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EPIDEMIOLOGICAL FEATURES OF *STRONGYLOIDES* INFECTION IN OKINAWA, JAPAN: COMPARATIVE STUDY WITH OTHER ENDEMIC AREAS

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Abstract: The epidemiological features of *Strongyloides stercoralis* infection in Okinawa, Japan, were studied by comparing with those in Thailand, Laos and Brazil. The prevalence rates of *Strongyloides* infection in the present study were 9.6% (133/1,380) in Okinawa, 47.6% (99/208) in Chiang Mai, Thailand, 23.8% (106/445) in Khammouane, Laos, and 12.0% (32/267) in Maceio, Brazil, respectively. The age inclination in aged subjects and sex dominance in males were significant features of *Strongyloides* infection in Okinawa, suggesting that new infection from the environment does not occur in present-day Okinawa. The epidemiological feature was considered to provide a favorable field to investigate therapeutic efficacy unaffected by reinfection from environment after treatment. Absence of helminth infection other than *Strongyloides* was an additional feature in Okinawa. The features may also be convenient to study host response and pathogenicity in the *Strongyloides* infection unaffected by concurrent infection with other helminths.

Key words: *Strongyloides stercoralis*, strongyloidiasis, epidemiology, Okinawa, Thailand, Laos, Brazil

INTRODUCTION

Strongyloides stercoralis is a nematode parasite of man with a high prevalence in many tropical and subtropical countries. A warm and moist climate is essential for its natural transmission, and man becomes typically infected through skin contact, by penetration of infective larvae developing in the soil. It has also been well known that the parasite can multiply within host by internal autoinfection. Due to the autoinfection, the parasite can survive for many years in its host and it is frequently imported in temperate regions without outside source of reinfection. The biological nature of the parasite influences not only the clinical manifestation of strongyloidiasis but also epidemiological feature in endemic and non-endemic areas.

Okinawa prefecture lies in the southernmost part of Japan and is the only prefecture located in subtropical

zone. Under the circumstance, the inhabitants in Okinawa have been suffering in the past from many important parasitic diseases, such as malaria and filariasis. However, these parasitic diseases have already been almost completely eradicated in recent years and only strongyloidiasis is currently highly prevalent in the prefecture. In the recent surveys, the mean prevalence rate was found to be as high as 10% among the inhabitants over 40 years old (Asato *et al.*, 1992). On the other hand, the prevalence in the young generation is extremely low, suggesting that new infection from the environment rarely occurs among inhabitants in present-day Okinawa and that presumably the majority (more than 90%) of cases are long-standing cases acquired the infection in childhood and persisted until adulthood (Sato *et al.*, 1986). Under the condition, epidemiological feature of strongyloidiasis in Okinawa is considered to be different from those of other endemic areas where *S.*

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stercoralis infection currently manifested among the inhabitants.

The purpose of the present study was to compare the epidemiological features of strongyloidiasis in Okinawa with those of endemic areas in Thailand, Laos and Brazil, where many parasitic infections are currently prevalent among the inhabitants.

MATERIALS AND METHODS

Survey Areas and Populations Examined:

Okinawa prefecture, also referred as to the Ryukyu Islands, consisted of about 60 small islands. One of the islands, Kume Island, located about 100 km east of Okinawa Island was selected as survey area in the present study. The similar surveys were also conducted in two countries of Southeast Asia and in a country of South America. In Southeast Asia, a village (Sanpatong village) in Chiang Mai province, northern Thailand, and two villages (Sisamsung and Phavang villages) in Khammouane province, southeast Laos, were selected as survey areas. These areas were located in similar tropical environment, however, socio-economic situation was much different among the areas. Sanpatong village was located in rural area in Chiang Mai province, however, infrastructure of the village was well developed. Although the two rural villages in Laos were self-sufficient in food, incomes of the villagers was very low. The two slums (Vila Brejal and Vila Aratu) in Maceio City, Alagoas State, northern Brazil, were selected as survey areas in South America. The slums were located in the city, health facility in the slums being poorly developed as compared with other areas in the city.

The surveys were carried out on November 1991 in

Chiang Mai (Thailand), on November 1993 in Okinawa (Japan), on October 1994 in Maceio (Brazil) and on September 1996 in Khammouane (Laos).

In Table 1, sex and age distributions of the subjects in the present study are shown. In Okinawa, all subjects were adults over 20 years old and more than 90% of them were occupied by the aged subjects over 40 years old. The age distribution pattern in Chiang Mai was similar to that in Okinawa although the aged subjects over 70 years old examined in the area were considerably few in the present survey. On the other hand, in Maceio and Khammouane, more than 50% of the subjects belonged to children and the young under 20 years. The average age (\pm SD) was 59.6 (\pm 13.4) in Okinawa, 47.9 (\pm 15.1) in Chiang Mai, 22.6 (\pm 16.7) in Maceio, and 25.5 (\pm 20.9) in Khammouane, respectively. Sex ratio of the subjects was almost the same in Chiang Mai and Khammouane but the number of female subjects was greater than that of males in Okinawa and Maceio.

Stool Examination:

The stool examinations were performed by fecal concentration (formalin-ether concentration), Harada-Mori fecal culture and an agar plate fecal culture methods. The last method was recently developed in Okinawa, in which fecal samples (about 3 g) were placed on the primary agar plate for bacterial culture and incubated at 28°C for 3 days (Arakaki *et al.*, 1988). After the incubation, the surface of the agar plate was examined carefully under a stereoscopic microscope to find out motile larvae that crawled out of the fecal mass on the agar plate. When found, the larvae were differentiated morphologically from those of hookworm and free-living *Rhabditis*. If the tracks left by the larvae were observed but no larvae were found on the agar

Table 1 Number of subjects examined in 4 survey areas

Area	Sex	No. subjects examined (by age group)									
		-9	10-	20-	30-	40-	50-	60-	70-	80-	Total
Okinawa (Japan)	Male	0	0	7	44	78	97	166	116	25	533
	Female	0	0	11	78	110	163	293	162	30	847
	Total	0	0	18	122	188	260	459	278	55	1,380
Chiang Mai (Thailand)	Male	0	2	13	24	13	15	28	8	0	103
	Female	0	0	11	31	13	19	26	5	0	105
	Total	0	2	24	55	26	34	54	13	0	208
Khammouane (Laos)	Male	67	55	18	25	17	23	16	6	2	229
	Female	73	31	33	22	25	19	12	1	0	216
	Total	140	86	51	47	42	42	28	7	2	445
Maceio (Brazil)	Male	24	47	10	6	4	4	4	2	0	101
	Female	34	40	39	20	19	8	5	1	0	166
	Total	58	87	49	26	23	12	9	3	0	267

Table 2 Prevalence of parasitic helminths among the subjects examined in 4 survey areas

	Okinawa (n = 1,380)	Chiang Mai (n = 208)	Khammouane (n = 445)	Maceio (n = 267)
No. positive for helminth infection	133 (9.6)	193 (92.8)	384 (86.3)	186 (69.7)
Type of infection:				
<i>Strongyloides stercoralis</i>	133 (9.6)	99 (47.6)	106 (23.8)	32 (12.0)
<i>Ascaris lumbricoides</i>	0 (0)	0 (0)	193 (43.4)	111 (41.6)
<i>Trichuris trichiura</i>	0 (0)	7 (3.4)	112 (25.2)	118 (44.2)
Hookworm*	0 (0)	50 (24.0)	164 (36.9)	77 (28.8)
<i>Enterobius vermicularis</i>	0 (0)	6 (2.9)	10 (2.2)	2 (0.7)
<i>Opisthorchis viverrini</i>	0 (0)	162 (77.9)	243 (54.6)	0 (0)
<i>Schistosoma mansoni</i>	0 (0)	0 (0)	0 (0)	71 (26.6)
<i>Fasciola hepatica</i>	0 (0)	0 (0)	2 (0.4)	0 (0)
<i>Taenia</i> sp.	0 (0)	4 (1.9)	17 (3.8)	0 (0)
<i>Hymenolepis nana</i>	0 (0)	0 (0)	0 (0)	10 (3.7)

* The species did not identified in the present study.

surface, the presence of larvae was assumed and further appropriate examinations (i.e. fecal concentration and/or Harada-Mori fecal culture) were carried out for a correct diagnosis. For the above stool examination, two stool samples were collected from each subject on 2 different days.

Statistics:

The data were analyzed by the χ^2 (chi-square) test to determine significance level among the subject groups. A *P* value for smaller probability than 0.05 and 0.01 was considered to be significant and highly significant, respectively.

RESULTS

In Table 2, the prevalence rates of helminth parasites among the subjects in the present surveys are shown. About 70% or more of the subjects were found to be positive for one or more helminth parasites in the

survey areas except in Okinawa. *Ascaris lumbricoides* and *Trichuris trichiura* were dominant infection in Maceio, Brazil. While in Chiang Mai and Khammouane, Southeast Asia, liver fluke, *Opisthorchis viverrini*, showed as the highest prevalence rate as 77.9% in Chiang Mai and 54.6% in Khammouane. *A. lumbricoides*, *T. trichiura* and hookworm, although the species did not identified in the present study, were also common parasites among the subjects in Khammouane, but *A. lumbricoides* and *T. trichiura* infections were rare in Chiang Mai. A total of 133 subjects (9.6%) were confirmed harboring parasite infection in Okinawa, but *Strongyloides* was the only helminth species detected among the subjects. The highest infection rate of *S. stercoralis* was obtained in Chiang Mai, showing 47.6%, which was followed by 23.8% in Khammouane, 12.0 in Maceio and 9.6% in Okinawa, respectively. Hookworm infection was higher in rate than that of *S. stercoralis* in Maceio and Khammouane, but was only about a half of that of *S. stercoralis* in Chiang Mai.

Table 3 Prevalence of *Strongyloides* infection by age group in 4 survey areas

Age group	Okinawa	Chiang Mai	Khammouane	Maceio
-9	—	—	21/140 (15.0)	5/58 (8.6)
10-	—	1/2 (50.0)	21/86 (24.4)	13/87 (14.9)
20-	0/18 (0)	9/24 (37.5)	16/51 (31.4)	5/49 (10.2)
30-	1/122 (0.8)	26/55 (47.3)	15/47 (31.9)	3/26 (11.5)
40-	4/188 (2.1)	12/26 (46.2)	9/42 (21.4)	1/23 (4.3)
50-	18/260 (6.9)	17/34 (50.0)	13/42 (31.0)	1/12 (8.3)
60-	55/459 (12.0)	25/54 (46.3)	9/28 (32.1)	4/9 (44.4)
70-	46/278 (16.5)	9/13 (69.2)	2/7 (28.6)	0/3 (0)
80-	9/55 (16.4)	—	0/2 (0)	—
Total	133/1,380 (9.6)	99/208 (47.6)	106/445 (23.8)	32/267 (12.0)

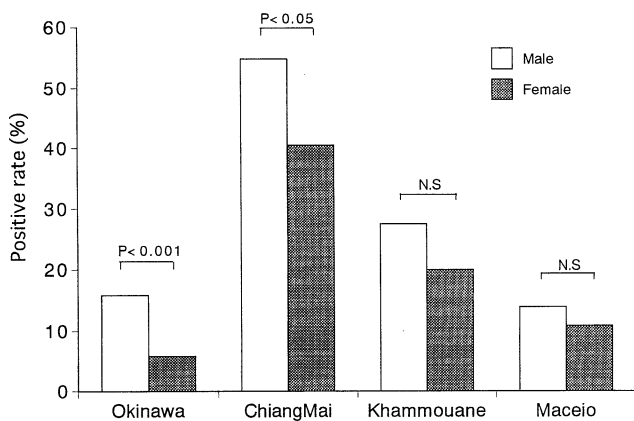


Figure 1 Comparison of positive rate of *Strongyloides* between male and female subjects in 4 survey areas.

The positive rates of *S. stercoralis* by age groups of the subjects are compared among the 4 survey areas in Table 3. In Okinawa, more than 95% of the positive persons were aged subjects over 50 years old, although the number of younger subjects were very few in the present survey. The positive rate increased steadily with the age of the subjects in Okinawa. On the other hand, *Strongyloides* infection was highly confirmed in younger subjects in the other areas; the mean positive rate in the subjects under 20 years old was more than 10% in Khammouane (18.6%) and Maceio (12.4%). Increasing tendency of the *Strongyloides* positive rate with subject's age was not clear in the areas in South-east Asia and South America.

Fig. 1 shows sex difference of the positive rate in each area. The positive rate in males was consistently higher than that in female subjects. Especially in Okinawa, there was a great difference in positive rate between males and females; the rate in male subjects was three-times higher than that in females, this difference being highly significant ($P < 0.001$). On the other hand, sex difference of positive rate was not so significant in the other areas, although male positive rate was significantly higher in Chiang Mai ($P < 0.05$).

DISCUSSION

There have been several reports on the prevalence of *Strongyloides* infection in the countries surveyed here; the positive rate reported ranged from 6% to 24% in Thailand (Yamaguchi *et al.*, 1982; Bayajian, 1992; Sukhavat, 1994), from 3% to 13% in Laos (Sormmani *et al.*, 1974; Chai *et al.*, 1998), and from 6% to 40% in Brazil (Dias, 1968; Asami, 1970; Marzochi *et al.*, 1978), respectively. These results on prevalence of *Strongyloides*

infection, however, may extremely underestimate the true prevalence because of low efficacy of detection methods used in the past. In the previous study in which strongyloidiasis cases were reinfection-checked without treatment several months later, the conventional methods of fecal examination, such as direct smear, fecal concentration and Harada-Mori fecal culture methods, were only 15-24% effective in reconfirming the infection (Sato *et al.*, 1995). On the other hand, an agar plate culture method, a newly developed fecal culture method, was confirmed to be much effective for detection of chronic, low-level infection with *Strongyloides*. In the present survey, therefore, the agar plate culture method was applied. The results indicate that *Strongyloides* infection was a major human public health problem in the survey areas. Especially in Chiang Mai, Thailand, positive rate as high as 47% was estimated among the subjects examined. The positive rate of 23% in Khammouane, Laos, was also significantly higher than those reported in the past in this country. On the other hand, the positive rate in Okinawa, Japan, was greatly low as compared to those in the other countries. One of the characteristic epidemiological features of strongyloidiasis in Okinawa, however, was observed in the age inclination of *Strongyloides* positive persons (Sato, 1986; Sato *et al.*, 1990). Namely, most of *Strongyloides* positive people (more than 95%) were included in middle to upper age groups over 40 years old in Okinawa. Only one positive case in 140 residents was found under the age of 40. Unfortunately, the subjects under 20 years old were not examined in this survey. However, it was reported that no case of *Strongyloides* infection was found in 205 subjects under 20 years old in Okinawa (Asato *et al.*, 1983). Whereas many young subjects were found infected with *Strongyloides* in the survey areas in Southeast Asia and South America. The extremely low incidence in the young generation in Okinawa suggests that the inhabitants have no opportunity to acquire new infection from environment in the island recently. From the epidemiological feature, Okinawa seemed to provide favorable field to investigate therapeutic efficacy of anthelmintics, because the follow-up examination can not be affected by reinfection-infection after treatment. Although there have been many reports on therapeutic effect on strongyloidiasis, the results obtained were considerably different from each other even in the case in which same drug was used in the similar regimen. The inconsistency may be attributed to the several factors. The most effective factor may be difference of applied methods in the follow-up fecal examination. Another factor affect-

ting therapeutic efficacy may be the duration of follow-up examination after the treatment. The *Strongyloides* infection has been known to relapse frequently in several months after seemingly successful treatment. The relapses due to unsuccessful treatment can not be distinguished from reinfection from environment during the follow-up examination. On the basis of the above epidemiological background, the authors could examine the exact efficacy of several anthelmintics for as long as a year after treatment without consideration of reinfection during the follow-up period (Sato *et al.*, 1992; Takara *et al.*, 1992; Toma *et al.*, 1993).

In Okinawa, the infections with soil-transmitted nematodes were highly prevalent until 1950's, but many of them have already been controlled. Ascariasis and trichuriasis were very rare in 1960's. Hookworm infection was still observed in more than 30% of Okinawan people in 1960's, but the prevalence rate also decreased extremely to less than 0.1% in the following two decades (Asato *et al.*, 1990). These changes are considered to be caused by the appropriate control measures, socio-economical and agricultural improvements. Apparently, most of *Strongyloides* carriers are also considered to acquire the infection during and/or immediately after the World War II when the standard of living was very low and human excrements were used as fertilizer. Long term of *Strongyloides* infection among aged people without new infection from environment may be due to internal autoinfection of the parasite. Therefore, the other epidemiological feature of strongyloidiasis in Okinawa seems to be that there is no concurrent infection with other helminths occurred among the people with *Strongyloides* infection. Actually, no intestinal helminth infection other than *Strongyloides* was observed in Okinawa in the present study, while helminth infections such as ascariasis and opisthorchiasis were concurrently detected in many subjects positive for *Strongyloides* infection in the other survey areas. This epidemiological feature may also be convenient for the investigation of immune response and clinical features of strongyloidiasis unaffected by concurrent infection with other helminth infection.

Finally, significant dominance of male subjects in prevalence of *Strongyloides* infection in Okinawa was also an epidemiological feature different from those in the other areas. In general, it has been recognized that males were more commonly infected with *S. stercoralis* than females (Soroczan, 1976; Scaglia *et al.*, 1984; Walzer *et al.*, 1982). The infection rate in males was 3 times higher than that in females in Okinawa in the present study. One of the reasons for the high preva-

lence in males may be that males have had frequent opportunities for the infection in their life style. It is also possible to consider that males were more susceptible to the infection than females, as known in experimental infection model with *S. ratti* and animal hosts (Katz, 1961; Dawkins *et al.*, 1980). In the previous study, the authors also demonstrated that the efficacy of treatment with various anthelmintics was significantly low in male subjects as compared to that in females (Kobayashi *et al.*, 1996). Due to the significant resistance to treatment, male subjects harbor the parasite for many years, and the obstinacy in males might result in a significant accumulation of male subject positive for *Strongyloides* under the improved sanitary condition in which persons do not acquire new infection from environment.

In conclusion, *Strongyloides* infection in Okinawa showed a significant age inclination and sex dominance. These epidemiological features may be derived from an environmental situation in which new infection from outside did not occur for many years, and also from the unique property of the parasite to maintain the infection for several decade years beyond the life span of the parasite. These epidemiological features in Okinawa are considered to provide many favorable conditions to investigate the parasite and its disease.

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