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Ethnic Differences for Developing Rheumatic Fever in a Low-Income Group Living in Hawaii

David K. Kurahara, MD, **Andrew Grandinetti, PhD**, **Judith Galario, BS**, **D. Venu Reddy, MD**, **Angela Tokuda, MS**, **Susan Langan, MPH, MS**, **Brian Tanabe, MD**, **Kara S. Yamamoto, MD**, and **Karen M. Yamaga, PhD**

From the University of Hawaii, John A. Burns School of Medicine, Departments of Pediatrics (DKK, JG, AT, DVR, KSY, BT), the Department of Tropical Medicine, Medical Microbiology, and Pharmacology (KMY), and the Pacific Biomedical Research Center (AG), Honolulu, Hawaii; Johns Hopkins University, Bloomberg School of Public Health, Department of Molecular Microbiology and Immunology, Baltimore, Maryland (SL).

Abstract

The risk factors responsible for acute rheumatic fever (ARF) are complex, in part, because group A streptococcus (GAS) infection is a prerequisite for this disease. We attempted to differentiate socioeconomic from genetic risk factors by studying subjects in a Hawaii pediatric cardiology clinic who qualified for Medicaid. This ethnically diverse group was unique because they maintained a low socioeconomic but generally healthy lifestyle with more limited risks than those living in extremely impoverished conditions.

Methods—Questionnaires were administered to consenting subjects in the clinic, who were divided into those diagnosed with ARF (n=26) and those with other (primarily congenital) heart diseases (n=41).

Results—The socioeconomic status of the ARF and non-ARF groups was lower than that of the Hawaii population in general, and little differences were noted between the groups. The ARF group, however, had slightly larger household sizes and more children than the non-ARF group. The greatest difference was in ethnicity. By the Fisher exact test, the number of Polynesians belonging to the ARF group was significantly greater than all other ethnicities (P=.005). Polynesians had an odds ratio >4.80 of developing ARF, which increased to 6.33 when number of children per household was considered.

Conclusion—The potential contribution of genetic predisposing factors for developing ARF was analyzed in subjects living in a homogeneously low socioeconomic level relative to the general Hawaii population. Polynesians were at highest risk when compared to other ethnicities living in similar socioeconomic conditions.

Address correspondence and reprint requests to David K. Kurahara, MD; John A. Burns School of Medicine; University of Hawaii; 1319 Punahou Street, Room 734; Honolulu, HI 96826; 808-983-8394; davidk@kapiolani.org.

Author Contributions
Design concept of study: Kurahara, Grandinetti, Reddy, Tokuda, Langan, Tanabe, Yamamoto, Yamaga
Acquisition of data: Kurahara, Galario, Reddy, Tokuda, Langan, Tanabe, Yamamoto, Yamaga
Data analysis interpretation: Kurahara, Grandinetti, Galario, Yamaga
Manuscript draft: Kurahara, Galario, Reddy, Langan, Yamamoto, Yamaga
Statistical expertise: Kurahara, Grandinetti, Langan, Yamaga
Acquisition of funding: Kurahara, Reddy, Tokuda, Tanabe, Yamamoto
Administrative, technical, or material assistance: Kurahara, Galario, Reddy, Langan, Yamamoto, Yamaga
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Keywords

Acute Rheumatic Fever; Epidemiology; Ethnicity; Risk Factors

Introduction

Evaluating the relative contribution of socioeconomic, environmental, and genetic predisposing factors in acute rheumatic fever (ARF) is a challenging task. The knowledge that the prerequisite trigger is *Streptococcus pyogenes* is helpful,[1] but as in many infectious diseases in which humans are the only hosts, socioeconomic conditions play major roles in contributing to the risk of developing ARF.[2] The risk of developing ARF may be decreased considerably by prompt treatment of *S. pyogenes* infections, emphasizing the importance of proper medical care access, patient education, and compliance in preventing ARF.[2] An added complication, however, is that ARF is one of many autoimmune diseases that may express intriguing host influences. For example, in another autoimmune disease, juvenile rheumatoid arthritis (JRA), the highest incidence is found in Norway (22/100,000) whereas in Japan, the incidence is among the lowest (.8/100,000).[3] Recently, we also found that incidence of JRA was rare in individuals of Japanese and Filipino ethnicity and extremely rare in Samoans.[4] However, Samoans were at greatest risk for developing ARF in Hawaii.[4] Other areas of the Pacific region have very high prevalence rates of ARF.[5, 6]

To determine some of the factors for these prevalence rates, we analyzed Medicaid subjects who were enrolled in a pediatric cardiology clinic serving families in Hawaii. The socioeconomic conditions of this group were expected to be relatively homogeneous, lower than the average family in Hawaii but not as impoverished as in developing countries, where overwhelming disease, malnutrition, inadequate health care, and immunocompromised status may mask more subtle host factors. Hawaii offers a unique environment in which to institute this study because of its multiethnic population, nearly universal healthcare, mild climate, and acute awareness of the high ARF incidence. Questionnaires were administered to two groups, those diagnosed with ARF and those with other heart conditions.

Materials and Methods

Subject Population

Consecutive ARF case-patients and congenital heart disease cohort control-patients enrolled in the pediatric cardiology clinic were recruited at Kapiolani Medical Center for Women and Children, which is the only pediatric tertiary-care hospital in Hawaii. Subjects were divided into the case group, who had been diagnosed with ARF using the modified Jones criteria by one of two pediatric rheumatologists,[7] or the control group with non-ARF heart conditions (primarily congenital in nature). Identical surveys for both groups were administered by using a structured interview process investigating economic, living, and educational conditions of the subject's family during the study period of 1998–2001. A detailed assessment was undertaken by determining the ethnicity of both the parents and grandparents of each subject. This study and questionnaire received approval from the pediatric hospital's institutional review board.

Statistical Analysis

Chi-square analysis was used to assess significance of specific risk factors between the two groups. Multiple logistic regression was then used to calculate odds ratios for ARF among this multiethnic population. Odds ratios were calculated by taking the exponential of the logistic regression function. Confidence intervals were estimated and presented to illustrate the

precision of the estimated odd ratios. Risk factors determined to be statistically significant by chi-square analysis were added incrementally to the multiple logistic models in order to assess the role of sociodemographic risk factors in explaining the previously reported ethnic disparities in ARF incidence.

Results

Subjects diagnosed with ARF (*n*=26) and those with other heart conditions (*n*=4l) were compared with each other and with the Hawaii population at large, based on the 2000 Census data (Table 1). The mean age in the ARF group was significantly higher than in the non-ARF group (*P*=.002), but that was to be expected since ARF is an acquired disease whereas most of the other heart conditions were congenital and would be diagnosed at a younger age. The percentage of males in both groups was similar and higher than that found in the rest of the Hawaiian population.

Because the clinic services individuals who qualify for Medicaid, the socioeconomic conditions were expected to be relatively homogeneous. These services were available only to those children who now reside in Hawaii, and therefore general environmental influences were similar between the two groups. Compared with the Hawaii 2000 Census data, both groups had much higher percentage of those households with an annual income <$25,000 per year (Table 1), and they were not significantly different from one another. The number of families in this low-income bracket may be even higher in the pediatric cardiology clinic, since the annual income of the household was determined whereas the census data provided only family annual incomes. The ARF group compared with the non-ARF group had a slightly greater household size (7.3 vs 5.5, respectively) and number of children (4.1 vs 3.0, respectively). Ownership was similar in both groups and not substantially different from the average family in Hawaii. However, having multiple families or family members of different generations living in a household was probably more common when finances were limited. Little difference was seen in the percentages of parents with high school diplomas when compared with the Hawaiian population.

The most marked difference between the two groups was found when ethnicity was analyzed (Table 2). Because of the limited sample size, all individuals identified as being ≥50% Polynesian were grouped. These included individuals with mixed Polynesian ancestry and those who reported only 50% Polynesian background. A detailed listing of different Polynesians is shown. Of the ARF patients, 54% were Polynesians while only 20% of the control group fell into this category (*P*<.05). In the ARF group were fewer individuals identified as Asian than in the non-ARF group. The ARF group had none identified as Caucasian. The ARF group also had fewer individuals with ≥3 ethnicities when compared to the non-ARF group. If the mixed (≥3 ethnicities) category was excluded from the calculations, however, the percentage of Polynesians in the ARF group would be 63.6% (14/22) and in non ARF group would be 25.9% (7/27), still showing a large percentage of Polynesians with ARF.

The level of risk for developing ARF was then calculated by using odds ratios (Table 3) with a multiple logistic regression model. Polynesians, when compared with all other ethnicities, revealed an odds ratio of 4.80 for developing ARF (P<.011). This factor did not change appreciably when household size, sex, and place of residence was included (data not shown) but did increase to 6.53 when number of children in the household was included.

Discussion

Many studies have established that socioeconomic conditions play a critical role in determining the risk for ARF, especially in developing countries. The fact that early attention to pharyngitis

coupled with compliance to antibiotic usage can greatly reduce the risk for ARF has been well documented by the declining rate of the incidence of ARF in industrialized countries.[2] Assessing the host's contribution to ARF is difficult, but we decided to study a population of children whose families qualified for Medicaid. The pediatric cardiology clinic cohort offered unique advantages because although all individuals were in the lower socioeconomic scale, they were not living in extreme poverty, as might be found in developing countries. Impoverished individuals may suffer from overwhelming disease burdens, malnutrition, and a lack of basic health care, and thus, more subtle host factors that contribute to ARF risks may be masked. In addition, based on high school graduation level, families attending the pediatric cardiology clinic attained a similar educational level as the state average. Although no direct evidence is available, the Samoan community, in general, is probably better educated about their risk for ARF because it has been noted to be high for a number of years in multiple publications,[5, 8–10] and local physicians are well aware of the increased risk of ARF among Pacific Islanders.

These studies are unique because although families making up the pediatric cardiac clinic patient population are of similar socioeconomic levels, they are ethnically diverse, which allows us to simultaneously evaluate a number of different ethnicities. However, classification of an individual's ethnicity is difficult. In previous studies, families have self-reported the child's predominant ethnicity. Since the revival of Hawaiian culture in the 1960s–70s, there is a tendency to over-report Hawaiian ancestry. Thus, a detailed assessment had to be undertaken to determine the ethnicity of both the parents and grandparents of each subject. The problem of how to classify individuals who are 50% of two ethnicities has no ideal solution. We did not want to count any individual twice even though they could technically fit into two different ethnic categories. We decided to consider these few individuals first as Polynesians (n=1), then Micronesians (n=2), Asians (n=3), and lastly Caucasians (n=1) but even if these individuals were excluded or were reclassified, the overall conclusions that those who were Polynesians were at high risk would still be valid because the number of individuals in the 50% category is low. The other alternative was to count these individuals as .5 in their respective ethnic group. Again, the overall conclusions would not be affected by this calculation.

Of those studied, the only condition that showed a difference between the ARF and non-ARF group was household size and the number of children living in the household. Families with a child with congenital heart disease may have been reluctant to have more children and thus have a smaller family. However, adjusting for the household size did not change the odds ratio for developing ARF in Polynesians (Table 3). Some of these families who had a child with congenital heart disease may have had subsequent children develop ARF, but this occurrence is difficult to evaluate. One way to study this possibility is by studying the birth order of the children in these families, which is being investigated. Not surprisingly, however, the number of children in the household did increase the risk reflecting the need for group A streptococcus (GAS) infection as the initiating trigger. This finding points to the fact that the number of adults in a household is not as important as the number of children in spreading respiratory disease. One possible reason for the increased incidence of ARF among Polynesians might be the presence of rheumatogenic strains of *S. pyogenes*. In Utah, the periodic outbreaks of ARF occur among middle-class Caucasians and are presumably due to rheumatogenic M18 isolates.[11] Relatively large outbreaks do not occur in Hawaii; rather, the incidence of ARF appears to be rather uniform from year to year. Preliminary results (Erdem G, et al, unpublished results) have not identified a single, predominant rheumatogenic strain, as occurs in Utah. Indeed, she has noted the presence of many unusual strains of GAS.[12] Hawaii's proximity to developing Pacific nations may lead to the introduction of streptococcal strains that are not commonly seen in the US mainland.[12] Many Pacific nations enjoy a rather simplified access to Hawaii through compacts with the United States.[13] Another possibility is that children could be carriers of rheumatogenic isolates. As in the Aboriginal population in Australia and the Maori in New

Zealand, these groups have high rates of pyoderma, which may offer another route of infection for ARF.[14]

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The finding that more children in the household enhances the risk of developing ARF suggests that other conditions, eg, those related to hygiene practices within the family, are important. This study did not address all environmental, social, and cultural practices that may influence disease spread. However, we argue that after removing major socioeconomic and educational factors, Pacific Islanders and Samoans, in particular, may have a genetically increased risk of ARF. Indeed in a short letter to the editor written in 1999, Steer et al[15] reported that the prevalence of rheumatic heart disease (RHD) in Samoa is the highest in the world. They obtained a prevalence of 77.8 per 1000 whereas the WHO study estimated the mean prevalence of RHD among children in developing countries as 2.2 per 1000. We contend that the risk for ARF among Polynesians is high even when such variables such as crowding, sex, and place of residence were included in the risk analysis (Table 3). These results contrast to those of Carapetis et al,[16] who suggest that the variation in ARF incidence between populations is due not to inherent genetic predisposition, but rather to exposure and treatment.

We conclude that complex genetic factors may exist that predispose Pacific Islanders to ARF. Host factors should be identified, as these will give valuable clues to others at risk who could be targeted for intensive preventive measures.

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Table 1

Socioeconomic and educational comparisons between ARF and non-ARF groups. Subjects were enrolled in a Medicaid-sponsored pediatric cardiology clinic (no. of subjects in parenthesis)*

Characteristics	ARF Group (*n*=26)	Non-ARF Group (*n*=41)	*P*value	Hawaii 2000 census (*n*=1.2 million)
Mean age in years	14.0 (26)	10.8 (41)	.002†	NA
% Male	62 (26)	56 (41)	.66‡	50 (1.2 million)
% Yearly income <$25,000	63.2 (19)	72.7 (33)	.54†	16.7 (289,012)
0–$1 4,999	15.8 (3)	42.4 (14)	.15§	7.9
$1 5,000–$24,999	47.3 (9)	30.3 (10)		8.8
$25,000–$39,999	26.3 (5)	12.1 (4)		57.8
$40,000–$74,999	10.5 (2)	15.2 (5)		
≥$75,000	0	0		34.3
Household size	7.3 (26)	5.5 (41)	.01†	2.9 (403,240)
No. children/house	4.1 (26)	3.0 (41)	.03†	NA
Number in subject's bedroom	1.4 (26)	1.7 (41)	.35†	NA
% In apartment	46.2 (25)	41.5 (41)	.34‡	39.4 (470,512)
% Home ownership	52.9 (26)	47.8 (39)	.2‡	56.5 (470,512)
% With high school diploma				84.6 (age 25+)
% of mothers	88.0 (25)	89.5 (38)	.9‡	NA
% of fathers	70.8 (24)	80.0 (35)	.42‡	NA

*No. of subjects varies with each characteristics because some did not answer all questions.

†*P* value determined by t test.

‡*P* value determined by chi-square likelihood ratio and compares all values in subcategory between ARF and non-ARF group.

§*P* value determined by test of logistic regression.

ARF=acute rheumatic fever; NA=not available.

Table 2

ARF and non-ARF subjects categorized by ethnicity. Percent of total calculated for each major category (no. of subjects in parentheses)

Ethnicity	% of ARF (*n*=26)	% of Non-ARF (*n*=40)	% in Hawaii from 2000 Census
≥50% Polynesian	53.8 (14)	17.5(7)	NA
>50% Samoan	319 (8)	59 (2)	1.3
>50% Hawaiian	12 (3)	89 (3).	6.6
>50% Tongan	4 (1)	3 (1)	<1.3
>50% Mixed Polynesian	(1)*	(1)†	NA
50% Polynesian	(1)‡	(0)	NA
≥50% Micronesian	15.4 (4)	12.5 (5)	NA
>50% Micronesian	(3)	(4)	<1.3
50% Micronesian	(1)§	(1)‖	NA
≥50% Asian	15.4 (4)	27.5 (11)	41.6
>50% Filipino	(3)	(5)	14.1
>50% Chinese or Korean	(1)	(1)	6.6
>50 % Mixed Asia	(0)	(2)¶	NA
50% Asian	(0)	(3)#	NA
≥50% Caucasian	0(0)	10.0 (4)	NA
>50% Caucasian	(0)	(3)	24.3
50% Caucasian	(0)	(1)**	NA
≥3 ethnicity; none ≥50%	15.4 (4)	32.5 (13)	NA
Total	100 (26)	100 (40)	

*Tongan/Hawaiian-Chinese.

†Samoan/Hawaiian-mixed.

‡Hawaiian/Caucasian.

§Micronesian/Filipino.

‖Micronesian/Korean.

¶Filipino/Asian, Filipino/Chinese.

#Korean/mix; Chinese/Caucasian, Japanese/Caucasian.

**Caucasian/Mixed.

ARF=acute rheumatic fever; NA=not available.

Table 3

Odds ratios for developing rheumatic fever among Polynesians adjusted for number of children per household

Model	Odds Ratio	95% Confidence Intervals	*P*
Polynesian vs all others	4.80	1.65–15.63	.011
Polynesian, # children in household	6.53	1.9–24.1	.022