Concurrent Infections of Malaria and Dengue

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***Abstract*: There are several tropical mosquito borne infections. Malaria and dengue are the two communal mosquito infections that are very significant and cause high morbidity also mortality for many patients around the world. Here In this review we will discuss about Introduction, history, current scenario, nature, infection in pregnancy and foetal, coinfection from various countries in Asia, future prospective, conclusion. Furthermore, the dealing procedures for these co-infections are not the same as those for mono-infections. Hence, a delay in implementing the appropriate treatment regimen for these concurrent infections due to poor diagnosis can be fatal. . Though malaria-dengue concurrent infections are seldom described from the Asian region, it is probably increasing particularly in the countries known to be endemic for both of the above diseases. A necessary reporting of the incidences of malaria-dengue concurrent infections is recommended**

***Index terms*: Malaria, Dengue, Concurrent-infections, Pathophysiology**.

Introduction

'Malaria', 'dengue' are rapidly spreading mosquito-borne diseases and of high importance in terms of both mortality and morbidity, posing a worldwide public health problem due to ease in globalised travel [1]. Malaria is caused by Plasmodium species. which is usually transmitted by Anopheles species. The major Plasmodium species infecting humans are Plasmodium falciparum (P. falciparum), Plasmodium vivax (P. vivax), Plasmodium ovale and Plasmodium malariae [2]. human infections with the simian malaria and Plasmodium knowlesi, have been reported from forested regions of South-East Asia, particularly, the Borneo Island [3] Dengue is a mosquito-borne disease that is due to infection by single stranded RNA viruses of four distinct types (DEN-1, 2, 3 and 4) under the family Flaviviridae. Each of these types is usually transmitted by Aedes aegpti [2].

History

Across 87 countries [4]. The global load of dengue has been growing over the previous 50 years, with a yearly incidence estimate of near about 350 million infections, and about half of the world globally; malaria was estimated to affect 229 million people and cause 409,000 deaths in 2019 d's population in endemic areas is at risk [5-7]. These diseases are often share similar clinical manifestations, with fever being the most common symptom [8]. Co-infections with two diseases are frequently overlooked and misdiagnosed as being a mono-infection because of clinical resemblances [9-11]. Malaria dengue infection has been escalating after the increased reporting of dengue cases in malaria-endemic areas in various parts of the world since the first reported co-infected case in 2005 [12-17]. A systematic review reveals infection with malaria and dengue diseases in 20 countries in 2018 [8], ranging from 0.2% in Sierra Leone [18] to 23.0% among dengue-positive febrile patients in Pakistan [19].

In Yemen, near about 1.5 lacks malaria cases were reported by health facilities in 2019, mostly caused by P. falciparum [4]. currently, dengue cases have escalated; where several outbreaks caused by dengue virus (DENV) serotypes 2 and 3 have been reported between 2010 and 2012 [18-20]. DENV type 2 has reported febrile patients with dengue-like illnesses in Hodeidah city, also known as Al Hudaydah, in 2012 [22]. In Yemen, an increase 6 times in the number of dengue cases was reported in 2016 compared with 2015 [23]. Diagnosis, care , control of malaria, dengue in Yemen have been affected by the unstable political situation and wars 2012, where only half of the health facilities in the country were functional as of December 2018 [24]. Problem is lack of diagnostic tests in Yemen which prompt physicians that any acute febrile illness (AFI) is malaria, treat it as such, leading to unnecessary treatment of other AFIs. Inappropriate treatment of malaria, dengue infections can lead to severe complications or even death [17, 25-28]. Unnecessary malaria treatment contribute to the emergence, spread of drug resistance [29].

Current scenario

Current infections of malaria, dengue are when these diseases occur simultaneously in an individual. Since there are similarities in clinical characteristics between these two infections and diagnosis of malaria, dengue infections might be either misdiagnosed or misinterpreted as mono-infections [30].As of today, there are various cases of malaria and dengue infections testified from various areas in the world succeeding the first case which was reported in July 2005 in France [31]. Even if documented cases of malaria, dengue concurrent infections are rare in Asia but there is evidence of their clinical brutality when compared to either of the infections single-handedly [31]. Dengue, malaria is difficult to clinically distinguish, but the treatment of these infections is very dissimilar. A delay in instituting an appropriate management can be fatal, which is emphasized in the cases discussed elsewhere [32].In fact, clinical and biological pictures of infection cases are different from particular infections, and bivariate judgments show more differences among malaria-dengue and dengue than between malaria, [31].

What is the concurrent malaria and dengue infection?

In general, malaria is a protozoon infectious [49-51]. The pathogen is one of 5 human pathogenic species of Plasmodium. The main vector is Anopheles mosquito, whereas dengue is a viral infection [52-54]. The main mosquito vector is Aedes. Malaria and dengue diseases can cause acute febrile illness. However, malaria can be chronic while dengue not. The specific triads of dengue, atypical lymphocytosis, hem concentration, thrombocytopenia clue for differential diagnosis of dengue infection from other tropical infections including to malaria [52-54].It is no doubt that in a tropical country, the high prevalence of malaria, dengue can be seen. Current malaria and dengue infection is uncommon. Current malaria and dengue infection is a scenario that malaria and dengue exists in a patient at the same time.

Clinical Presentation and Pathogenesis

Clinical presentations of malaria, dengue is similar. However, there are minor differences, as the causative organisms, their pathogenic mechanisms are different and need to be addressed. similar clinical presentations lead to misdiagnosis of the co-infection status. Thrombocytopaenia is a solid interpreter of dengue fever, also is associated with a probability of malaria [33-34]. Dengue and malaria are reported to coexist in thrombocytopenic patients, especially those presenting with acute febri illness, as reported from a study elsewhere [35]. Anaemia is a major symptom seen in malaria infections, which is a blood stages causing intense intravascular haemolysis. This is not able in dengue cases [36]. However, anaemia is frequent in current infections. A significant decrease in platelets, haemoglobin content, reduced aspartate aminotransferase levels, elevated alanine aminotransferase levels are also seen in concurrent infections [36].Other clinical manifestations in malaria are myositis, rhab- domyolysis and acute renal failure [37]. It is postulated that in malaria, tumour necrosis factor-a (TNF-a), increased blood viscosity, red cell sequestration in skeletal muscle, metabolic toxins released by the parasite, lactic acidosis may cause myositis and skeletal muscle necrosis, myoglobinuria [38, 39]. In a study done in French Guiana, the clinical presentations in the cases of malaria, dengue infections were more severe than those seen in mono-infections [31]. It was also concluded from the above study that concurrent infections tend to more severe for cases with haematologic abnormalities, thrombocytopaenia and anaemia, which are known risk factors of severe dengue fever and malaria. Whether this increased severity results from longer evolution duration or increased virulence or both remains to be identified [31]. [fig.1]

The clinical features of current infections, mono-infections with dengue are reported to be similar. Significantly, less severe outcomes of the infections in the patients may be attributed to early diagnosis, treatment [40]. From a study conducted during the 2012 dengue outbreak in Pakistan, it was reported the rate of co-infections was high in cases of dengue fever. There was no significant difference in severity of the disease, except that infected patients had a lower rate of jaundice [41]. Other clinical, laboratory parameters were comparable. Another study concluded that prolonged fever with normal to low haematocrit, marked thrombocytopenia were concurrent infection manifestations [42] Such findings were solely based on serological diagnosis and which is not considered to be the gold standard to confirm an acute DENV infection, as the non-specific reactivity for DENV, positive immunoglobulin M (IgM) of past infection cant be ruled out in those serological assays [43].Other underlying conditions in malaria and dengue infections are rhabdomyolysis and sickle cell disease. While dengue can cause rhabdomyolysis and malaria can also cause acute infection. For example, TNF-a, RBC sequestration in skeletal muscle, increased blood viscosity, and toxins from the parasite together with lactic acidosis can lead to this problem [44]. In the case of sickle cell disease and there have been multiple DENV serotype infections, malaria, sickle cell disease infection. The presence of co-infection disease could lead to severe complications [45].

Nature of concurrent malaria and dengue infection

There are few published reports on current malaria, dengue infection. Reports are from only some countries [55-62]. Of interest, some areas with high prevalence of malaria and dengue such as those countries in Southeast Asia have never reported any cases of concurrent malaria, dengue infection. Based on this report by Carme, in French Guiana and the specific rate of concurrent malaria, dengue infection from overall febrile patients was equal to 0.99% [57]. It can assume that there is a high chance of concurrent infection in this setting. Focusing on the clinical presentations, the common manifestations of current malaria, dengue infection include high fever, myalgia [55-62].

Concurrent infection of malaria in pregnancy and foetal infection

The first case of malaria, dengue co-infection in pregnancy was reported from a northern province in India where a six-month pregnant woman admitted for suspected malaria was later diagnosed with a P. vivax and P. falciparum infection. She was later diagnosed with dengue co-infection. , she recovered with foetal well-being due to timely diagnosis as well as appropriate management [46].

Demonstrates the importance of timely management, diagnosis has proven to be lifesaving for mother and foetus. In Indian study, a total of 300 blood samples from febrile pregnant women were tested to rule out dengue infection. Dengue infection was detected in 7.3% cases. Two women co-infections with malaria and dengue. The outcome of a patient co-infected with dengue, P. vivax malaria in the later study was reportedly intrauterine death of the foetus at Week 37 [47]. cross-sectional study in the Brazilian Amazon presented four co-infected pregnant women with more severe complications in comparison to other infected patients [48].[fig.3] This study revealed that the predominant dengue types in the co-infected group were DENV-2, DENV-4. Similarly, in a case series of 11 hospitalised co-infected patients from the Brazilian Amazon, two pregnant women presented with severe complications, as designated by the World Health Organization severe malaria criterion and warning signs for severe dengue [43]. Co-infections in pregnancy are a challenge for diagnosis and clinical management due to the additional stress of the physiological changes during pregnancy [47]. , urgent medical attention is required for a rapid and accurate diagnosis so that efficient medical management of the co-infections can reduce the high mortality rates in pregnancy-related cases.

Host immune responses in malaria and dengue co-infection

Heightened levels of TNF and interferon-g (IFN-g) have been systematically associated with increased clinical disease severity in both malaria and dengue fever in many case series [36]. The increased TNF levels with significantly high numbers of interactions in the chemokine or cytokine networks suggest that cytokines may be involved in the pathogenesis of malaria and dengue fever comorbidity. Interleukin-6 (IL-6) has been implicated in the pathogenesis of severe dengue, as this cytokine enhances the production of anti-platelet and the induction of tissue plasminogen activator, leading to an increased risk for bleeding. These findings on immune markers support that coinfected cases present with more severe inflammation and disease status compared to mono-infections [36] Circulating cytokines and inflammatory mediators can be used as biomarkers in early diagnosis. As the immunopathogenesis of malaria and dengue produce common multiple cytokines and inflammatory responses, which regulate the spectrum of the infection, understanding that the key factors associated with increased morbidity can lead to a better clinical prognosis. A study of host immune response patterns in malaria and dengue co-infection revealed that co-infected individuals produced higher median concentrations of IFN-g, IL-6, and chemokine (C–C motif) ligand 4 than the mono-infected groups. Network analyses of plasma chemokines revealed that co-infection exhibited a distinct immune profile with critical roles for TNF, IL-6 and IFN-g [36]

Conclusion

The current review of literature reveals that the concurrent infection of malaria and dengue, though seldom reported, is showing an increase in incidence in these diseases' endemic countries in Asia. Even with the scarce case reports in Asia, the co-infections of malaria and dengue have recently been recognised to be an important clinical problem. Considering the possibility of concurrent infection in cases of atypical clinical manifestations or acute febrile illness, an early diagnosis is essential. Thereby, the treatment regime can be lifesaving. There is a great need to increase awareness of this concurrent infection among physicians and other healthcare personnel, and there is also a need for them to report the incidences.

Figures and Tables:

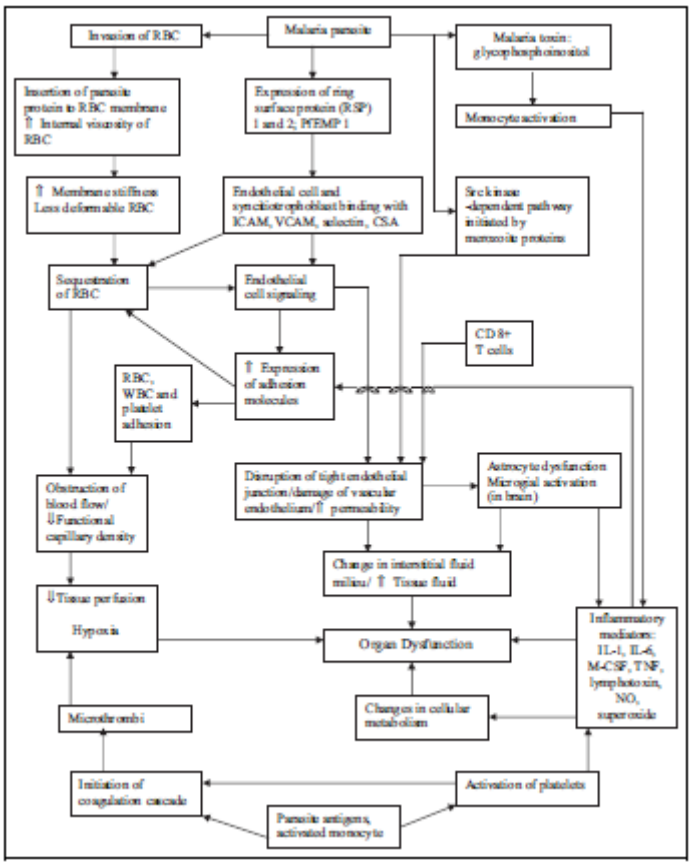

Figure: 1. Pathogenesis of malaria and complications of malaria.

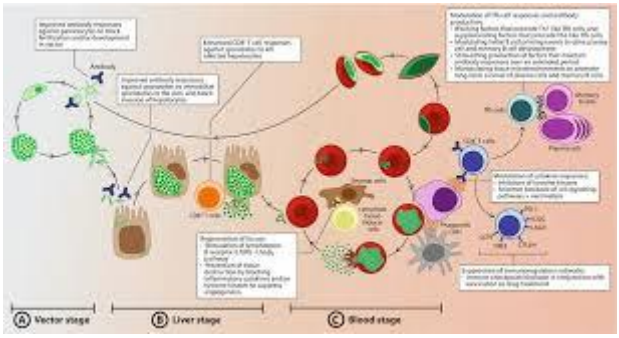

Figure:2. Stages of life cycle of maleria.

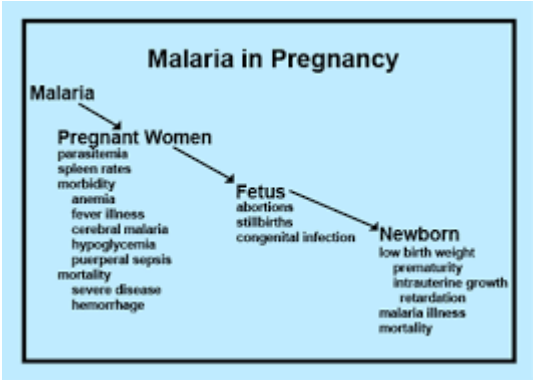

Figure:3. Infection of malaria in pregnancy and foetal infection.

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