International Journal of Microbiology Research
ISSN: 0975-5276 & E-ISSN: 0975-9174, Volume 8, Issue 1, 2016, pp.-720-722.
Available online at http://www.bioinfopublication.org/jouarchive.php?opt=&jouid=BPJ0000234

PREVALENCE OF MALARIA, ENTERIC FEVER, DENGUE AND RICKETTSIAL DISEASES IN FEVER CASES AT TERTIARY CARE HOSPITAL

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Received: December 23, 2015; Revised: January 16, 2016; Accepted: January 17, 2016

Abstract- Aim: Malaria, Enteric fever, Dengue and Rickettsial diseases are major diseases, still prevalent in most of the countries including India. Number of studies on contribution of these diseases in an acute febrile illness is less in this region. Hence, study was conducted to know prevalence of these diseases in Shimoga, Karnataka, India. **Methodology:** Data was collected from Microbiology Laboratory registers retrospectively for one year from October 2014 to September 2015. Samples from patients of all age group and from both Out Patient Department (OPD) and In Patient Department (IPD) who presented with fever, and were clinically suspected to have dengue, malaria, enteric fever or rickettsial diseases were included in this study. Other febrile patients were excluded. Serological tests for dengue, typhoid and rickettsial diseases was performed by following the manufacturer's instructions and for malaria, examination of thick and thin peripheral blood smear was done. Analysis was done using MS Excel 2010. **Results:** Among 554 febrile patients, rickettsial diseases was detected in 140(25.3%), enteric fever in 84(15.1%), dengue in 18(3.3%) and malaria in 06(1%) cases. Mixed infection was noted in 18(3.2%). **Conclusion:** Prevalence of rickettsial diseases 140(25.3%) is significantly high, especially in children's followed by enteric fever 84(15.1%). Simple serological tests and peripheral blood smear for malaria are useful in diagnosis of fever cases.

Keywords- Malaria, Enteric fever, Dengue, Rickettsial diseases, Serological tests, Peripheral smear.

Citation: Wadekar M.D., et al., (2016) Prevalence of Malaria, Enteric Fever, Dengue and Rickettsial Diseases in Fever Cases at Tertiary Care Hospital. International Journal of Microbiology Research, ISSN: 0975-5276 & E-ISSN: 0975-9174, Volume 8, Issue 1, pp.-720-722.

Introduction

Fever is a common presenting symptom in developing countries [1]. The most common causes of fever are infections (30%-40%) [2]. Malaria, Enteric fever, Dengue and Rickettsial diseases still remain a diseases of major public health importance in tropics and also are classified under the causes of pyrexia of unknown origin (PUO) [3].

According to WHO, Malaria is known to be endemic in 108 countries including India, where only *Plasmodium falciparum* and *Plasmodium vivax* are prevalent [4,5]. The symptoms of malaria are non-specific which causes difficulty in clinical diagnosis, resulting in poor disease monitoring and inappropriate use of anti-malarial drugs [5,6]. *Plasmodium falciparum* malaria is a medical emergency that requires accurate diagnosis and appropriate treatment. Therefore, precise laboratory diagnosis and species identification is essential [6].

Enteric fever is caused by gram-negative bacilli (*Salmonella typhi*, *S paratyphi* A, B and C), which is transmitted by faecal-oral route by contaminated food or water or by contaminated hands [3]. The annual incidence has been reported as more than 13 million cases in Asia and causing more than six lakhs deaths worldwide annually [7]. The socio-economic status of the disease has a significant importance, because the typhoid survivors may take several months to recover and to resume work [8]. Confirmed diagnosis of enteric fever by blood or bone marrow culture requires isolation and identification of the organism, which may take up to seven days [9]. A commonly used diagnostic procedure, Widal test is useful in developing countries like India where facilities for isolations and cultures are often not available especially in smaller hospitals [10]. Although typhoid and malaria are caused by two different agents, both share social circumstances which are imperative to their transmission. Therefore, a person living in such environment is at risk of contracting both these diseases, either concurrently or an acute infection superimposed on a chronic one [5].

Dengue is a vector-borne viral disease of humans that is transmitted by mosquitoes of the genus Aedes [11]. Dengue has been known to be endemic in India for over two centuries. Among 18 endemic states, the most affected regions are Delhi, West Bengal, Kerala, Tamil Nadu, Karnataka, Maharashtra, Rajasthan, Gujarat and Haryana [12]. Dengue causes clinical manifestations which may range from asymptomatic infections to dengue fever (DF) and also can cause severe disease, dengue haemorrhagic fever/dengue shock syndrome (DHF/ DSS) [13]. As there are no vaccines or drugs available to prevent or treat dengue specifically, its early laboratory diagnosis can ensure initiation of appropriate clinical management [14].

Rickettsial diseases are caused by arthropods like lice, fleas, ticks and mites, which are under reported in India but are significant contributors of pyrexia [15,16]. These diseases may pose a serious threat to public health if not diagnosed or misdiagnosed [17]. Difficulty in diagnosis of these infections arise owing to conditions such as a reduced level of suspicion, nonspecific signs and symptoms, and the absence of widely available sensitive and specific diagnostic tests [15].

There is a need to know the prevalence of malaria, enteric fever, dengue and rickettsial diseases in this region, where no published data is available and hence this study was conducted.

Materials and Methods

We collected data from Microbiology laboratory registers retrospectively for the last one year from October 2014 to September 2015. Analysis was done using MS Excel 2010.

For this study, we analyzed data from only patients who presented with fever, and were clinically suspected to have dengue, malaria, enteric fever or rickettsial diseases. Samples from such patients of all age group and from both Out Patient Department (OPD) and In Patient Department (IPD), referred to Microbiology laboratory for diagnosis of all four infections were included the study. Samples of other febrile patients were excluded.

554 febrile patients were referred to microbiology laboratory for diagnosis of these infections. Serological tests for dengue, typhoid and rickettsial diseases was performed by following the manufacturer's instructions and for malaria, examination of thick and thin peripheral blood smear was done.

For diagnosis of Malaria, blood sample should be collected few hours after the height of the paroxysm of fever and before anti-malarial treatment. Thick and thin blood smears are made at same time from capillary blood. Smears are stained by Leishman's stain and examined for malarial parasites.

With aseptic precautions, two to five ml of blood samples were collected by venipuncture and transported to the Microbiology laboratory with duly filled requisition forms. The serum was separated by centrifugation of the whole blood sample and if delay in testing, stored in the refrigerator at -20°C. Dengue infection was diagnosed by using Dengue Day 1 test which is a rapid immunochromatographic test (ICT) from J Mitra Co. Pvt Ltd Okhla Ind area Ph-1, New Delhi, India. Test kit consists of two devices; one device for detection of NS 1 antigen and second device for differential detection of IgM and IgG antibodies to dengue virus. This test is intended as an aid to an early diagnosis of dengue infection by detecting NS1 antigen and also for presumptive diagnosis between primary (if sample is reactive for IgM antibodies) and secondary infection (if sample is reactive for IgG antibodies).

Commercially available stained Salmonella antigen from ARKRAY Healthcare Pvt Ltd's kit containing S. typhi 'O', S. typhi 'H', S. paratyphi 'AH' and S. paratyphi 'BH' suspensions were used for diagnosis of enteric fever. Test procedures were performed according to manufacturer's instructions in the kit insert. Appropriate control tubes with normal saline were kept. The bacterial suspension (antigen) is mixed with suspected patient's serum in various dilutions. Appearance of agglutination in highest dilutions determines the titre of the antibodies in patient serum. Antibody titres of ≥ 1: 80 for 'O', 'H', 'AH'& 'BH' antigens were considered as positive.

Rickettsial diseases were diagnosed by Weil– Felix test (PROGEN, Tulip Diagnostics (P) Ltd., Verna, Goa, India). The Weil–Felix test is based on the principle that some strains of *Proteus* share common somatic constituents with certain species of *Rickettsia*. Sera from patients infected with *Rickettsia* will, therefore, produce agglutination with *Proteus* antigen suspensions. Antigen suspension of *Proteus* OX19 antigen reacts strongly with the sera of patients with typhus group rickettsiae and rocky mountain spotted fever, *Proteus* OX2 with the sera of patients with spotted fever infections, while the *Proteus* OXK with the sera of patients infected with scrub typhus. Serum samples positive in the slide test were confirmed with the tube test. Titers of more than 1:80 for OX2 and OX19 and more than 1:160 for OXK were considered diagnostically significant.

Patients suffering from more than one infective aetiologies were considered as mixed

Results

Of 554 patients who presented with fever, 248(44.7%) were positive for any of the four infections. 336(60.7%) patients were male and 218(39.3%) were female. Majority of patients 220(39.7%) were between age group of 1-18 years. Rickettsial diseases was detected in 140(25.3%), enteric fever in 84(15.1%), dengue in 18(3.3%), and malaria in 06(1%). Mixed infection was noted in 18(3.2%). Out of these 'mixed infection' patients, 8(1.4%) had enteric fever with rickettsial diseases, 8(1.4%) had dengue with rickettsial diseases and 2(0.4%) had malaria with rickettsial diseases.

Table-1 *Age and sex wise distribution of febrile patients*

Age (years)	Total No. (%)	Sex	
		M No. (%)	F No. (%)
1 – 18	220(39.7)	154(27.8)	66(12.0)
18 -45	214(38.6)	110(19.9)	104(18.7)
> 45	120(21.7)	72(13.0)	48(8.6)
Total	554(100)	336(60.7)	218(39.3)

Table-2 *Prevalence of infections*

Disease	Positive No.(%)
Enteric fever	84(15.1)
Malaria	06(1)
Rickettsial diseases	140(25.3)
Dengue	18(3.3)
Total(n=554)	248(44.7)

Table-3 *Pattern of mixed infections*

Disease	Positive No.(%)
Enteric fever + Rickettsial diseases	8(1.4)
Malaria + Rickettsial diseases	2(0.4)
Dengue + Rickettsial diseases	8(1.4)
Total	18(3.2)

Discussion

In our study of 554 patients, rickettsial diseases was diagnosed in 140(25.3%), enteric fever 84(15.1%), dengue 18(3.3%), and malaria 06(1%). In a similar study from Karnataka, 100 patients of acute febrile illness were diagnosed with scrub typhus (33%); dengue (25%); enteric fever (14%); malaria (8.0%) [18]. Infectious diseases are the most common causes for the fever and also are the leading causes of mortality and morbidity. In India, a retrospective study from Mumbai among 160 patients who died from acute febrile illness reported malaria in 23%, leptospirosis in 22% and dengue fever in 2%, while up to 54% died due to unexplained fever, a proportion of which is likely to have been caused by bacterial infections [19]. Mixed infection was noted in 18(3.2%) patients. Concurrent infections with more than one etiological agent can result in an illness with overlapping symptoms, resulting in a situation where the diagnosis and management of such a patient could be challenging [1]. The clinician should look for other causes of fever especially if atypical presentations arouse suspicion of other possible aetiologies. Although infectious diseases are the most common sources for PUO, its distribution and spectrum is changing overtime. The distribution varies in different countries according to health status and socioeconomic conditions [20]. Males 336(60.7%) were more commonly suffering from fever than females 218(39.3%). This may be due to their easy exposure to mosquitoes and mites because of their outdoor activities.

Rickettsiosis is an under diagnosed group of diseases presenting as acute febrile illness affecting previously healthy active persons and has high mortality in untreated cases [21]. Weil felix was the first test to detect rickettsial diseases, which is easy to perform and also cheap [22]. The reported seropositivity in clinically suspected infections is up to 33% [23]. This study showed widespread existence of rickettsial diseases 140(25.3%) in this region of Karnataka and hence there is a need to undertake studies wherever possible to understand the current scenario in a better perspective. Malaria is known to be severely underreported and insufficiently controlled in India, and malaria overtreatment, at the cost of other potentially severe infections, has also been reported.[19] Although there are so many cases of concurrent typhoid and malaria due to cross reactivity, true co-infection also exists and should be borne in mind as both typhoid and malaria infections thrive in similar social conditions. Deepika Verma et al. showed the prevalence of co-infection was found by culture methods and peripheral blood smear for malaria parasite as only 1.6% as compared to 8.5% by serological methods [5]. Diseases with classic clinical findings can also manifest as fever only, causing difficulty in diagnosis [24]. Most dengue infections are asymptomatic or cause mild symptoms, which are characterized by undifferentiated fever with or without rash. Hence laboratory diagnosis of dengue virus infections along with clinical correlation with proper case definition had improved case detection as well as proper treatment. Dengue Day 1 test used is this study helps in rapid detection of early infection and also for differential detection of primary and secondary infection [25].

Conclusion

Maximum patients suffered from rickettsial diseases in this area. Other infections in order of frequency were enteric fever, dengue and malaria. Significant numbers of patients were found to be suffering from various combinations of these infections. The vector control is important preventive measure in community and also proper sanitation, public health education and vaccination (Enteric fever) are the long term preventive measures which are essential to control these diseases

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