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Title: MORBIDITY, MORTALITY AND SURVIVORSHIP BIAS IN PREVALENT AND INCIDENCE RHEUMATIC HEART DISEASE: A PROSPECTIVE COHORT STUDY

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Background & Aims: Rheumatic heart disease (RHD), a consequence of a dysregulated immune response to Streptococcus pyogenes infection, remains the most commonly acquired cardiovascular condition in under 25-year-olds. Predominantly occurring in low- and middle-income countries (LMICs), RHD typically affects the young working age population, with an estimated 2.8 million new and 40.5 million prevalent cases globally in 2019, although rates of RHD complications in endemic settings remain uncertain. Accordingly, we undertook a prospective cohort study of RHD in Fiji with the aim of validating our previous retrospective study based on routine data and record-linkage from this setting.

Methods: We prospectively ascertained RHD patients in the Central Division of Fiji from: i) prevalent cases reviewed in echocardiography clinic at the Colonial War Memorial Hospital during 2011-2012, and ii) incident cases diagnosed in hospital until October 2016. The primary outcome comprised the earliest of RHD-attributable death, new heart failure, new stroke, or acute rheumatic fever recurrence. Deaths were considered RHD-attributable if RHD (or valvular heart disease) was specifically mentioned as a cause, or where the cause of death was a recognised RHD complication without an alternative explanation. Secondary outcomes included these events individually, infective endocarditis, cardiac surgery and progression of symptoms. Follow-up was at approximately six monthly intervals until the end of October 2016 (i.e. 30 months). Rates of RHD-attributable death and new hospitalisation for heart failure or stroke in the prospective cohort were also compared to those in a group with similar characteristics from our previously reported retrospective study.

Results: We successfully recruited 111 (66.1%) of 168 prevalent cases between May 2014 and September 2015, but were unable to recruit the remainder of whom 24 (14.3%) could not be contacted and 11 (6.5%) had died. We also recruited 52 incident cases before completion of follow-up in October 2016. The median follow-up period was 19.3 months (IQR 13.8-22.3) amounting to a median of three reviews (IQR 2-3 reviews) of each participant. The combined prospective cohort of 163 individuals were mostly young (median age 19.2 years, IQR 13.8-33.9), with more than half (62.0%) recorded as female. The primary outcome occurred in five of 109 (4.6%) of the prevalent group and three of 48 (6.5%) from the incident group without existing heart failure or stroke at recruitment, with yearly incidence rates of 3.0 (95% CI, 1.2-7.2) and 5.5 (95% CI, 1.8-16.9) in prevalent and incident groups respectively. For comparison, we identified 628 individuals who had attended the echocardiography clinic during our previous retrospective study covering 2008-2012. During 2011-2012, RHD-attributable death or new hospitalisation for heart failure or stroke occurred in 25 (median age, 31 years). This equated to a yearly incidence of 1.4% (95% CI, 0.8-2.5) among the 412 individuals with prevalent RHD at the start of 2011, and 5.7% (95% CI, 3.4-9.6) among 216 individuals with incident RHD diagnoses before the end of 2012. The same endpoint occurred at rates of 1.7 (95% CI, 0.6-5.4) and 3.3 (95% CI, 0.8-13.3) in the prevalent and incident groups in the prospective cohort respectively.

Conclusions: Our study represents one of very few prospective studies of RHD morbidity and mortality from an LMIC, providing an important insight into the natural history of RHD in this population. Rates of complications were higher among incident versus prevalent cases in both retrospective and prospective analyses, an important feature of the disease’s epidemiology, with broader implications for wider RHD surveillance efforts. Given the marked concordance between the two designs, robust retrospective routine data studies, which can potentially reach a wider, more representative population, offer a much needed to tool to inform efforts limiting the impact of RHD globally.