S4 Table. Summary of education and GAS infection, ARF and RHD

| Study details | Aim of study | Study design | Study population and setting | Measure of parental education | Measure of outcome (GAS, ARF, RHD) | Outcome incidence/ prevalence | Results univariate | Results Multivariate | Study quality |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Adanja et al 1988 | To test the hypothesis regarding the influence of socioeconomic and some other factors on the occurrence of ARF.  | Case control | 148 with first ARF attack, 444 controls matched for age, sex and place of residence (1:3) Serbia | Low education of mother: < 4 years elementary school educationLow education of father: < 4 years elementary school education | ARF using revised Jones criteria | NA | **Positive association**Low education of mother 18.9% vs. 10.4% RR 2.58 (1.38-4.83) **No association** Low education of father |  | Poor to fair: cannot determine temporal association of exposure and outcome; no multivariate analysis.  |
| Dobson et al 2012 | To investigate the role of environmental factors for RHD in Fiji. | Case control | 80 children aged 5- 15 years with RHD and 80 age and sex matched controlsFiji | Maternal education: Primary school, Secondary school | Definite RHD diagnosed on echocardiogram using WHO criteria  | NA | **No association** Maternal education level |  | Poor: no power calculations, unstated number of controls from different source, participation rate 61%.  |
| Grave 1957 | To investigate the factors of social and emotional forces in the aetiology of rheumatic fever.  | Case control | 122 children aged 2-12 with ARF, 100 controls from outpatient clinics within same age rangeSydney, Australia | Years of maternal education | ARF diagnosed on criteria of the Rheumatic fever council of the American Heart Association | NA | **No association**Years of maternal education |  | Poor: unmatched controls and no adjusting for differences, no power calculations, no test of significance  |
| Riaz et al 2013 | To identify the risk factors of ARF and to explore the risk factors of developing RHD among ARF patients. | Case control | 103 RHD cases, 103 ARF cases, 207 controlsBangladesh | Education level of mother and father: Secondary and above, Primary or less, Illiterate | ARF diagnosed using modified Jones criteriaRHD diagnosed by doppler echocardiography | NA | **Positive association** Mother illiterate: non-ARF 33.8% (reference), ARF 46.6% (χ26.7 p=0.033), RHD 50.5% (χ211.7 p=0.003)**No association**Education level of father |  | Fair: no matching, blinding of assessors not stated.  |
| Kurahara et al 2006 | To determine factors in prevalence rates of ARF in a multiethnic population.  | Case control | 26 cases ARF, 41 controls with other heart condition (all on Medicaid)Hawaii, USA | Mother or father with a high school diploma | ARF diagnosed using modified Jones criteria | NA | **No association** Mother or father with a high school diploma |  | Fair: no matching, small sample size |
| Okello et al 2012 | To investigate the role of socioeconomic and environmental factors in the pathogenesis of RHD in Ugandan patients.  | Case control | 243 RHD cases, 243 controls aged between 5 and 60Uganda | Education level of case: no education, Primary, Secondary, Vocational, University  | RHD diagnosed using history ARF, clinical examination, echocardiogram criteria  | NA | **Positive association** Education level Primary or less 53.9% vs 25.9% OR 3.34 (2.24-4.99) | **No association** Education level | Fair: unmatched controls, but randomly chosen and multivariate analysis performed, time period of participant selection not stated.  |
| Vlajinac et al 1991 | To investigate the independent, unconfounded effect of risk factors for ARF identified in a previous study conducted on this population. | Case control | 148 with first ARF attack, 444 controls matched for age, sex and place of residence (1:3) Serbia | Low education of mother: < 4 years elementary school education | ARF diagnosed using revised Jones criteria | NA |  | **Positive association**Low education of mother RR 2.52 (1.29-4.92) | Fair: temporal association of exposure and outcome not explicitly stated; |
| Vlajinac et al 1989 | To test the hypothesis that socio-economic factors are related to rheumatic fever and an additional comparison for those with and without a history of sore throat.  | Case control  | 148 with first ARF attack, 444 controls matched for age, sex and place of residence (1:3)Serbia  | Low education of mother < 4 years elementary school education | ARF diagnosed using revised Jones criteriaFrequent sore throat= >1/year | NA | **Positive association** Without sore throat: Low education of mother RR 2.23 (1.16-4.25)**No association**With sore throat: Low education of mother |  | Poor to fair: temporal association of exposure and outcome not explicitly stated; stratified only by sore throat frequency.  |
| Zaman et al 1998 | To explore further the nutritional factors that may be associated with ARF.  | Case control | 60 ARF cases, 104 controls aged 5-20 years with recent GAS infectionDhaka, Bangladesh | Parental schooling in years | ARF diagnosed using updated Jones criteria | NA | **Positive association** Parental schooling 10.3 vs. 17.8 (p<0.0001) |  | Fair to good: no power calculations.  |
| Meira et al 2005 | To study the progress of valvar disease by means of clinical and echocardiographic evaluations and to identify the independent variables that predict severe chronic valvar disease. | Case series | 258 children and adolescents diagnosed with ARF between 1983 to 1998Belo Horizonte, Brazil | Mother’s schooling: <4 years | ARF diagnosed using revised Jones criteria |  | **No association** Mother’s schooling | **Positive association** Mother’s schooling < 4 years RR 3.93 (1.46-10.57) | Fair: reasonable breadth of factors, multivariate analysis, no power calculation  |
| Mirabel et al 2015 | To address the outcomes and modalities of RHD screening through a cohort of children with and without RHD who took part in the first large RHD echocardiography based surveillance programme.  | Cohort | 114 cases of RHD selected from a cohort of 157 and 227 controls selected randomly from classmates, matched for ethnicity and classroomNew Caledonia | Mother’s education: Primary, Secondary, Higher education | Persistence of RHD diagnosed using World Heart Foundation criteria.   | RHD: 890/100,000  | **Positive association** Mother’s education:Primary 46.3% vs 54.2%Secondary 50% vs. 29.2%Higher 3.7% vs. 16.7% (p=0.048) | **No association** Mother’s education | Fair: no power calculation, >20% lost to follow up.  |
| Bassili et al 2000 | To evaluate the current regimen of secondary prophylaxis available to disadvantaged Egyptian children suffering from RHD who were attending various children’s hospitals in Alexandria.  | Cross section | 150 children with RHD | Maternal education: ≤6 years, >7 yearsPaternal education: ≤6 years, >7 years | Diagnosis of RHD based on a documented previous history of ARF with characteristic murmur confirmed by Doppler echocardiography | NA | **No association**Maternal or paternal education  |  | Poor to fair: no power calculation, limited factors included |
| Likitnukal et al 1994 | To evaluate the factors influencing streptococci colonization of school age children.  | Cross section | 1,547 school children aged 6-11 yearsBangkok, Thailand | Maternal and paternal education levels:≤Lower primary school≤ Upper primary school≤ Secondary school | Throat swab culture for βHS and GAS | GAS 18%βHS 47% | **No association** Maternal or paternal education levels |  | Poor: high attrition, no power calculation.  |
| Rizvi et al 2004 | To determine the prevalence of RHD in a rural population in a single subdistrict and study the risk factors for RHD.  | Cross section | 10,412 participants interviewed & 9,483 screened across11 rural villagesPakistan | Education among patients:IlliterateAble to read or having any formal education | ARF diagnosed using updated 1992 Jones criteriaRHD diagnosed using echocardiography for cases with clinical murmurs | RHD5.7/ 1000  | **No association**Patient education level |  | Fair to good: generally good methods, unconventional measure for crowding index. |
| Lue et al 1979 | To collect information on streptococcal infections, prevalence and severity of ARF and RHD and their long term follow up. | Ecologic | Various | Literacy rates among urban and “well to do children” | GAS diagnosed on throat swab cultureDiagnosis of ARF was made based on the revised or modified Jones criteria. RHD diagnosis from hospital record | Various. Range for GAS 1.6-29.5%Range for RHD 0.3 to 2.7/ 1,000  | **No association**Literacy rates and GAS Literacy rates and RHD |  | Poor: heterogeneity in methods, populations and results. Ill-defined ecologic units.  |
| Morton & Lichty 1970 | To describe the evidence which suggests the existence of a region within Colorado in which excess risks of occurrence of rheumatic fever were associated with socioeconomic factors manifest in 1959-61.  | Ecologic | 75 cases RHDColorado, USA | Per cent of children aged 14-17 years in schoolMedian school years completed of persons aged 25 years of more | ARF cases and ARF/RHD death data from Colorado Department of Public Health  | Varied by region. Average mean annual rate 14.0/100,000; range 7.6 to 64.6 /100,000 | **Possible association** Region with lowest proportion in school aged 14-17 (84.8% vs. population mean 89.4%) and lowest median school years completed (9.9% vs. population mean 11.7%) had highest ARF rate (64.6 vs. population average 14.0/100,000) (no test of significance) |  | Poor: poor analysis, no multivariate.  |
| Rosati et al. 1978 | To investigate the frequency of MS, rheumatoid arthritis, RHD and post-streptococcal nephritis in a population ethnically homogeneous and stable in size and composition, exclusively on the basis of differences in climatic and socioeconomic conditions. | Ecologic | 813 cases of RHD | Proportion of population who were illiterate  | RHD diagnosed on hospital records of heart disease as a clinical manifestation of rheumatic fever diagnosed using revised Jones criteria | Various. 0.42 to 0.89/1,000 | **Possible association**Regions with highest illiterate proportion had highest frequency of RHD: Zone 1: 16%, 0.89/1000Zone 2: 11%, 0.76/1000Zone 3: 8%, 0.42/1000Zone 4: 6%, 0.46/1000(no test of significance) |  | Poor: ecologic unit too broad, no direct analysis.  |

ARF: Acute rheumatic fever βHS: Beta haemolytic streptococci ECG: Electrocardiogram emmST: emm sequence type GAS Group A streptococci NA: Not applicable OR: odds ratio RHD: Rheumatic heart disease RR: Risk ratio USA: United States of America WHO: World Health Organization