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Clinical outcomes for young people with screening-detected and clinically-diagnosed rheumatic heart disease in Fiji

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ABSTRACT

Background: Echocardiographic screening is under consideration as a disease control strategy for rheumatic heart disease (RHD). However, clinical outcomes of young people with screening-detected RHD are unknown. We aimed to describe the outcomes for a cohort with screening-detected RHD, in comparison to patients with clinically-diagnosed RHD.
Methods: A retrospective cohort study included all young people with screening-detected RHD in the Central Division of Fiji in the primary cohort. Screen-negative and clinically-diagnosed comparison groups were matched 1:1 to the primary cohort. Data were collected on mortality, clinical complications and healthcare utilisation from the electronic and paper health records and existing databases.
Results: Seventy participants were included in each group. Demographic characteristics of the groups were similar (median age 11 years, 69% female, median follow-up 7 years). There were nine (12.9%) RHD-related deaths in the clinically-diagnosed group and one (1.4%) in the screening-detected group (Incident Rate Ratio: 9.6, 95% CI 1.3–420.6). Complications of RHD were observed in 39 (55.7%) clinically-diagnosed cases, four (20%) screening-detected cases and one (1.4%) screen-negative case. There were significant differences in the cumulative complication curves of the groups ($p < 0.001$). Rates of admission and surgery were highest in the clinically-diagnosed group, and higher in the screening-detected than screen-negative group.
Conclusions: Young people with screening-detected RHD have worse health outcomes than screen-negative cases in Fiji. The prognosis of clinically-diagnosed RHD remains poor, with very high mortality and complication rates. Further studies in other settings will inform RHD screening policy. Comprehensive control strategies are required for disease prevention.

1. Introduction

Rheumatic heart disease (RHD) is the chronic sequel of acute rheumatic fever (ARF), an autoimmune reaction to infection with the Group A Streptococcus bacterium. People with RHD are at increased risk of complications such as congestive heart failure (CHF), infective endocarditis, arrhythmia, stroke, complications of pregnancy and childbirth, and premature death.

Echocardiography is a sensitive test for the diagnosis of RHD [1]. Screening using echocardiography may identify individuals with RHD that have not previously presented to clinical services, and echocardiographic screening research activities have been conducted in many countries for two decades [2,3]. There are an estimated 33 million prevalent cases of RHD globally [4], although this estimate does not include asymptomatic cases as uncovered in screening studies, suggesting the actual global burden may be considerably greater [5].

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However, whilst data exist on the natural history of RHD for patients presenting with clinically-diagnosed ARF or RHD [6], data are limited on the clinical outcomes for people with screening-detected RHD. It is therefore not known whether echocardiographic findings on screening represent only trivial to mild disease, or if some predispose to serious complications, increased healthcare utilisation and premature death. These data are required for development of evidence-based policy for population-level screening.

We previously reported severe disease on echocardiography in some young people with screening-detected RHD in Fiji [7]. In this study, we aimed to describe the clinical outcomes for a cohort of young people with screening-detected RHD, and to compare these outcomes to a cohort without RHD and to a cohort with clinically-diagnosed RHD.

2. Methods

2.1. Design and setting

We used a retrospective cohort study to describe and compare the clinical outcomes of a screening-detected RHD cohort with two matched groups of screen-negative and clinically-diagnosed RHD participants.

This study took place in the Central Division of Fiji, a country in the South Pacific with a population of approximately 900,000. Forty-one percent of the population reside in the Central Division [8]. Fiji has a very high prevalence of RHD (definite RHD 7 per 1000 school-aged children on echocardiography) [9]. Fiji has conducted sporadic echocardiographic screening for RHD since 2006 and has an active RHD control program managed by the Ministry of Health and Medical Services. All inpatient and outpatient medical care for children and young adults with RHD in the Central Division is provided at the Colonial War Memorial Hospital in Suva.

2.2. Participants

Cases were defined by interrogating a database compiled from individual screening activity logs in Fiji, as previously described [10]. All young people aged 5–15 years who were diagnosed with RHD on echocardiographic screening from 2006 to 2013 and recommended to commence secondary prophylaxis were included in the primary cohort [11–13]. We excluded any child known to have RHD prior to screening, or who was later assessed to have a non-RHD diagnosis such as congenital heart disease. We also excluded cases assessed to have possible or probable RHD [14] or borderline RHD [15]. We excluded cases screened outside the Central Division as data for other divisions were unreliable or unavailable.

We then defined two matched comparison groups: a control group of screen-negative participants, and a comparison group of participants with clinically-diagnosed RHD. Participants for these groups were matched 1:1 for each screening-detected case by date of screening/diagnosis, age, gender and ethnicity. Screen-negative cases were identified by manually searching the school screening enrolment logs for the child of the closest age to the case at the same school, where gender and ethnicity were matched. Echocardiography reports were then checked to ensure none had congenital or other abnormalities.

Clinically-diagnosed cases were identified by manually searching the Fiji National RHD register. At the time of the study, the register was a locally-stored, Microsoft Access database managed by the RHD control program, containing demographic and clinical information for all cases of ARF and RHD notified to the program since 2005. Patients without RHD (registered as ARF only) or residing outside the Central Division were excluded. Register data were filtered to display age and gender matched individuals with a clinical diagnosis date within 12 months of the screening date of the screening-detected case. The individual with the closest age was enrolled as the match. In the few instances where there was no available match for cases of other Pacific Islander ethnicity, a match was selected from the indigenous iTaukei population. Matching was performed blinded to any additional clinical or demographic information.

2.3. Outcomes

The study period was defined from the date of screening or clinical diagnosis until July 31, 2015, or the date of death where applicable. Outcomes collected were known clinical complications of RHD (CHF, infective endocarditis, stroke, ARF recurrence, and death). Data were also collected on healthcare utilisation episodes including admissions, surgery and medication prescriptions. Documented prescription of a medical treatment for cardiac failure was coded as CHF. Reliable data were not available for complications of pregnancy and childbirth.

2.4. Data collection

The main data source was the Fiji electronic health information system (PATIS Plus) which includes hospital admission coding according to the International Statistical Classification of Diseases and Related Health Problems (ICD-10) for the main divisional and subdivisional hospitals nationally, and detailed medication prescribing records. Coding data for hospital admissions are fairly reliable, although there are some known deficiencies [16]. The second major source of data was individual patient files held at the Colonial War Memorial Hospital. These paper files were manually inspected page-by-page for details of admissions, surgery, medications and complications. Additional data were extracted from the Fiji National RHD Register and existing lists of cardiac surgical cases held by the RHD control program.

Two data collectors used a standardised data extraction tool to inspect the PATIS record, individual patient file and any other available data sources and reached consensus on items to include in the analysis. When assessing admission episodes for clinically-diagnosed cases, any admission where the initial diagnosis of RHD was made was excluded, and only subsequent admissions counted. All records were reviewed by an experienced paediatrician and reasons for admission, surgery and death were classified as RHD-related or not.

A list of participants who had died was compiled from all data sources. We then undertook a primary review of death certificates held at the Fiji Health Information Unit to determine cause of death. Death certificate information is generally available and reliable as reporting deaths is mandatory prior to burial or cremation [17].

2.5. Statistical analysis

Descriptive statistics were used to calculate frequency of clinical outcomes. Incident rates were calculated using the total period of observation of each group as the denominator. Incident rate ratios (IRR) with 95% confidence intervals were used to compare outcomes between the primary cohort (screening-detected) and the screen-negative and clinically-diagnosed groups. Kaplan-Meier failure curves were used to compare mortality and cumulative RHD complications, and the log-rank test used to assess for differences between groups. Results were analysed using Stata 14.2 (Statacorp, College Station, TX, USA).

2.6. Ethical approval

The study protocol was approved by the Fiji National Research Ethics Review Committee (2014.134) and the Royal Children's Hospital Human Research Ethics Committee, Australia (2015–02).

3. Results

3.1. Characteristics of cohort groups

Seventy screening-detected cases were included. The median age at screening was 10.9 years, median age at end of study was 17.6 years and median length of observation was 7.4 years. Females accounted for 69% of cases and 83% were iTaukei (indigenous Fijian). These cases were matched with 70 screen-negative and 70 clinically-diagnosed cases, and the demographic characteristics of the three groups were very similar (Table 1).

3.2. Healthcare interactions

There were 28 admissions (16 RHD-related) in the screening-detected group compared to 4 (none RHD-related) in the screen-negative group and 113 (78 RHD-related) in the clinically-diagnosed group (Table 2). Admission incident rates were higher in the screening-detected than screen-negative group (IRR 7.1, 95% CI 2.5–27.9) and higher in the clinically-diagnosed than screening-detected group for overall admissions (IRR 4.3, 95% CI 2.8–6.8) and RHD-related admissions (IRR 5.2, 95% CI 3.0–9.5). Admission bed days were higher in the screening-detected than screen-negative group (IRR 3.7, 95% CI 2.7–5.3) and higher in the clinically-diagnosed than screening-detected group (IRR 6.6, 95% CI 5.6–7.8).

Three screening-detected and fifteen clinically-diagnosed patients had cardiac valve surgery during the study. Surgical episodes were more frequent in the clinically-diagnosed group than the screening-detected group, both overall (IRR 7.5, 95% CI 2.6–29.2) and for RHD-related surgery (IRR 6.4, 95% CI 1.8–33.9, Table 2). There was only one episode of surgery (not RHD related) in the screen-negative group, although this result was not statistically significantly different to the screening-detected group with this sample size.

3.3. RHD complications

In the screening-detected group, 14 (20%) developed complications of RHD, particularly CHF (Table 2). There was one episode each of

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