Publications
Prevalence and Clinical Manifestations of Malaria in Aligarh, India

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Abstract: Malaria is one of the most widespread infectious diseases of tropical countries with an estimated 207 million cases globally. In India, there are endemic pockets of this disease, including Aligarh. Hundreds of Plasmodium falciparum and P. vivax cases with severe pathological conditions are recorded every year in this district. The aim of this study is to find out changes in liver enzymes and kidney markers. Specific diagnosis for P. falciparum and P. vivax was made by microscopic examination of Giemsa stained slides. Clinical symptoms were observed in both of these infections. Liver enzymes, such as AST, ALT, and ALP, and kidney function markers, such as creatinine and urea, were estimated by standard biochemical techniques. In Aligarh district, P. vivax, P. falciparum, and mixed infections were 64%, 34%, and 2%, respectively. In case of P. falciparum infection, the incidences of anemia, splenomegaly, renal failure, jaundice, and neurological sequelae were higher compared to those in P. vivax infection. Recrudescence and relapse rates were 18% and 20% in P. falciparum and P. vivax infections, respectively. Liver dysfunctions and renal failures were more common in P. falciparum patients, particularly in elderly patients. Artesunate derivatives must, therefore, be introduced for the treatment of P. falciparum as they resist to chloroquine as well as sulfadoxine-pyrimethamine combinations.

Key words: Plasmodium falciparum, Plasmodium vivax, malaria, prevalence, clinical features, Aligarh, India

INTRODUCTION

Malaria is endemic in 104 countries with estimated 207 million clinical cases and 627,000 deaths, representing a major global public health problem [1]. It mainly affects children, pregnant women, and non-immune adults who frequently die as victims of cerebral manifestations and anemia [2]. Both of these malarial complications are responsible for a great number of spontaneous abortions, stillbirths, premature deliveries, and low birth weight [3]. Children with impaired consciousness and respiratory distress are at the highest risk of death associated with malaria [4]. Among the 4 Plasmodium species responsible for human malaria, P. falciparum has been the most prevalent overall, particularly in Africa. Neurological involvement in P. falciparum malaria is common and nearly a quarter of children who survived cerebral malaria develop neurological sequelae [5]. P. vivax is responsible for a significant proportion of malaria cases worldwide and is increasingly reported as a cause of severe disease [6]. In the past few years, P. vivax infection was recognized as a cause of severe malaria in young children even causing death [7-9].

In India, 60-65% of the malaria infections are reported due to P. vivax, while 30-35% due to P. falciparum [10]. India is one of the major contributors to malarial morbidity and mortality in the world [11]. Malaria has been a serious problem in some parts of India due to the slow progress in its control. During the past decade, most malaria-endemic countries shifted their national treatment policies to artemisinin combination therapy (ACT). Keeping above facts in view, the present study aimed to determine the prevalence and clinical manifestations of malaria in Aligarh, India.

MATERIALS AND METHODS

This study is based on the confirmed cases of malaria admitted in the hospitals and nursing homes of Aligarh, India during 2011-2013. Blood samples were collected from the patients admitted to the Jawaharlal Nehru Medical College hospital and a few other nursing homes of Aligarh. Clinical profiles of the patients were recorded at the time of sample collection.
Clinico-pathological studies of *Plasmodium falciparum* and *Plasmodium vivax* – malaria in India and Saudi Arabia

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Abstract

Malaria is one of the most devastating diseases of tropical countries with clinical manifestations such as anaemia, splenomegaly, thrombocytopenia, hepatomegaly and acute renal failures. In this study, cases of thrombocytopenia and haemoglobinemia were more prominent in subjects infected with *Plasmodium falciparum* (Welch, 1897) than those with *Plasmodium vivax* (Grassi et Feletti, 1890). However, anaemia, jaundice, convulsions and acute renal failure were significantly high (3–4 times) in subjects infected with *P. falciparum* than those infected with *P. vivax*. The incidence of splenomegaly and neurological sequelae were 2 and 6 times higher in *P. falciparum* infections compared to the infections of *P. vivax*. Both in *P. vivax* and *P. falciparum* malaria, the cases of splenomegaly, jaundice and neurological sequelae were almost double in children (<10 years) compared to older patients. The liver enzymes were generally in normal range in cases of low and mild infections. However, the AST, ALT, ALP activities and serum bilirubin, creatinine, and the urea content were increased in *P. falciparum* and *P. vivax* malaria patients having high parasitaemia, confirming liver dysfunction and renal failures in few cases of severe malaria both in India and Saudi Arabia.

Keywords

Pathology, liver enzymes, splenomegaly, malaria, India, Saudi Arabia

Introduction

Malaria is one of the most widespread infectious diseases of tropical and sub-tropical countries which continue to claim around 655,000 lives throughout the WHO African region (WHO, 2011). There are 99 countries and territories with ongoing malaria transmission. Globally, an estimated 3.3 billion people are at risk of malaria, with maximum cases recorded from sub-Saharan Africa. It mainly affects children, pregnant women and non-immune adults who frequently die as victims of cerebral manifestations and anaemia (Quintero et al. 2011). In the African region, approximately 90% of deaths among children under the age of five occur due to malaria. Children with impaired consciousness and respiratory distress are at the highest risk of death associated with malaria (Marsh et al. 1995). Neurological involvement in *P. falciparum* malaria is common and nearly a quarter of children who survive cerebral malaria, develop neurological sequelae (Idro et al. 2007). *P. vivax* infection is responsible for a significant proportion of malaria cases worldwide and is increasingly reported as a cause of severe disease (Lanca et al. 2012). However in the past few years, *P. vivax* infection has been increasingly recognized as a cause of severe malaria in young children even causing death (Sharma and Khanduri 2009, Singh et al. 2011, Limaye et al. 2012). Despite having lower densities than *P. falciparum*, *P. vivax* causes similar absolute reduction in red blood cell mass because it results in proportionately greater removal of uninfected red blood cells (Douglas et al. 2012). Recent findings indicate that *P. vivax* is also responsible for a dramatic toll in many endemic areas other than Africa. Cerebral malaria, acute kidney injury, liver dysfunction, severe respiratory distress, abnormal bleeding, severe anaemia and multiple organ failure were the recently reported symptoms of *P. vivax* – malaria (Prakash et al. 2003, Picot and Bienvenu 2009, Sonkar et al. 2011). In view of above facts, the present study was aimed at assessing the clinico-pathological symptoms of malaria in India and Saudi Arabia.
Prevalence of mutation and phenotypic expression associated with sulfadoxine-pyrimethamine resistance in Plasmodium falciparum and Plasmodium vivax

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Abstract: Therapeutic efficacy of sulfadoxine-pyrimethamine (SP), which is commonly used to treat falciparum malaria, was assessed in isolates of Plasmodium falciparum (Welch, 1897) and Plasmodium vivax (Grassi et Feletti, 1890) of Aligarh, Uttar Pradesh, North India and Taif, Saudi Arabia during 2011–2012. Both the species showed mutations in dihydrofolate reductase (DHFR) enzyme as they have common biochemical drug targets. Mutation rate for pfdhfr was higher compared to pvdhfr because the drug was mainly given to treat falciparum malaria. Since both the species coexist, P. vivax was also exposed to SP due to faulty species diagnosis or medication without specific diagnosis. Low level of mutations against SP in P. falciparum of Saudi isolates indicates that the SP combination is still effective for the treatment of falciparum malaria. Since SP is used as first-line of treatment because of high level of resistance against chloroquine (CQ), it may result in spread of higher level of mutations resulting in drug resistance and treatment failure in near future. Therefore, to avoid further higher mutations in the parasite, use of better treatment regimens such as artesunate combination therapy must be introduced against SP combination.

Keywords: molecular study, malaria, drug resistance, India, Saudi Arabia

Malaria is the most prevalent parasitic disease worldwide, responsible for an estimated 225 million clinical cases each year. It mainly affects children, pregnant women and non-immune adults who frequently die as victims of cerebral manifestations and anaemia (Quintero et al. 2011). It is major cause of death in tropical and sub-tropical countries where it claims approximately 655 thousand lives each year (World Health Organization 2010). This disease is managed by anti-malarial drugs as no effective vaccine is yet available. However, the parasite has developed resistance against most commonly used antimalarial chloroquine (CQ), posing a major problem for malaria control programme (Mitra et al. 2006).

In case of doubtfull species diagnosis, sulfadoxine-pyrimethamine (SP) combination is usually prescribed by clinicians to avoid any risk on the life of patient and, thereby, increases SP pressure on parasite population. With the spread of chloroquine resistant malaria in different countries including India and Saudi Arabia, SP alone or in combination with artesunate is used as an alternate drug. This drug combination targets the folate biosynthetic pathway of Plasmodium species; blocking the nucleic acid biosynthesis and thus causing parasite death (Peterson et al. 1988, Triglia et al. 1997). Pyrimethamine acts on the dihydrofolate reductase enzyme of Plasmodium falciparum (Welch, 1897) (PFDHFR) and inhibits the folate biosynthesis pathway of the parasite (Gregon and Plowe 2005). Point mutation in PFDHFR reduces its capacity to bind with the drug, resulting in the emergence of resistant parasite strains (Mbugi et al. 2006, Gesase et al. 2009). There are mutations at more than three loci in the parasite enzyme in endemic countries (Peterson et al. 1988, Sirawaraporn et al. 1997).

Pyrimethamine resistance develops in a progressive manner and treatment failure occurs. Since both P. falciparum and P. vivax (Grassi et Feletti, 1890) contain the same target enzymes, the antifolate drug also affects P. vivax – see Imwong et al. (2003), Hastings et al. (2004), de Pecoulas et al. (2004), Kaur et al. (2006), Barnadas et al. (2008). Keeping these facts in mind, study on the prevalence of mutations and phenotypic expressions associated with sulfadoxine-pyrimethamine resistance in P. falciparum and P. vivax is attempted in the samples obtained from India and Saudi Arabia.

MATERIALS AND METHODS

Blood samples collected from the patients with fever who attended the Medical College and other malaria clinics of Aligarh, India during 2011–2012, and the Communicable Diseases Control Centre, Taif, Saudi Arabia, from the patients who visited Jazan and Yemen earlier, were included in this study. Thick and thin blood smears of these patients were screened by E-600...