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ANALYZING THE PREVALENCE AND INCIDENCE OF TYPHOID FEVER, MALARIA AND THEIR COINFECTIONS IN FEBRILE SUBJECTS OF URBAN INDIA: A CROSS-SECTIONAL STUDY

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Abstract

Background: Typhoid fever and malaria remain major public health threats in developing countries and tropical regions. In endemic regions, people are at a very high risk of developing both the disease at the same time with significant overlapping of associated symptoms and signs

Aims: The present cross-sectional clinical trial was undertaken to assess the prevalence, typhoid fever, malaria, and their coinfections in urban Indian subjects with fever.

Materials and Methods: In 180 subjects, demographic data and clinical features of all the study subjects were recorded. For assessing typhoid fever, a slide agglutination test was done using H (flagellar) and O (somatic) antigen kits for S.typhi. The collected data were subjected to statistical evaluation for results formulation.

Results: Total positive malaria cases were 37.22% (n=67). Among 67 positive cases, 43.28% (n=29) were seen to have P.vivax, 40.29% (n=27) had P. Falciparum and mixed infection were seen in 16.41% (n=11) subjects. Typhoid and malaria coinfection was seen in 6.66% (n=12) of study subjects. On correlating typhoid fever, malaria, and coinfections with demographic characteristics and clinical characteristics in the study subjects, it was seen that the age groups of 2 years to 10 years were associated with malaria, and the association was statistically significant with p=0.03.

Conclusion: Within its limitations, the present study concludes that the coinfections are common owing to the high prevalence and overlapping symptoms of malaria and typhoid fever. Poor hand washing habits are associated with typhoid fever significantly.

Keywords: Coinfections, Malaria, P. Falciparum, S. typhi, Typhoid fever

Introduction:

Malaria is a commonly encountered disease seen in subjects with fever globally. However, Malaria is more prevalent in developing countries like India, and is caused by single or more species of Plasmodium including Plasmodium ovale, Plasmodium knowlesi, Plasmodium vivax, Plasmodium malariae, and Plasmodium falciparum. WHO (World Health Organization) suggests 300-500 million cases of malaria every year. Total Malaria burden is contributed by Southeast Asia with 2.5 million cases alone, where 76% of these cases are from India only. Approximately 50 percent of the World's population is at risk of developing malaria. Malaria is also associated with significant morbidity with the largest death rate reported in the sub-Saharan region of Africa. As per the 2011 World malaria report, approximately 216 million malaria cases were reported globally in the year 2010 with nearly 655,000 deaths.[1]

Concerning India, malaria epidemiology is complex owing to various ethnicities, geographical variations, and different species of transmitting vectors existing in India. A total of 9 species of Plasmodium are seen in different Indian tropical regions, were widely prevalent, principle vectors, and commonly seen Plasmodium species in urban India are P. malariae, P. falciparum, Anopheles culicifacies, and P. vivax, whereas in urban population, An. stephensi is primarily seen. Secondary vectors of malaria seen widely are An. Varuna and An. Annularis. Species found in malaria subjects of Andaman and Nicobar islands is An. sun-daicus, whereas An. Dirus, An. nivipes, An. Philippinensis, and An. minimus is commonly seen in northeast India. The vector associated with malaria in foothills and hills is An. Fluviatilis.[2]

After independence in 1947, India reported 7.5 million malaria cases in 330 million subjects, whereas, in 1964, these cases dropped to 100,000 malaria cases, owing to successful eradication programs implemented. However, a marked increase was again reported in India where 6.4 million cases were reported in 1976 with the associated increase in P. falciparum species. P. Falciparum species is

recently reported in approximately 50% of malaria cases in India.[3]

Typhoid fever also known as enteric fever describes a prolonged fever (febrile state) caused by different serotypes of Salmonella species. Typhoid fever is commonly caused by Salmonella enterica serotype paratyphi (including S. paratyphi A, B, and C) and by S. Typhi (Salmonella enterica serotype Typhi), where S.typhi is the most common serotype causing typhoid fever. Typhoid is also more prevalent in developing countries like India and is transmitted by poor handwashing habits, improper human excreta disposal, using untreated water, and/or ill-equipped latrine and associated water supply.[4]

Typhoid fever and malaria remain major public health threats in developing countries and tropical regions. Despite different etiologic factors including gram-negative bacilli, protozoa, and microorganisms respectively, they share common clinical features including fever state. In endemic regions, people are at a very high risk of developing both the disease at the same time with significant overlapping of associated symptoms and signs.[5]

Owing to overlapping signs, symptoms, and clinical features, there is a high probability of wrong diagnosis and treatment of subjects with prolonged fever. Hence, it is vital to have a reliable and accurate diagnostic tool, which allows accurate diagnosis and treatment to reduce mortality, morbidity, drug wastage, and/or drug abuse. Despite high prevalence and mortality, coinfection, and malaria, and typhoid are less researched concerning their prevalence.[6] Hence, the present cross-sectional clinical trial was undertaken to assess the prevalence, typhoid fever, malaria, and their coinfections in urban Indian subjects with fever.

Materials and Methods

The present cross-sectional clinical trial was undertaken to assess the prevalence, typhoid fever, malaria, and their coinfections in urban Indian subjects with fever. The study included a total of 180 subjects, both males and females within the age group of 2 years to 78 years with a mean age of 36.7 years. The inclusion criteria were the subjects with the fever suspected as typhoid fever or malaria, the subjects who did not take any antibiotics or antimalarial drug within the last 2 weeks, and the subjects who were willing to participate in the study. The exclusion criteria were the febrile subjects who had associates systemic diseases, subjects having a confirmatory diagnosis of tuberculosis, subjects who have taken antibiotics/anti-malarial drugs within the last 2 weeks, and the subjects not willing to participate in the study.

After final inclusion, informed consent was taken from all the study subjects followed by detailed history recording including demographic data. After demographic data, the clinical features of all the study subjects were recorded. After recording all the parameters, blood collection was done for laboratory investigations to diagnose the underlying disease. 10 ml intravenous blood was collected from the adult subjects, whereas, 3-4 ml blood was collected from the children. To isolate S.paratyphi and S.typhi, 7ml blood from the adults was inoculated to 45ml Brain Heart Infusion Broth, and 2ml children blood was added to 9ml broth.

For assessing typhoid fever, a slide agglutination test was done using H (flagellar) and O (somatic) antigen kits for S.typhi. Concerning malaria, both thin and thick blood films were made and assessed by laboratory technicians, and the results were reported. Cross-assessment of the results was done by other experienced in the field, not aware of the previously reported results, and the final results were noted. In reactive samples, antibody titration was done, was cut-off value was taken at a titer of $\geq$ 1: 80 against H and O S.typhi antigen based on instructions by the kit manufacturer.

The collected data were subjected to the statistical evaluation using SPSS software version 21.0, 2012, Armonk, NY, ANOVA, and t-test. The results were formulated keeping the level of significance at $p<0.05$.

Results

The study included 180 subjects both males and females within the age group of 2 years to 78 years with a mean age of 36.7 years. The demographic and disease characteristics of the study subjects are described in Table 1. It was seen that in age groups of 2-10, 11-25, 26-45, and ≥46 years, there were 17.77% (n=32), 42.22% (n=76), 32.7% (n=59), and 7.2% (n=13) study subjects. Concerning gender, there were 57.7% (n=104) males and 42.2% (n=76) females in the present study. 83.8% (n=151) study subjects were unemployed, whereas, 16.1% (n=29) subjects were employed. For educational status, there were 62.2% (n=112), 35% (n=63), and 2.7% (n=5) subjects who were illiterate, with undergraduate/lesser education, and with postgraduate or higher education.

For typhoid assessment, Widal test showed no agglutination, 1:20, 1:40, 1:80, 1:160, and ≥1:320 agglutination in 7.54% (n=4), 11.32% (n=6), 16.98% (n=9), 22.6% (n=12), 28.3% (n=15), and 9.43% (n=5) of study subjects was seen (Table1).

For prevalence of malaria, total positive cases were 37.22% (n=67). Among 67 positive cases, 43.28% (n=29) were seen to have P.vivax, 40.29% (n=27) had P. Falciparum, and mixed infection was seen in 16.41% (n=11) subjects (Table 1, Graph 1).

Typhoid and malaria coinfection was seen in 6.66% (n=12) study subjects, where 25% (n=3) had P. vivax infection, 58.3% (n=7) had P. Falciparum infection, and 16.6% (n=2) had mixed infection by both.

On correlating typhoid fever, malaria, and coinfections with demographic characteristics and clinical characteristics in the study subjects, it was seen that the age groups of 2 years to 10 years were associated with malaria, and the association was statistically significant with p=0.03. No

statistically significant correlation was seen of malaria or typhoid fever with gender, employment status, and educational status with p>0.05 as shown in Table 2.

Similarly, on correlating the clinical characteristics with typhoid fever or malaria, no significant correlation was seen between typhoid fever and malaria with headache, fever, vomiting, joint pain, fatigue, chills, diarrhea, nausea, and constipation with respective p-values of p>0.05 as depicted in Table 3.

Poor hand washing habits were significantly associated with typhoid fever (p=0.01), whereas, water source, toilet habits, and uncooked food intake were not associated significantly with typhoid fever with respective p values of 0.34, 0.89, and 0.55 respectively. Concerning malaria-related factors, travel history and usage of the net at bed were not associated with malaria significantly, where respective p-values were 0.93 and 0.24 as shown in Table 4.

Table 1: Demographic and disease characteristics in the study subjects

Characteristics	Subgroups	%	N
Age Range (years)	2-10	17.77	32
	11-25	42.22	76
	26-45	32.7	59
	≥46	7.2	13
Gender	Males	57.7	104
	Females	42.2	76
Employment Status	Unemployed/students	83.8	151
	Employed	16.1	29
Educational Status	Illiterate	62.2	112
	Undergraduate/Lesser	35	63
	Postgraduate or more	2.7	5
Widal-test (Typhoid Prevalence) (n=53)	No agglutination	7.54	4
	1:20	11.32	6
	1:40	16.98	9
	1:80	22.6	12
	1:160	28.3	15
	≥1:320	9.43	5
Malaria Prevalence	Total Positive cases	37.22	67
	P. vivax	43.28	29
	P. Falciparum	40.29	27
	Both	16.41	11

Table 2: Association of typhoid fever, malaria, and coinfections with demographic characteristics in the study subjects

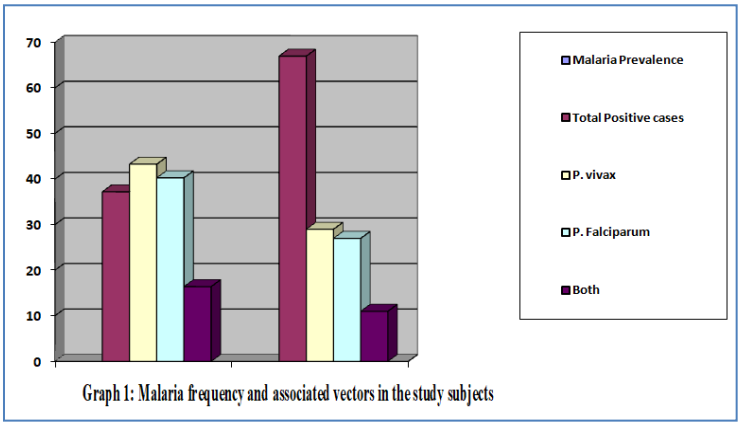
Parameter	Subgroups	Typhoid fever (n=32)			Malaria (n=67)			Coinfections (n=12)		
		%	N	p	%	N	p	%	N	p
Age Range (years)	2-10 (n=32)	25	8	0.94	96.87	31	0.03	25	8	0.06
	11-25 (n=76)	18.4	14		42.10	32		7.89	6	
	26-45 (n=59)	20.33	12		30.50	18		5.08	3	
	≥46 (n=13)	15.38	2		15.38	2		7.69	1	
Gender	Males (n=104)	17.30	18	0.32	40.38	42	0.339	75	78	0.484
	Females (n=76)	22.36	17		31.57	24		5.26	4	
Employment Status	Unemployed/students (n=151)	17.88	27	0.84	43.70	66	0.20	8.60	13	0.90
	Employed (n=29)	27.58	8		96.55	28		20.68	6	
Educational Status	Illiterate ((n=112)	18.75	21	0.97	35.71	40	0.83	6.25	7	0.88
	Undergraduate/Lesser ((n=63)	20.63	13		41.26	26		14.28	9	
	Postgraduate or more (n=5)	20	1		20	1		11.1	1	

Table 3: Association of typhoid fever, malaria, and coinfections with clinical characteristics in the study subjects

Parameter	Subgroups	Typhoid fever (n=32)			Malaria (n=67)			Coinfections (n=12)		
		%	n	p-value	%	n	p-value	%	N	p-value
Headache (n=165)	Yes	18.18	30	0.60	35.75	59	0.66	15.15	25	0.06
	No	23.03	38		41.21	68		16.95	28	
Fever (n=71)	Continuous	18.30	13	0.97	33.80	24	0.56	4.22	3	0.5
	Intermittent	18.30	13		38.02	27		7.04	5	
Vomiting (n=76)	Present	22.36	17	0.23	39.47	30	0.54	3.94	3	0.36
	Absent	14.47	11		34.21	26		7.89	6	
Joint Pain (n=137)	Present	21.16	29	0.69	35.76	49	0.85	5.10	7	0.42
	Absent	18.24	25		37.22	51		10.21	14	
Fatigue (n=164)	Present	17.68	29	0.29	37.80	62	0.05	6.70	11	0.84
	Absent	28.04	46		17.07	28		6.09	10	
Chills (n=149)	Present	16.77	25	0.20	38.25	57	0.33	6.04	9	0.53
	Absent	26.17	39		28.85	43		8.72	13	
Diarrhea (n=66)	Present	15.15	10	0.06	36.36	24	0.01	7.57	5	0.43
	Absent	25.75	17		34.84	23		4.54	3	
Nausea (n=60)	Present	21.66	13	0.16	36.6	22	0	6.66	4	0.84
	Absent	13.33	8		35	21		5	3	
Constipation (n=31)	Present	16.12	5	0.80	38.70	12	0.05	12.90	4	0.15
	Absent	19.35	6		35.48	11		3.22	1	

Table 4: Variables associated with typhoid fever and malaria in the study subjects

Characteristics	Subgroup	Positive % (n)	Negative % (n)	p-value
Malaria associated factors				
Travel History	Positive (n=23)	34.78 (8)	65.21 (15)	0.93
	Negative (n=157)	35.66 (56)	64.33 (101)	
Using net at bed	Yes (n=130)	39.23 (51)	60.76 (79)	0.24
	No (n=50)	30 (15)	70 (35)	
Typhoid fever associated factors				
Source of water	Tapwater (n=50)	22 (11)	78 (39)	
	Well (n=14)	14.28 (2)	85.71 (12)	0.34
	Spring (n=95)	15.78 (15)	84.21 (80)	0.24
	River (n=21)	28.57 (6)	71.4 (15)	0.75
Hand washing habit	Good (n=28)	35.71 (10)	64.28 (18)	0.01
	Poor (n=152)	15.78 (24)	84.21 (128)	
Food Habits (uncooked)	Yes (n=59)	20.33 (12)	79.66 (47)	0.55
	No (n=121)	18.18 (22)	81.81 (99)	
Using Toilet	Yes (n=160)	18.75 (30)	81.25 (130)	0.89
	No (n=20)	20 (4)	80 (16)	



Graph 1: Malaria frequency and associated vectors in the study subjects

Discussion

The results of the present study were in agreement with the studies of Igharo EA et al in 2012 and Opara AU et al[7] in 2011 with 37.6% and 39% prevalence respectively and were in contrast to the results of Mbuh FA et al[8] in 2003 and Nwuzo AC et al[9] in 2009 with 27% and 13% prevalence respectively.

For the prevalence of malaria, the total positive cases were 37.22% (n=67). Among 67 positive cases, 43.28% (n=29) were seen to have P.vivax, 40.29% (n=27) had P. Falciparum and mixed infection were seen in 16.41% (n=11) subjects. Typhoid and malaria coinfection was seen in 6.66% (n=12) study subjects, where 25% (n=3) had P. vivax infection, 58.3% (n=7) had P. Falciparum infection and 16.6% (n=2) had mixed infection by both. This was similar to Malisa and Nyasi[10] in 2010 with comparable results.

It was seen that in age groups of 2-10, 11-25, 26-45, and ≥46 years, there were 17.77% (n=32), 42.22% (n=76), 32.7% (n=59), and 7.2% (n=13) study subjects. Concerning gender, there were 57.7% (n=104) males and 42.2% (n=76) females in the present study. 83.8% (n=151) study subjects were unemployed, whereas, 16.1% (n=29) subjects were employed. Sundufu AJ et al[11] in 2012 showed higher prevalence of males by 64.4%. This can be attributed to less immune response.

For typhoid assessment, Widal test showed no agglutination, 1:20, 1:40, 1:80, 1:160, and ≥1:320 agglutination in 7.54% (n=4), 11.32% (n=6), 16.98% (n=9), 22.6% (n=12), 28.3% (n=15), and 9.43% (n=5) of study subjects was seen. This was consistent with the study of Akinyemi KO et al[12] in 2007, showing 27.6% typhoid prevalence, and was against the findings of Alhassan HM et al[13] in 2012. This can be due to different regions, seasons, and hygiene practices. As shown in the present study, poor hand washing habits are associated with typhoid fever significantly.

Conclusion

Within its limitations, the present study concludes that the coinfections are common owing to the high prevalence and overlapping symptoms of malaria and typhoid fever. High Widal test positivity can be attributed to mixed infection treatment frequently given. Also, cross-reactivity of typhoid fever and malaria is seen on the Widal test that can lead to typhoid fever over diagnosis. This over diagnosis can lead to non-judicial use of antibiotics and hence, associated side effects. Delayed diagnosis owing to mentioned factors can result in prolonged disease, demanding accurate assessment tools for diagnosis of malaria and typhoid fever.

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