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ORIGINAL ARTICLE

An epidemiological study to assess the true incidence and prevalence of rheumatic heart disease and acute rheumatic fever in New Caledonian school children

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Aim: To provide in New Caledonian school children (i) the prevalence of rheumatic heart disease (RHD) detected by annual screening program using new World Heart Federation diagnostic criteria; (ii) the point prevalence of acute rheumatic fever (ARF); and (iii) to investigate socio-demographic risk factors associated with RHD.

Methods: This study linked data from national ARF/RHD programs by combining ARF incidence data from the register with RHD prevalence data from echocardiographic screening data for a single age year of the population for overall point prevalence ARF/RHD rates. For the analysis, cases of echocardiographic detection of RHD are presumed to be synonymous with undiagnosed ARF. All results were weighted to minimise the bias introduced from absent pupils of each annual screening program. Incidence and prevalence were age-standardised to the WHO World Standard Population. Each 2013 cumulative prevalence of definite and borderline RHD was studied using a multivariate logistic regression adjusted for socio-demographic factors.

Results: The overall age-standardised incidence of clinical and undiagnosed ARF (i.e. echocardiographic-detected RHD) was combined as point prevalence and estimated to be 99/10 000 cases in 2012 and 114/10 000 cases in 2013. This included 40/10 000 prevalent cases of asymptomatic RHD detected by screening each year. Being Melanesian, OR 23.2 (95% CI: 3.4–157.3), or Polynesian, OR 21.5 (95% CI: 2.9–157.7), was associated with a higher prevalence of having definite RHD compared with being Caucasian. Being a girl was associated with a higher risk of having borderline RHD, OR 1.9 (95% CI: 1.03–3.3).

Conclusion: Without echocardiographic screening, ARF/RHD burden is substantially underestimated.

Key words: acute rheumatic fever; register; rheumatic heart disease; school children; screening.

What is already known on this topic

1 Rheumatic heart disease and acute rheumatic fever remain endemic in New Caledonia.
2 Echocardiographic screening detects more cases of RHD than clinical reports alone (by register).
3 The risk of definite RHD increases with age.

What this paper adds

1 The 2011 World Heart Federation standardised echocardiographic criteria were used for the first time in New Caledonia.
2 To provide weighted and age-standardised prevalence of RHD and incidence and point prevalence of ARF.
3 To provide weighted socio-demographic risk factors in the 9 to 10-year old population, which reveal the difference between the onsets of definite or borderline RHD.

World-wide, acute rheumatic fever (ARF) and rheumatic heart disease (RHD) affect between 15.6 and 19.6 million children, adolescents or young adults.[1,2] The Global Burden of Disease 2010 Study estimated that RHD is responsible for 345 110 deaths each year and accounts for over 10 million disability-adjusted life years.[3] The incidence of ARF peaks in children aged 5 to 14 years; in this age group, it is estimated that there are 300 000 to 350 000 new cases per year.[3–5]

Acute rheumatic fever and RHD remain a substantial burden in low-resource settings, as demonstrated in the Pacific,[6–10] in the indigenous populations of Australia,[11,12] certain populations of New Zealand[13–16] and other parts of the world.[17–19] In the Pacific and indigenous Australian populations, prevalence ranges between 0.5% and 1.0% for school children and 3% for adults aged 35 to 44 years.[3]

Living conditions, especially household crowding,[6,20] poverty, hygiene and poor living standards[14–16,19,21] are known risk factors for developing these diseases. Previous studies have demonstrated that the risk of having definite or borderline RHD increases with

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age, especially from the youngest ages (5 years old) to adolescence and young adulthood.[5,7]

Acute rheumatic fever and RHD result from a primary infection in the upper respiratory tract or from a re-infection (relapse) associated with an inappropriate inflammatory response to the group A beta-haemolytic streptococci.[22,23] ARF occurs after a few weeks' latency period and is diagnosed according to Jones' criteria.[24,25] In practice, the patient may not consult physicians, or physicians may not identify these patients; thus, there is a high risk of missed diagnoses.[26]

Echocardiographic screening is more sensitive and specific for RHD than cardiac auscultation, detecting 3 to 25 times more cases.[4,17] It also enables classification of disease into either definite or borderline RHD by applying combined morphological and Doppler criteria.[27] Over recent years, echocardiographic screening has increased in certain countries with a high incidence of RHD.[7–9,17,18] However, misclassification of lesions is common, and it is often difficult to determine if the identified lesions of RHD are a result of ARF.[28] The World Heart Federation (WHF) has therefore standardised the echocardiographic criteria to reduce borderline cases.[28]

Active screening for RHD through cross-sectional surveys is seen as more advantageous than health facility-based screening as it captures cases who are asymptomatic (or subclinical) or unable to access health care.[3] In New Caledonia, the Agency for Health and Social Welfare conducts an annual echocardiographic screening program to detect asymptomatic or subclinical RHD (and thus undiagnosed/subclinical ARF cases) in the target population of children enrolled in the fourth grade of primary school.

A previous analysis was undertaken of 114 pupils who had asymptomatic or subclinical RHD detected by this screening program between 2008 and 2010. Crude prevalence of RHD was found to be 100/10 000 for girls and 78/10 000 for boys, 135/10 000 for Melanesian school children and 18/10 000 for Caucasian school children; however, there was no weighting undertaken to account for absent pupils or any age-standardization to aid comparisons over time or with other populations.[6] Also, the study did not distinguish between definite and borderline RHD cases, and no true incidence estimates were made for ARF. Since this study, the WHF has updated their recommended diagnostic criteria for RHD.

The objectives are to provide in New Caledonian school children, weighted and age-standardised estimates of (i) the prevalence of RHD detected by annual screening using new World Heart Federation diagnostic criteria; (ii) the true point prevalence of ARF; and (iii) to investigate socio-demographic risk factors associated with RHD.

Methods

Study design

An epidemiological study was conducted between 1 January 2012 and 31 December 2013. Written informed consent was given by the parents of every child who participated in the study.

Geography and population of New Caledonia

New Caledonia is an archipelago located east of Australia, north of New Zealand and just west of Fiji and Vanuatu. New Caledonia comprises a main island, the Loyalty Islands and several smaller islands. The 2009 and 2014 census estimated the population to be 245 580 and 268 767 (4349 nine to 10-year olds) respectively. From the 2009 census, 4494 and 4349 children were aged 9 and 10 years old.[29] Of these 8843 children, 44.9% were Melanesian, 5.7% were Polynesian, 22.9% were Caucasian, 6.3% were mixed ethnicities, 3.1% were other ethnicities and 1.4% were Asian.[29]

Participants

The target population of the screening program is the fourth grade. However, if pupils are absent from school the day of the initial screening, they are screened the following year when in fifth grade. Thus, the initial study sample includes a small proportion of fifth graders. The age range of fourth- to fifth-grade pupils in New Caledonia is 6–12 years – this broad age range is a result of the New Caledonian integrated learning policy which integrates pupils who have learning difficulties into mainstream classes. For the purpose of this study, the analysis is limited to 9 to 10-year olds (8026 school children who represent 87.3% of all children screened). In New Caledonia, school enrolment is compulsory; therefore, the school-based sample almost equates to the whole New Caledonian population for this age group (8843 children).

Data sources and measurement

There were two data sources for this study: (i) the national ARF and RHD register; and (ii) the two annual screening program for asymptomatic (or subclinical) RHD in 2012 and 2013.

1 The ARF/RHD register establishes records of all ARF and RHD cases detected by:
   Physicians working in public clinics and general practice (clinical ARF; symptomatic or clinical RHD; asymptomatic or subclinical RHD). New Caledonian physicians are obliged to notify all new clinical ARF cases according to the Jones' criteria and to perform a diagnostic echocardiogram looking for potential RHD, because ARF leads to RHD in 30 to 80% of cases.[2,30,31] Therefore, in order to diagnose RHD, following an episode of clinical ARF, an echocardiogram is always performed according to the 2011 WHF echocardiographic criteria[28] (Table 1). Asymptomatic or subclinical RHD and decompensated RHD, without a clear history of preceding ARF, can also be detected and notified to the register by cardiologists and the major tertiary hospital in New Caledonia.
2 The annual screening program for asymptomatic (or subclinical) RHD takes place in two stages: (i) school detection; and (ii) cardiologist confirmation. The process has been previously described.[4,6] Initial standard echocardiograms are performed on each fourth/fifth grade child to look for structural or functional cardiac abnormalities. If an abnormality is detected on the screening echocardiogram, a repeat echocardiogram is conducted at a cardiology clinic for confirmation of definite and borderline asymptomatic RHD according to the 2011 WHF echocardiographic criteria[28] (Table 1). Echocardiographic detection of RHD was presumed to be synonymous with undiagnosed ARF (Table 2).

Annual screening data, which was limited to the 9 to 10-year olds, was used from both 2012 and 2013. The Ministry of

Table 1 2011 World Heart Federation criteria for echocardiographic diagnosis of rheumatic heart disease (RHD) used for the confirmation of screening programs, New Caledonia, 2012–2013

Echocardiographic criteria for individuals aged ≤20 years
Definite RHD (either A, B, C or D):
A) Pathological MR and at least two morphological features of RHD of the MV
B) MS mean gradient ≥4 mmHg†
C) Pathological AR and at least two morphological features of RHD of the AV‡
D) Borderline disease of both the AV and MV§
Borderline RHD (either A, B or C):
A) At least two morphological features of RHD of the MV without pathological MR or MS
B) Pathological MR
C) Pathological AR
Normal echocardiographic findings (all of A, B, C and D):
A) MR that does not meet all four Doppler echocardiographic criteria (physiological MR)
B) AR that does not meet all four Doppler echocardiographic criteria (physiological AR)
C) An isolated morphological feature of RHD of the MV (e.g. valvular thickening) without any associated pathological stenosis or regurgitation
D) Morphological feature of RHD of the AV (e.g. valvular thickening) without any associated pathological stenosis or regurgitation

†Congenital MV anomalies must be excluded. Furthermore, inflow obstruction as a result of non-rheumatic mitral annular calcification must be excluded in adults. ‡Aortic root and hypertension must be excluded. §Combined AR and MR in high prevalence regions and in the absence of congenital heart disease is regarded as rheumatic. AR, aortic regurgitation; AV, aortic valve; MR, mitral regurgitation; MS, mitral stenosis; MV, mitral valve; RHD, rheumatic heart disease; WHF, World Heart Federation.

Table 2 Socio-demographic characteristics of study participants, in the school children of 9 to 10 years, New Caledonia, 2012–2013

Socio-demographic characteristics	Children without RHD†		Children with definite RHD		Children with borderline RHD	
	n = 6905	%	*n* = 53	%	*n* = 44	%
Class categories						
General	6796	98.4	49	92.4	44	100.0
Class for inclusion	109	1.6	4	7.6	0	0.0
Ethnicity						
Asian	155	2.2	0	0.0	1	2.3
Caucasian	1975	28.6	1	1.9	12	27.3
Melanesian	3645	52.8	43	81.1	25	56.8
Polynesian	815	11.8	9	17.0	5	11.4
Mixed race	315	4.6	0	0.0	1	2.3
Linear age (years)						
Mean ± SD	9.7 ± 0.4	100.0	9.9 ± 0.5	100.0	9.7 ± 0.5	100.0
Range	9.0–10.9		9.1–10.9		9.0–10.9	
Province of residence						
Loyalty Islands	638	9.3	6	11.3	4	9.1
North	1301	18.8	7	13.2	5	11.4
South	4966	71.9	40	75.5	35	79.5
Sex						
Male	3564	51.6	26	49.1	16	36.4
Female	3341	48.4	27	50.9	28	63.6
Screening year						
2012	3477	50.3	26	49.1	23	52.3
2013	3428	49.7	27	50.9	21	47.7

†Pupils who had normal results.

Education provided a full list of all school children enrolled in the fourth/fifth grade along with socio-demographic variables. The Agency for Health and Social Welfare could thus verify before the annual screening program whether any pupils were currently on the ARF and RHD register. Ethnicity and other variables were specified by parents on the written consent form, and then they were verified by the nurse during the initial school detection from the child's health record.

The ARF and RHD register includes the number of known cases of clinical ARF (with or without RHD) detected in New Caledonia. All children who were 9 years old with a previous episode of clinical ARF were registered and counted as the incidence of ARF in 2012. The remaining 9-year olds of the population underwent echocardiographic screening to detect new cases of RHD in 2012.

Variables

The following variables were used: (i) the incidence of clinical ARF found within the register at the start of each annual screening period (stratified into definite RHD and no RHD cases); (ii) the prevalence of asymptomatic borderline RHD found in the annual screening programs for 2012 and 2013; (iii) the prevalence of asymptomatic definite RHD found in the annual screening programs for 2012 and 2013; (iv) the point prevalence of ARF (clinical and subclinical) calculated through adding the incidence of clinical ARF in the register at the start of the period to the prevalence of asymptomatic definite RHD found in the annual screening programs; and (v) the point prevalence of cases of borderline and definite RHDs at the end of 2013. All RHD cases were assessed by a cardiologist according to the 2011 WHF echocardiographic criteria.[28]

Statistical analysis

Prevalence and incidence estimates were age-standardised to the WHO World Standard Population in order to enable comparisons over time and with other populations.[32] To produce more valid estimates representative of the overall theoretical study population, a raking ratio[33] procedure was also undertaken to minimise bias from student absenteeism on screening day. Each 2013 cumulative prevalence of definite and borderline RHD was studied using a

multivariate logistic regression adjusted for socio-demographic factors. The analyses were conducted with 9.3 SAS software.

Results

There were 8026 pupils eligible for screening. Of these, 367 were absent on the day of the screening, 322 did not have parental consent and 38 had previously been diagnosed with clinical ARF and were thus listed in the ARF/RHD register, including 22 cases of definite RHD (Fig. 1).

Weighted and age-standardised incidence and prevalence of ARF and RHD

At the start of 2012, the incidence of clinical ARF was 58.9/10 000 ($n = 16$). This included 36.8/10 000 ($n = 10$) for definite RHD and 22.1/10 000 ($n = 6$) for ARF without RHD. At the start of 2013, the incidence of clinical ARF was 73.3/10 000 ($n = 22$). This included 43.1/10 000 ($n = 12$) for definite RHD and 30.2/10 000 ($n = 10$) for ARF without RHD (Table 3).

The annual screenings identified that the weighted and age-standardised prevalence of definite asymptomatic RHD for each of the 2 years was 40.3/10 000 ($n = 16$ in 2012 and 15 in 2013). These cases of RHD were also the new cases of undiagnosed ARF with asymptomatic definite RHD which were not previously included within the register.

Therefore, the new overall weighted and age-standardised point prevalence of clinical ARF and undiagnosed ARF (i.e. echocardiographic RHD) was 99.2/10 000 in 2012 and 113.6/10 000 in 2013. This suggests that without echocardiographic screening programs, the prevalence of ARF/RHD is underestimated by between 35% and 40% each year (Table 3).

Socio-demographic characteristics and logistic regression

In the univariate analysis, the risk of having definite RHD increased significantly with linear age ($P = 0.0097$), but this was not significant in the multivariate analysis ($P = 0.0971$). Adjusting for class categories, the multivariate analysis demonstrated that Melanesians, OR 23.2 (95% CI: 3.4–157.3), and Polynesians, OR 21.5 (95% CI: 2.9–157.7), had a higher risk of having definite RHD compared with Caucasians. No cases of definite RHD were found among Asian or mixed ethnicities. No statistically significant interaction between sociodemographic variables was detected in both regression models. Gender was associated with borderline RHD, with girls having a 1.9 (95% CI: 1.03–3.3) times higher risk of having borderline RHD than boys (Table 2).

Discussion

The present study has established a new overall weighted age-standardised prevalence of clinical and undiagnosed ARF (with or without RHD) in 9 to 10-year old school children in New Caledonia. This is based on the ARF register and echocardiographic screening program data, which have revealed that a high proportion of ARF go undetected in the community. This not only highlights the value of school screening programs for detecting asymptomatic RHD but also emphasises the limitations of registers that are based solely on clinical encounters.

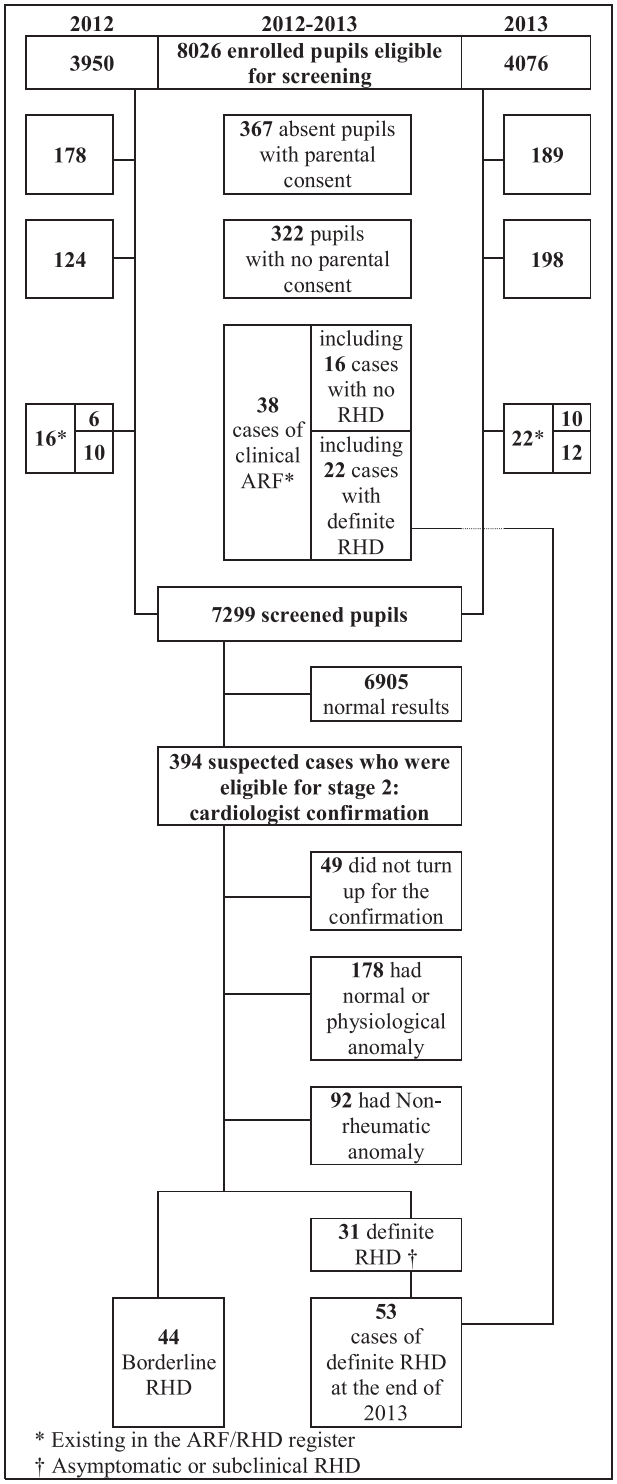

Fig. 1 Outcome of echocardiographic screening for rheumatic heart disease, New Caledonia, 2012–2013.

Being of Melanesian or Polynesian ethnicity was associated with a higher prevalence of definite RHD, and being a girl was

Table 3 Annual prevalence of rheumatic heart disease (RHD) and incidence and point prevalence (per 10 000) of acute rheumatic fever (ARF) in the target population of 9 to10 years, New Caledonia, 2012 and 2013

	n	Rate†	CI 95%	Rate‡	CI 95%
2012					
Incident cases of clinical ARF in the register at the start of 2012					
With definite RHD	10	27.4	10.4–44.4	36.8	12.4–61.2
With no RHD	6	16.4	3.3–29.5	22.1	3.2–41.0
Prevalent cases detected in annual screening programme					
Of asymptomatic borderline RHD	23	62.9	37.3–88.6	71.7	39.5–103.8
Of asymptomatic definite RHD	16	43.7	22.3–65.1	40.3	18.5–62.0
Point prevalence of ARF in New Caledonia at the end of 2012	32	87.5	—	99.2	—
2013					
Incident cases of clinical ARF in the register at the start of 2013					
With definite RHD	12	32.8	14.3–51.4	43.1	18.2–67.9
With no RHD	10	27.0	10.3–43.7	30.2	10.5–49.9
Prevalent cases detected in annual screening programme					
Of asymptomatic borderline RHD	21	56.8	32.5–81.0	51.4	28.3–74.5
Of asymptomatic definite RHD	15	41.0	20.3–61.7	40.3	18.9–61.8
Point prevalence of ARF in New Caledonia at the end of 2013	37	100.8	—	113.6	—

†Weighted rates to minimise potential bias from absent pupils. ‡Weighted and age standardised rates. The sample size of the study was 7337 participants (38 participants who were already in the register at the start of the periods plus 7299 participants who were screened in 2012 and 2013). CI, confidence interval (per 10 000).

associated with a higher prevalence of borderline RHD. This is important information to assist with targeted public health programs for the prevention of ARF.

The study had some limitations. The study demonstrated that the register underestimates the true number of ARF cases, but also the importance of combining cases from register with cases identified by screening program for establishing true number of cases. However, it also likely that the screening program underestimates the true number of cases of asymptomatic RHD. Indeed, some pupils missed both echocardiographic assessments, so their RHD status could not be ascertained. Although the weighting method[33] addressed bias from absent pupils in the first echocardiographic assessment, it did not address bias introduced from absenteeism at the cardiology clinic confirmation stage. This confirmatory stage is an important component of asymptomatic RHD screening programs because it increases the specificity of these programs.[7,17,27,28]

For the first time, the annual screening programs used the new 2011 World Federation echocardiographic criteria[28] and undertook weighting and age standardisation of estimates. Furthermore, definite RHD secondary to undiagnosed ARF was distinguished from definite RHD secondary to clinical ARF.

Previous studies from other endemic areas have demonstrated that the risk of having definite or borderline RHD increases with age.[5,7] For definite RHD, univariate results demonstrated this same increase with linear age but not with age group. The multivariate analysis did not support this evidence because age (in linear years or age group) was not significantly linked to the occurrence of definite RHD. It is possible that these findings were a result of the narrowly circumscribed population of 9–10 years, which delineated only two age groups.

The univariate results also demonstrated that age was not significantly linked to the occurrence of borderline RHD. Girls seem to have an increased risk of having definite or borderline RHD compared with boys. This trend has previously been described,[11,19] but the present findings suggest that girls may only be at higher risk of having borderline RHD than boys. These findings may refine the socio-demographic risk profile differences between definite and borderline RHDs.

Previous studies show that indigenous Australian and Māori populations (New Zealand) have a higher risk of having definite RHD compared with Caucasians.[11–16] This study supports this evidence because Melanesians and Polynesians were at a higher risk than Caucasians. However, this higher risk may be explained by differences in living conditions which have been suspected to increase the risk of RHD[6,14–16,19–21] without reliable conclusion about such risk factors.

An overall aged-standardised point prevalence around 99 to 114/10 000 cases of RHD (and ARF) may appear low compared with some other studies, although we do not have comparable age ranges. In Cambodia, the prevalence of only asymptomatic RHD was 215/10 000 cases (95% CI: 168–262), and in Mozambique, 304/10 000 cases (95% CI: 232–376) in school populations aged 6 to 17 years.[17] An older recruitment age should therefore be considered by undertaking repeat screening in adolescents attending secondary school to follow-up cardiac abnormalities according to standardised echocardiographic criteria. However, the current screening program is feasible and results in early identification of RHD. Monitoring of children with borderline RHD will be implemented because of the number of borderline RHD cases detected in the screening program.

Conclusion

Ongoing data collection regarding this study of pupils will likely improve the statistical power of the current results. This will allow us to further investigate the incidence, prevalence and socio-demographic profile of ARF and RHD in New Caledonia.

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