.\(^11\)

In summary, risk prediction for pregnant women with heart disease should consider the unique profile of cardiovascular disease in LMICs and the contribution of a number of risk factors.
Counselling individual patients is an integral component of medical care in which an estimate of risk is recognized to be this very composite of disease-specific risk, risk arising from individual variability related to biological susceptibility, and co-morbid conditions combined with environmental circumstances, often induced by lack of resources and expertise. All these elements are difficult to integrate into a single risk estimate to which individual patients can attach a particular value.

The current dataset extends our statistical knowledge of risk and if health system issues could be incorporated in risk prediction it may improve our ability to counsel patients and avoid a substantial portion of maternal morbidity and mortality.

Conflict of interest: None to declare.

References