

Assessing the Role of Echocardiography in Pregnancy in First Nations Australian Women: Is It an Underutilised Resource?

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Background

Rheumatic heart disease (RHD) remains prevalent within First Nations Australian communities. RHD is more common in females and peak prevalence corresponds with childbearing age. Significant valvular disease can complicate pregnancy. Current practice in Northern Australia is to refer pregnant women for echocardiography if there are signs or symptoms of possible cardiac pathology or a history of acute rheumatic fever (ARF) or RHD. It is not currently routine practice to offer echocardiographic screening for all pregnant women at high risk of RHD.

Aim

This study aimed to assess the current referral practices for echocardiography and disease patterns in pregnant women in the Northern Territory, Australia—a region with a known high prevalence of RHD in the First Nations population.

Method

A retrospective analysis of all echocardiography referrals of pregnant women over a 4-year period was performed. Data included indication for echocardiography, clinical history, echocardiographic findings, and location of delivery. Comparisons were made using Fisher's exact and Mann-Whitney *U* tests.

Results

A total of 322 women underwent echocardiography during pregnancy: 195 First Nations and 127 non-Indigenous women (median age, 25 vs 30 years, respectively; $p < 0.01$). Indications for echocardiography differed by ethnicity, with history of ARF or RHD being the most common indication in First Nations women, and incidental murmur the most common in non-Indigenous women. First Nations women were more likely to have abnormal echocardiograms (35.9% vs 11.0% in non-Indigenous women; $p < 0.01$) or a history of ARF or RHD (39.4% vs 0.8%; $p < 0.01$), but less likely to have documented cardiac symptoms as an indication for echocardiography (8.2% vs 20.5%; $p < 0.01$). New cardiac diagnoses were made during pregnancy in 11 (5.6%) First Nations and two (1.6%) non-Indigenous women ($p = 0.02$). Moderate or severe valve lesions were detected in 26 (13.3%) First Nations women (all previously diagnosed), and 11 (5.6%) had previous cardiac surgery. No severe valve lesions were identified in the non-Indigenous group. Interstate transfer to a tertiary centre with valve intervention services was required during pregnancy or the puerperium for 12 (6.2%) First Nations women and no non-Indigenous women.

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Conclusions

Amongst pregnant women in the Northern Territory who had an indication for echocardiography, First Nations women were more likely to have abnormal echocardiograms. This was mainly due to valvular disease secondary to RHD. Cardiac symptoms were infrequently recorded as an indication for echocardiography in First Nations women, suggesting possible underappreciation of symptoms. Having a low threshold for echocardiographic investigation, including consideration of universal screening during pregnancy, is important in a high RHD-burden setting such as ours. A better understanding of the true prevalence and spectrum of disease severity in this population would enable health services to invest in appropriate resources.

Keywords

Echocardiography • Rheumatic heart disease • First Nations Australians • Pregnancy • Obstetric-cardiology

Introduction

Rheumatic heart disease (RHD) remains a substantial health burden within First Nations Australian communities [1–3]. RHD is a complication of acute rheumatic fever (ARF) resulting from an abnormal immune response to group A streptococcal infection [4]. The subsequent inflammatory response results in cardiac valve damage due to scarring and fibrosis. Most patients diagnosed with RHD do not have a documented history of ARF [5]. RHD is more common in females (2:1), and peak incidence occurs in the third and fourth decade, corresponding with childbearing age [2]. Although RHD has been effectively eliminated from high-income populations, First Nations populations of Northern Australia have some of the highest global rates [2,3,6]. In this setting, the published prevalence within this population is between 2.5% and 5% of people aged 5–20 years [2,3]. Detection of ARF is increasing, especially in more subtle ('possible' and 'probable') cases, but this increase in detection is predominantly in children presenting with arthritis only, most of whom do not progress to RHD [7]. Meanwhile, community screening activities and registry data identify cases of RHD which have developed insidiously without any diagnosed precursor event, highlighting the challenge of RHD prevention [3,5,8].

Globally, one-quarter of maternal deaths are due to non-obstetric causes [9], with approximately 40% being attributable to cardiovascular disease [10]. In Australia, cardiovascular disease has been documented as the commonest cause of indirect (non-obstetric) maternal death at 16% of all maternal deaths [11]. Significant valvular disease may complicate pregnancy. Traditionally, there has been concern about stenotic valve lesions, particularly mitral stenosis (almost solely due to RHD in this population) and associated pulmonary hypertension [12]. However, there is evidence that significant regurgitant lesions may also carry increased morbidity and mortality risk during pregnancy [13]. In high-prevalence locations, RHD is a major cause of maternal cardiovascular morbidity and mortality [14,15]. Symptoms and signs of cardiovascular disease may be difficult to distinguish from symptoms of normal pregnancy, such as reduced exercise tolerance and peripheral oedema [10]. There are limited data on maternal mortality due to

RHD, and most are from small studies from low- and middle-income countries, yielding highly variable results [13,16]. A recent population-based study involving Australian and New Zealand maternity units demonstrated that RHD was associated with significant cardiac and perinatal morbidity [15]. This morbidity is higher for First Nations women [15]. The maternal mortality ratio is more than four times higher for First Nations Australian women compared with their non-Indigenous counterparts [11].

First Nations Australians make up 30% of the population of the Northern Territory (NT) [17]. Three-quarters of First Nations people live in rural and remote communities of the NT and migrate between communities [17]. There are several factors that result in limited interaction with health services, including cultural safety, health literacy, high staff turnover, and physical access [18–22]. Current practice in the NT sees many pregnant women assessed initially by remote area nurses [23]. Access to general practitioners for clinical assessment, including auscultation, can be limited [23]. The maternal mortality rate rises with increasing remoteness [11].

The exact prevalence of RHD in pregnant First Nations women is unknown. Rates are extrapolated from research in the paediatric population or from registry data [2,15]. According to the current Australian national clinical practice guidelines on RHD, "In high-risk populations, all [pregnant] women with a murmur (or regardless of the presence or absence of murmur in some settings) should be investigated clinically ... and with an echocardiogram... There is growing recognition of the importance of early echocardiographic screening of all pregnant women in high-risk populations." [24] However, echocardiographic screening has not been translated broadly into practice. Concurrently, research suggests that registry data underestimates the burden by 100%; therefore, for every known case of RHD, there is likely to be another as yet undetected case [3,25]. It is unclear whether current practice identifies all pregnant women with significant cardiac pathology or what number of women with clinical signs or a history of RHD being referred for echocardiography have significant disease. The aims of this study were to assess the current referral practices of echocardiography among pregnant women in the NT and describe identified cardiac pathologies with a focus on RHD.

Methods

We performed a retrospective analysis of echocardiograms available within the primary echocardiography database of the NT (NT Cardiac database; Synapse Cardiovascular, FUJIFILM New Zealand, Auckland, New Zealand). During the study period, echocardiography was provided by the private cardiology practice, NT Cardiac, in Darwin and Alice Springs with regular visiting services to rural towns and remote communities. All echocardiography studies that were performed between July 2014 and July 2018 on pregnant women were included in the analysis. A keyword search was used to identify studies performed during pregnancy from the 'indication' field within the database. These keywords included 'pregnancy', 'pregnant', 'gestation', and '/40'. All echocardiograms identified were reviewed by a cardiologist (J.M.) to ensure diagnostic accuracy and consistency. These findings were cross-referenced with the official clinical echocardiogram report. The World Heart Federation diagnostic criteria for RHD were used to determine definite cases of RHD [26]. In patients who had several echocardiograms during a single pregnancy, the most recent one within the study period before delivery was included. Postpartum echocardiograms were excluded. Electronic hospital medical records were used to collect individual patient data on identification as First Nations people, residence by remoteness classification, medical history (including a history of ARF, RHD, or other heart disease), and need for interhospital transfer for delivery.

The indication for echocardiography was determined and classified as one of the following: 'history of ARF or RHD', 'symptoms of possible heart disease', 'incidental murmur', or 'known cardiac disease'. Echocardiographic diagnoses were

classified as: 'definite RHD', 'congenital heart disease', 'other heart disease', or 'normal cardiac structure and function'. Indications for echocardiography were then cross-referenced with resultant echocardiographic diagnosis. Echocardiograms identifying RHD were further assessed for disease severity (defined by the Australian RHD guideline [24]), and files were reviewed for history of RHD or ARF, signs and symptoms of RHD, and impact of RHD diagnosis on the management of the pregnancy. Stata 18 statistical software (StataCorp LLC, College Station, TX, USA) was used for analysis. Fisher's exact test was used for analysis of categorical variables. The Mann-Whitney *U* test was used to test associations between independent, continuous variables, with associations with a $p < 0.05$ deemed to be statistically significant.

Ethical approval was provided by the Human Research Ethics Committee of the NT Department of Health and Menzies School of Health Research (HREC-2018-3186).

Results

A total of 322 pregnant women met the criteria for inclusion in the study (Table 1). Most (195; 60.5%) were First Nations women. The median age was 28 years (interquartile range [IQR], 23–32 years), with First Nations women being younger (25 years; IQR, 21–30 years) than non-Indigenous women (30 years; IQR, 27–33 years; $p < 0.01$). Approximately one-quarter of the overall study population were found to have an abnormal echocardiogram (84/322; 26.1%). Abnormal echocardiograms were more common amongst First Nations women (70/195; 35.9) compared with non-Indigenous women (14/127; 11.0%; $p < 0.01$). The abnormal finding represented new diagnoses

Table 1 Overview of the study cohort of pregnant women undergoing echocardiography.

Variable	First Nations women	Non-Indigenous women	P-value
Total number of patients	195	127	
Age (yrs, median)	25 (IQR, 21–30)	30 (IQR, 27–33)	<0.01
Prior cardiac surgery	14 (7.2)	3 (2.4)	0.07
Indications			
Incidental murmur	73 (37.4)	51 (40.1)	0.5
Cardiac symptoms	16 (8.2)	26 (20.5)	<0.01
History of cardiac disease (not RHD/ARF)	29 (15.0)	49 (38.6)	<0.01
History of RHD and/or ARF	77 (39.4)	1 (0.8)	<0.01
Echocardiographic Outcomes			
Abnormal result	70 (36.0)	14 (11.0)	<0.01
Rheumatic heart disease	58 (29.7)	2 (1.6)	<0.01
Congenital heart disease	7 (3.6)	6 (4.7)	0.7
Other heart disease	5 (2.6)	6 (4.7)	0.3
Clinical outcomes			
Required transfer interstate for delivery for cardiac reasons	12 (6.0)	0	0.04

All values are n (%) unless otherwise specified.

Abbreviations: IQR, interquartile range; RHD, rheumatic heart disease; ARF, acute rheumatic fever.

made during pregnancy for 11 of 195 (5.6%) of First Nations women and two of 127 (1.6%) non-Indigenous women ($p=0.02$).

Indications for Echocardiography

Indications for echocardiography differed significantly by ethnicity. A total of 78 women had a history of ARF and/or RHD. The leading indication was a history of RHD or ARF in First Nations women (77/195; 39.4%) and incidental murmur in non-Indigenous women (51/127; 40.1%) (Table 1). The burden of known history of ARF and/or RHD in First Nations women compared with non-Indigenous women was therefore 39.5% (77/195) vs 0.8% (1/127), $p<0.01$ (Table 1).

Symptoms suggestive of possible cardiac pathology, and history of non-RHD cardiac disease, were both significantly less commonly documented indications for an echocardiogram among First Nations vs non-Indigenous women. Pre-existing heart disease other than RHD was a documented indication for echocardiography for 29 (15.0%) First Nations women and 49 (38.6%) non-Indigenous women. The non-RHD cardiac diagnoses in First Nations women comprised cardiomyopathy, prior infective endocarditis, supraventricular tachycardia, mild valvular heart disease, and repaired simple congenital heart disease (CHD). In non-Indigenous women, diagnoses comprised history of supraventricular tachycardia, mild valvular disease, simple or repaired CHD, or cardiomyopathy.

Echocardiographic Diagnosis of RHD

There were 60 women (60/322 total; 18.6%) found to have echocardiographically confirmed RHD or prior valve intervention for rheumatic fever and heart disease (58 First Nations women [58/195 total First Nations; 29.7%] and two non-Indigenous women [2/127 total non-Indigenous; 1.6%]) (Table 2). Of the total 58 RHD diagnoses in First Nations women, almost half (26; 44.8%) had moderate or severe valvular disease and 11 (19.0%) had prior valvular intervention or surgery. The mitral valve was involved in all cases, most commonly mitral regurgitation (Table 3). Twelve (12) First Nations women with RHD required precautionary interstate transfer to a quaternary hospital (with cardiothoracic surgery support) for delivery. Eleven (11; 19.0%) echocardiographically confirmed RHD cases were new diagnoses, all mild in severity. Indications for these 11 echocardiograms were symptoms ($n=1$), incidental murmur ($n=5$), and history of other heart disease ($n=5$).

Of the non-Indigenous women, one was a migrant from India, and the other's ethnicity was unknown. One had moderate mitral regurgitation, and the other had mild aortic regurgitation. The former was transferred interstate (i.e., to another state) for delivery.

Association Between Documented Indication and Echocardiographic Findings

Associations between identification of RHD and the indication for echocardiography (cardiac murmur on auscultation,

Table 2 Characteristics of echocardiographically confirmed burden of rheumatic heart disease for First Nations and non-Indigenous women.

Variable	First Nations women	Non-Indigenous women
Total number of echocardiographically confirmed cases	58	2
History of ARF only	4 (6.9)	0
Known RHD	43 (74.1)	0
New RHD detected during pregnancy	11 (19.0)	2 (100)
Rheumatic heart disease		
Mild	32 (55.2)	1 (50.0)
Moderate	20 (34.5)	1 (50.0)
Severe	6 (10.3)	0

All values are n (%) unless otherwise specified.
Abbreviations: RHD, rheumatic heart disease; ARF, acute rheumatic fever.

symptoms suggestive of cardiac pathology, and/or history of ARF and/or RHD) were explored. Incidental murmur as the indication for an echocardiogram, in the absence of known pre-existing cardiac disease, was mostly (115/124; 93%) found to be benign. Incidental murmur was associated with an abnormal echocardiogram in eight of 73 (11%) First Nations women (five RHD, three other) and one of 51 (2%) non-Indigenous women (one RHD) (Table 4).

Discussion

In this study, we found that a quarter of the pregnant women referred for echocardiography in Australia's NT had structural cardiac disease evident on the echocardiogram. This

Table 3 Native valve abnormalities among women with echocardiographically confirmed rheumatic heart disease.

Valve	Disease type	n (total 49)
Isolated mitral valve disease	Mitral regurgitation	24 (49.0)
	Mitral stenosis	2 (4.1)
	Mixed mitral disease	12 (24.5)
Mixed mitral and aortic disease	Mitral regurgitation and aortic regurgitation	6 (12.2)
	Mixed mitral valve disease and aortic regurgitation	4 (8.1)
Isolated aortic valve disease		1 (2.0)

All values are n (%).

Table 4 Incidental murmurs as an indication for referral for echocardiography during pregnancy.

Variable	First Nations women	Non-Indigenous women	Total
Number of women	73	51	124
Normal echo	65 (89%)	50 (98%)	115/124 (93%)
Abnormal echo	8 (11%)	1 (2%)	9/124 (7%)
Rheumatic heart disease			
Mild	5	0	5
Moderate	0	1	1
Severe	0	0	0
Congenital heart disease			
Other heart disease	3	0	3

burden was mostly evident among First Nations women, among whom more than a third (70/195; 36%) had echocardiographic abnormalities (mostly RHD [58/70; 75%]), although they were on average 5 years younger than the non-Indigenous women in the study. First Nations women were more likely to have newly detected cardiac disease discovered during the pregnancy and more likely to need transfer to a major metropolitan quaternary hospital for delivery of the pregnancy.

Noting the sample was highly selected, representing only those who attended for echocardiography, we nevertheless identified factors that raise the question of whether a lower threshold is required for echocardiography in pregnant First Nations women in this study setting. Firstly, the proportion of all tests done that were found to be abnormal was significantly higher in First Nations than in non-Indigenous women (36% vs 11%). Secondly, it was less common for health care providers to note the presence of cardiac symptoms among First Nations women as a reason to refer for echocardiography, suggesting possible underappreciation of symptoms [22]. Given the major potential for adverse consequences of cardiac disease during pregnancy, childbirth, and the puerperium, having a low threshold for investigation is important in a high RHD-burden setting such as ours.

Rheumatic heart disease (RHD) remains a substantial health burden for First Nations peoples in Australia. A significant proportion of First Nations women in the NT receive limited antenatal care due to remoteness, service access, and sociocultural factors [18,23]. The clinical assessment of pregnant women remains vital in screening for diseases that may negatively affect the health of the mother and/or foetus, including hypertension, diabetes, infectious diseases, and RHD. However, the accuracy of auscultation for detecting valvular heart disease due to RHD is poor compared with

echocardiography [27]. Clinical identification of RHD in remote First Nations populations is hampered further because of limited access to primary care physicians [18]. Furthermore, given the hyperdynamic nature of pregnancy, which makes flow murmurs more prominent [28], most women with an incidental murmur had a normal echocardiogram result.

In our cohort, almost all non-Indigenous women with heart disease on echocardiography had a known diagnosis before pregnancy. The burden of heart disease, both previously known and unknown, was significantly higher in the First Nations group, with many cases of clinically significant disease. However, a history of ARF or RHD did not always correlate with RHD being seen on the echocardiogram. This reflects that not all ARF leads to RHD, established RHD can regress [29], and conversely, RHD can also have insidious onset [5].

Historically, stenotic valve lesions have caused the most concern during pregnancy because of effects of increased circulating volume, tachycardia, and reduced peripheral vascular resistance on the physiological changes, due to a fixed obstruction [12]. The risk is further elevated in the presence of secondary pulmonary hypertension [12]. Data from the international Registry of Pregnancy and Cardiac disease on rheumatic mitral valve disease in pregnancy reveal a hospital admission rate of almost one-quarter in women with any mitral stenosis [13]. However, 13.7% of women with mitral regurgitation also required hospital admission [13]. Mitral regurgitation was the most common rheumatic valve lesion in our cohort. The impact of moderate-to-severe mitral regurgitation on maternal outcomes may be underestimated in this high-risk population.

The role of echocardiography screening in pregnancy in the Australian context has not been explored in detail. Most work has been performed in low- and middle-income countries. A prospective screening study from Eritrea discovered a 2.3% rate of subclinical RHD in pregnant women [30]. Beaton et al. [10] studied the role of echocardiography as a screening tool for pregnant women in Uganda. They discovered a prevalence of 1.7% of heart disease in a cohort of >3,500 pregnant women. Most cases were RHD (87.9%), with very few cases previously known, of which 11% had severe valve lesions [10]. It was noted that symptoms of possible heart disease, including excessive oedema and syncope, did not differ significantly between the women with and without heart disease. An important benefit of timely detection of significant cardiac disease before labour was the facilitated transfer of patients to a more resourced centre for delivery. In our cohort, all women requiring transfer were known to have RHD before pregnancy. All newly detected cases were mild in severity and as such unlikely to cause compromise to the pregnancy [13]. However, identifying mild RHD early in life does allow for the initiation of secondary antibiotic prophylaxis to prevent progression of disease [29]. Determining how valvular disease had progressed before and during the pregnancy was outside of the scope of this study.

There were no deaths from rheumatic heart disease (RHD) during pregnancy or childbirth in our cohort, consistent with outcome data from the NT [31]. RHD in pregnancy is a leading cause of cardiac complications in pregnancy globally [14]. In some under-resourced low-and middle-income countries, the maternal mortality rate from RHD is as high as 34% [16]. The prospective cohort study of RHD in pregnancy, using the Australasian Maternity Outcomes Surveillance System (AMOSS), identified one death and demonstrated that RHD was associated with significant maternal and perinatal morbidity [15]. A single-centre retrospective study from Australia demonstrated low mortality for pregnant women with RHD [32]. The authors noted that appropriate risk stratification enabled the avoidance of peripartum complications due to the disease [32].

This study was not designed to determine the prevalence of RHD in pregnant women living in the NT. There is no prospective research that has assessed this in Australia. The AMOSS study estimated a population prevalence of 2.2% in the NT, based on retrospective data from clinically indicated historical echocardiogram reports [15]. This aligns with data for the RHD prevalence in the general population of the NT [2]. However, this may be a gross underestimate in the young female population. Data from a more recent echocardiographic screening study of 5- to 20-year-old children living in a remote community of the NT identified a prevalence of 5%, more than twice that of previously published data [3]. This suggests that there may be clusters within Northern Australia that have especially high rates. The higher proportion of new heart disease diagnoses in the First Nations women in our cohort, many of which were RHD, indicates a similar trend in women of childbearing age. An important next step is to perform a cross-sectional prevalence survey to estimate the burden of RHD during pregnancy in this high-risk setting. Prevalence data would help health services assign the necessary resources. For individual women, early identification of RHD would affect current and future pregnancies and contribute to improving outcomes for both mothers and fetuses.

Limitations

This study reports data from the main echocardiography database used in the NT, but limitations of the search mechanism may have resulted in missed cases. This study aimed to assess the referral patterns for women undergoing echocardiography during pregnancy. Therefore, individuals who may have been newly diagnosed with RHD in the postpartum period (another risk period when RHD can become clinically apparent) were excluded. The small size of the study cohort limited the power of statistical comparisons, such as the likelihood of an incidental murmur representing true cardiac disease in First Nations women vs non-Indigenous women. Tertiary but not primary care electronic medical records were used for information on medical history; hence, some relevant medical information may have been omitted.

Conclusions

Rheumatic heart disease (RHD) poses a substantial health burden within First Nations communities of Northern Australia, with high relevance for women of childbearing age. Our study demonstrates a clinically significant burden of disease that necessitates consideration of intervention, which may not be identifiable by clinical assessment alone. Timely detection of cardiac disease during pregnancy can ensure that planning for delivery can be medically and culturally safe, including location of delivery, type of care needed, and mental and social preparation for the mother and family [31]. A better understanding of the true prevalence and spectrum of disease severity in this population would enable more informed health service investments. We recommend a lower threshold for considering the need for echocardiography, and consideration of screening for all women identified as being at elevated risk of RHD.

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Conflicts of Interest

There are no conflicts of interest to disclose.

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