



Cellular Immunity and Resistance to Schistosomiasis in the Philippines (CRISTAL)

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ABSTRACT

- Schistosomiasis remains a major public health problem in the Philippines, with two million Filipinos infected and 12 million of the population at risk of infection [1]. Very high prevalence rates have been recently reported in a number of endemic provinces in the Philippines.
- Schistosoma japonicum* (*Sj*) is the sole schistosome species in the Philippines. The disease is caused by other species in other countries: *S. mansoni*, *S. mekongi*, *S. intercalatum*, and *S. haematobium* [2].
- Acquired by water contact, through the freshwater snail intermediate host (*Oncomelania hupensis quadrasi*). Adult worms establish in the mesenteric veins, where the female worm produces eggs that are subsequently trapped in the liver and induce potent granulomatous inflammatory responses, leading to hepatosplenomegaly and fibrosis.
- The use of Praziquantel has significantly reduced mortality and severe end-organ morbidity, with most countries adopting annual mass drug administration (MDA) [2].
- However, complicating the situation is the fact that *Sj* is a zoonosis, and can infect a wide array of animals such as dogs [3], wild rats, cattle, and in particular, water buffaloes [4].
- Thus, it is evident that the incidence, prevalence, and morbidity of the disease will not be controlled by MDA alone and there is a need for innovative cost-effective strategies, such as vaccines, to control schistosomiasis in the long term.



- Main Objective:** To assess the role of immune cells in resistance or susceptibility to *Schistosomiasis japonicum* reinfection in the Philippines before and after treatment with Praziquantel.
- Schistosomiasis infection status 16 months following treatment was determined by Kato-Katz examination of stool. The intensity of infection (continuous eggs per gram of stool) was also assessed. These outcomes will be associated with various immune parameters.

METHODOLOGY

The study design is a longitudinal, observational study. Three hundred forty six individuals ages 10 to 50 years old and infected with schistosomiasis were enrolled into the study. Another set of 60 Schisto-negative healthy individuals who have never travelled to a schistosomiasis-endemic area were enrolled to serve as normal controls.

- (1) Community preparation, courtesy calls, and barangay assembly for the orientation of the study



- (2) GPS mapping of all households, house tagging, and conduct of household census interview via tablets for paperless entry



- (3) Consent signing activity of target participants for stool screening



- (4) Stool screening using three stool Kato-Katz technique for all consenting villagers 10-50 years old; a barcoded sample tracking database was used to monitor submission compliance



- (5) Schisto-positive consented participants were invited to the satellite laboratory for Study Visit 1 activities: liver ultrasound, physical examination, Praziquantel treatment, blood collection, PBMC isolation, water contact activity interview, urine CCA test, nutritional measurements, and main study consent signing; with majority of the activities recorded on a networked tablet database





- (6) Follow up visit, 4 weeks after Praziquantel treatment for: socio-economic status interview, phlebotomy work, water contact activity interview, urine CCA test, Albendazole treatment; with majority of the activities recorded on a networked tablet database

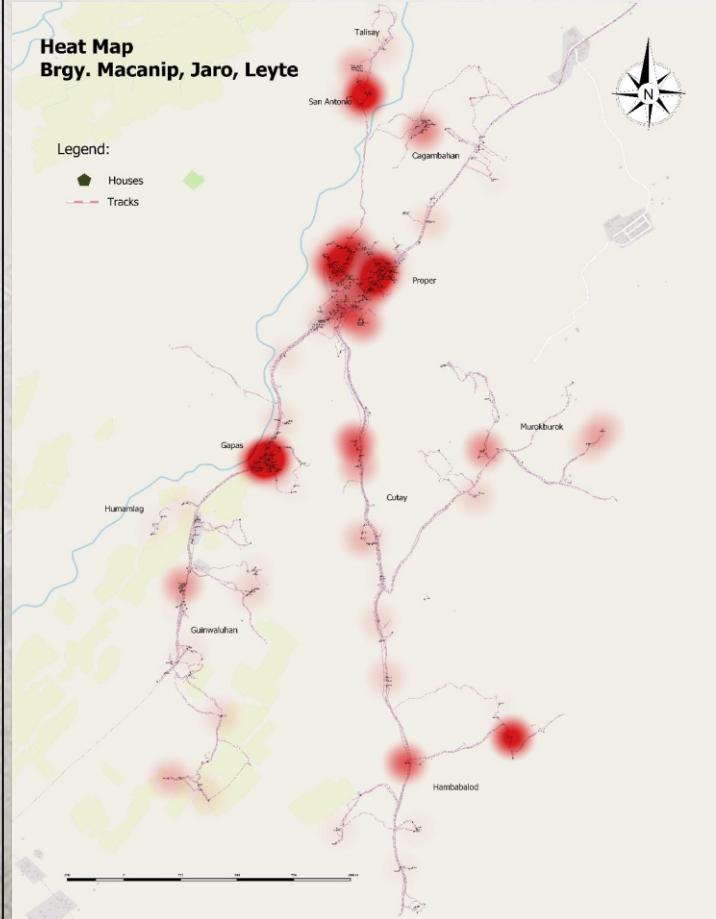


- (7) Close out visit, 16 months after study initiation for: liver ultrasound, physical examination, Praziquantel treatment, phlebotomy work, water contact activity interview, urine CCA test, pregnancy test, nutritional measurements; with majority of the activities recorded on a networked tablet database

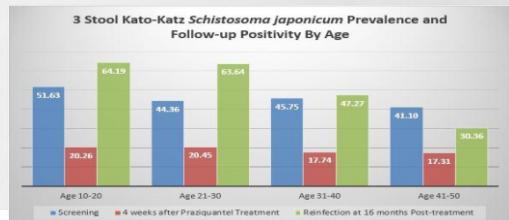


RESULTS

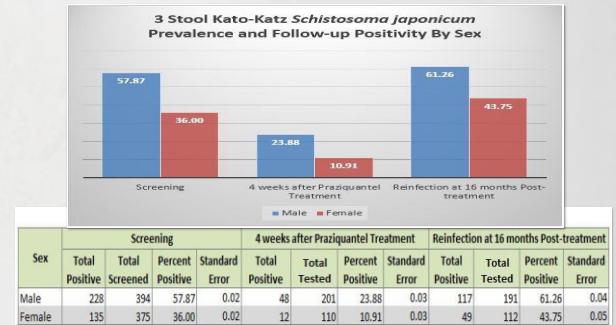
- Heat map produced from stool screening data showing *Schistosoma japonicum* hotspots:



Sito	Three-Stool Kato-Katz <i>Schistosoma japonicum</i> Prevalence by Sitio				4 weeks after Praziquantel Treatment				Reinfection at 16 months Post-treatment			
	Total Positive	Total Screened	Percent Positive	Standard Error	Total Positive	Total Tested	Percent Positive	Standard Error	Total Positive	Total Tested	Percent Positive	Standard Error
Cagambahan	21	45	46.67	0.07	4	18	22.22	0.10	8	19	42.11	0.11
Cutay	27	50	54.00	0.07	9	24	37.50	0.10	15	24	62.50	0.10
Gapas	50	112	44.64	0.05	10	45	22.22	0.06	24	44	54.55	0.08
Guinwaluhan	17	26	65.38	0.09	4	16	25.00	0.11	13	17	76.47	0.10
Hambalod	29	54	53.70	0.07	6	26	23.08	0.08	11	26	42.31	0.10
Humlag	29	73	39.73	0.06	4	21	19.05	0.09	12	22	54.55	0.11
Murckburuk	16	27	59.26	0.03	4	14	28.57	0.12	11	16	68.75	0.12
Proper Zone 1	81	148	52.90	0.05	4	49	8.16	0.04	27	49	55.31	0.07
Proper Zone 2	68	143	47.33	0.04	11	56	19.64	0.05	20	51	39.22	0.07
Proper Zone 3	21	86	24.42	0.05	2	20	10.00	0.07	8	15	40.00	0.13
San Antonio	7	11	63.64	0.15	1	5	20.00	0.18	1	5	20.00	0.18
Talisay	17	28	60.71	0.09	1	17	5.88	0.06	8	15	53.33	0.13



Age Grp (Years)	Screening				4 weeks after Praziquantel Treatment				Reinfection at 16 months Post-treatment			
	Total Positive	Total Screened	Percent Positive	Standard Error	Total Positive	Total Tested	Percent Positive	Standard Error	Total Positive	Total Tested	Percent Positive	Standard Error
10 to 20	174	337	51.63	0.03	31	153	20.26	0.03	95	148	64.19	0.04
21 to 30	59	133	44.36	0.04	9	44	20.45	0.06	28	44	63.64	0.07
31 to 40	70	153	45.75	0.04	11	62	17.74	0.05	26	55	47.27	0.07
41 to 50	60	146	41.10	0.04	9	52	17.31	0.05	17	56	30.36	0.06



Sex	Screening				4 weeks after Praziquantel Treatment				Reinfection at 16 months Post-treatment			
	Total Positive	Total Screened	Percent Positive	Standard Error	Total Positive	Total Tested	Percent Positive	Standard Error	Total Positive	Total Tested	Percent Positive	Standard Error
Male	228	394	57.87	0.02	48	201	23.88	0.03	117	191	61.26	0.04
Female	135	375	36.00	0.02	12	110	10.91	0.03	49	112	43.75	0.05



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