# Erupt of malaria, dengue and chikungunya in Pakistan: Recent insights about prevalence, diagnosis and treatment

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**Abstract**: Malaria, dengue and chikungunya are the most rampant mosquito-borne infections predominantly in Pakistan. They pose a serious threat and cause a havoc for the victims owing to the life threatening signs and symptoms marked with elevated morbidity and mortality rate. It seems hard to discriminate due to common indications, consequently, deserves appropriate diagnosis prior elevated toll of death. Present article encompasses depth insights about their prevalence, diagnosis and clinical manifestation if erupt in the pandemic. However, host-vector-host cycle is the root cause of transmission and diverse mosquito species confer dissimilar infections. Indeed these infections are seasonal but other factors like flood, open irrigation channels, immense agricultural land, rich fauna and water reservoirs can't be overlooked. Dire need was felt to acknowledge and aware the public about local transmission, vector control, entomologic, research resources, diagnosis and advancement in healthcare system to alleviate them absolutely in future.

**Keywords**: Malaria, dengue, chikungunya, prevalence, diagnosis, treatment.

## INTRODUCTION

The infectious diseases are an important threat to the health and are one of leading cause of death globally. According to the World Health Organization (WHO) the infectious diseases accounts for 17% of expiries every year. The infectious diseases play a very important role in the world's economy (Tchankouo-Nguetcheu *et al*., 2012). More than 100 viruses of Bunyaviridae, Togaviridae and Flaviviridae are known and these viruses can infect humans through many vectors (Gubler, 2001). Malaria, dengue and chikungunya are the three types of mosquito-borne diseases and are comparatively serious due to various lethal symptoms. It is very hard to differentiate the disease without proper diagnostic tests because these diseases have quite similar symptoms and needs specialized efforts to identify before treatment. The mosquitos borne infectious diseases can produce an epidemiological pattern that the transmission can fluctuate from low level of endemic to high level epidemic (Yaqub, 2017).

Malaria is one of the most common health problem, it is endemic in ninety-one countries. It has caused greater than a million death's every year and has affected forty percent of population. It is estimated that malaria has affected 300 million people every year (Khan *et al*., 2013). Tropical regions are most affected, in such region malaria is a major health problem. Most of malaria cases are found in sub-Saharan African countries. In most of these regions, even though the deaths tool due to malaria has decreased yet it is still a leading health problem (Breeveld *et al*., 2012).

Malaria is a protozoan parasitic infection caused by Plasmodium specie, female anopheles mosquito transmit malaria in human population (fig. 1). Anopheles mosquitoes have about 577 species, malaria infection is transmitted by 77 species that can act as a vector (Khan *et al*., 2012). There are five major Plasmodium species that are infecting humans, *Plasmodium vivax*, *Plasmodium falciparum*, *Plasmodium malariae*, *Plasmodium ovale*, and *Plasmodium knowlesi*. In humans, malarial parasite first grows and multiply in the liver cells and then later in the red blood cells. During the erythrocytic cycle of the parasite the clinical symptoms of malarial infection appears (fig. 1). The plasmodium life cycle is started with a mosquito bite when it ingests the malaria parasite. The

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ingested gametocytes inside the gut of mosquito produce male and female gametes that will unite to form a zygote. In the gut wall ookinete penetrates the lining to form an oocyst, sporozoites release as the oocyst ruptures and migrate in the mosquito's body and from the salivary glands it is again ready to infect another host. When a mosquito bites a healthy human the sporozoites get enters the circulation. Sporozoites migrate to liver destroy the cells and divide into merozoites. The merozoites escape into the circulation and target red blood cells. In red blood cell merozoites develop into ring forms called trophozoites and schizonts. It will produce further merozoites and the gametocytes are also produced. When it is taken up by a mosquito, the parasite infects the insect and the cycle will keep continue with infecting a new host (Sahu *et al*., 2016).

***Prevalence of malaria in Pakistan***

The second most widespread disease in Pakistan is malaria, according to the WHO report about 1.6 million cases are reported every year (Khattak *et al*., 2013). It has been estimated that 60% population of Pakistan lives in areas with high prevalence of malaria. The transmission of malarial infection is seasonal. In Pakistan, the Federally Administrated Tribal Areas (FATA) are mainly affected. The major outbreaks of malaria are reported in Khyber-Pakhtunkhwa Khawa (KPK), Sindh, Baluchistan province, while the malaria transmission is less common in Punjab (Khan *et al*., 2012). In numerous districts the malarial outbreak is due to flooding. Despite of many malarial control programs were initiation still every 500,000 malarial cases leads to 50,000 deaths (Kakar *et al*., 2010). The most prevalent species of malaria is *Plasmodium vivax*, it accounts for 200,000 cases in 2011, and however, remaining cases were reported with *Plasmodium falciparum* and cases of *Plasmodium falciparum* infection have increased in recent years. A total of 64% and 36% cases are reported due to the *Plasmodium vivax* and *Plasmodium falciparum* respectively (Khattak *et al*., 2013; Kakar *et al*., 2010). In Pakistan, the period of transmission for *Plasmodium falciparum* is between August and December as *Plasmodium falciparum* infection are increasing it has increased from 34%-54%. The incidence of positive cases rose from 45% to 68% in 2006 in Baluchistan and Sindh provinces. A total of 240,591 cases were reported of which 73,857 that is 31% were *Plasmodium falciparum* infected cases. The 37% of malarial incidences were in districts and agencies that shares border with Iran and Afghanistan. The malarial control programs are initiated at government level to control the epidemic, new effective tools have been presented such as mosquitoes net that are pretreated with insecticides, vaccination, quick diagnostic tests and artemisinin-based combination drug therapy (Kakar *et al*., 2010).

Dengue virus belongs to genus Flavivirus and family Flaviviridae, it is an enveloped single stranded RNA virus. Dengue is a febrile illness, it is transmitted to slight extent by "*Aedes albopictus*" but it is mainly transmitted "*Aedes aegypti*" (fig. 2). The infection is caused by one of the four serotypes, these serotypes are antigenically related known as Dengue Virus I, II, III and IV (Ali *et al*., 2013). All serotypes can cause retro-orbital pain, flu-like symptoms, including joint pain, fever and headache (fig. 2). If same serotype infects an individual then type specific antibodies are produced while if the infection is because of different serotypes then an antibody dependent mechanism is mediated as in Shock syndrome and Hemorrhagic Fever (Atique *et al*., 2016). The cycle begins when the virus enters in the human body by the bite of "*Ades aegypti*", among four serotypes Dengue virus II cause more severe disease, while Dengue virus II causes milder illness, co-circulation of dengue virus serotypes has given less importance though it is common in tropical countries (Dhanoa *et al*., 2016).

Like malaria the transmission of dengue virus involves human vector-human cycle. A female mosquito ingests the dengue virus from human blood while feeding. Inside the mosquito mid gut, the virus infects and starts replication. The virus infects haemocoel and the salivary glands of the mosquito. The virus from the salivary gland, is then transmitted to other humans during its feeding time (Sahu *et al*., 2016). In human dengue has a dormant period of around 5 days, it is common to show mild to severe flu-like symptoms in infected individuals, while in rare cases the infection leads to hemorrhagic fever (Manore *et al*., 2014). More than half of population of the world is at risk of dengue infection and presently, WHO has reported its presence in more than 125 countries and recent modelling suggest as many as 39 million infections occur annually (Furuya-Kanamori *et al*., 2016). Dengue infection might be asymptomatic in some individuals, it has a potential to cause more severe illness like Shock syndrome and Hemorrhagic fever (Ali *et al*., 2013; Rafique *et al*., 2017).

***Dengue prevalence in Pakistan***

In 1943 the virus was first isolated in Japan, while in 1953 to 1954 the first dengue hemorrhagic fever outbreak occurred in Manila, city of Philippines (Ali *et al*., 2013). In 1994, Pakistan reported its first ever case of dengue infection, before that dengue infection prevalence in Pakistan is not clear (Paul *et al*., 1998). Dengue infection is once limited to Karachi but now it is epidemic in Lahore and continued to spread northeastern cities of Pakistan, it is also emerged as an epidemic in KPK and Punjab province (Wesolowski *et al*., 2015).

In 2005, it caused serious morbidity and mortality, now it is endemic, in 2006 the outbreak in Karachi was mainly because of presences of two serotypes of dengue virus

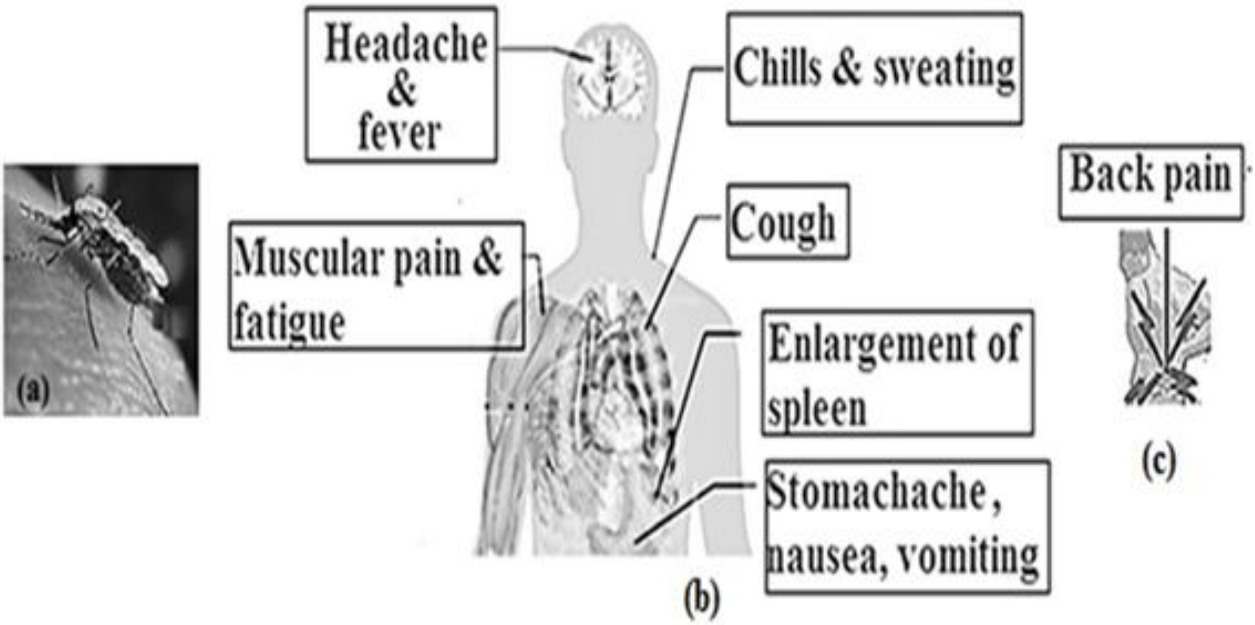


**Fig. 1**: *Anopheles stephensi* (a) mosquito for transmission of malaria. Major symptoms concerning malaria (b & c).

that was dengue virus I and II, the cases reported are also complicated with hemorrhagic or shock syndrome (Jahan, 2011). In 2006, from KPK one death while 31 cases were reported. In Punjab where most affected cities were Rawalpindi and Lahore 800 cases were reported. In 2007, Dengue spread to the northern and southern Pakistan again with 1208 cases and 22 deaths it was in low intensity as compared to the previous year. In 2008, from all over Pakistan 3280 cases and 30 deaths were reported. Punjab is more affected as compared to Karachi. In 2008 there were 20 deaths and 1450 positive cases from Punjab while 585 cases and 6 deaths were reported from Karachi. In 2009, from all over Pakistan 950 cases and 16 deaths reported. In 2010, greater than 9000 cases reported throughout Pakistan, 16 deaths reported from Karachi, 5000 cases with 35 deaths happened in Sindh. In 2011 over all 22,562 cases were reported with 363 deaths toll in Pakistan, Punjab (Lahore) majorly affected from dengue epidemic and registered 17,493 cases with 290 deaths. Similarly, from Sindh 953 cases were reported end up with 18 deaths (Rasheed *et al*., 2013). In 2013, there were 4955 cases and 30 deaths were reported from Karachi while 500 cases reported from Hyderabad and about 9024 dengue cases and 70 deaths were reported from Swat region respectively (Wasim *et al*., 2014).

The virus transmission is principally because of trade and travel between cities or countries. The WHO has reported one hundred million cases of dengue with about 30000 deaths. Dengue virus causes epidemic cycle after being endemic in most of countries, for two to three years. Since 2006 every year outbreak and co-circulation of dengue serotypes have been reported. In Pakistan, usually after the rainy season the incidence of dengue cases increase, other factors contributing the dengue transmission are flood, open irrigation channels, immense agricultural land, rich fauna and water reservoirs (Dawani *et al*., 2018).

Chikungunya word was derived from a verb "Kimakonde" that means "to become deformed" refers to those who are experiencing joint pain (Dawani *et al*., 2018). Chikungunya is a new mosquito borne infection, which is receiving too much concern these days. *Aedes aegypti* and *Aedes albopictus* (fig. 3) both are the vector for this infection. Chikungunya was first identified in 1953 (Manore *et al*., 2014). Both chikungunya and dengue have some parallels but difference in interaction pattern between host and mosquito species exists that expresses a substantial dissimilarity. The mortality rate of chikungunya is less in comparison with dengue. The disease shows joint pain that is also like dengue infection and incubation period in the mosquitoes is for 7 to 15 days as like dengue. After being infected with chikungunya infection the individual gets a lifelong immunity against this infection (Manore *et al*., 2014). Chikungunya is also the mosquito borne viral infection, it transmitted to healthy humans when an infected mosquito bites an individual. The symptoms of chikungunya include nausea, rash, fatigue, fever, sever joint pain that can vary in duration, headache and muscle pain (Dawani *et al*., 2018).

***Prevalence of Chikungunya***

Chikungunya virus was first recognized in Tanzania in 1954, and according to a report around 3000 individuals

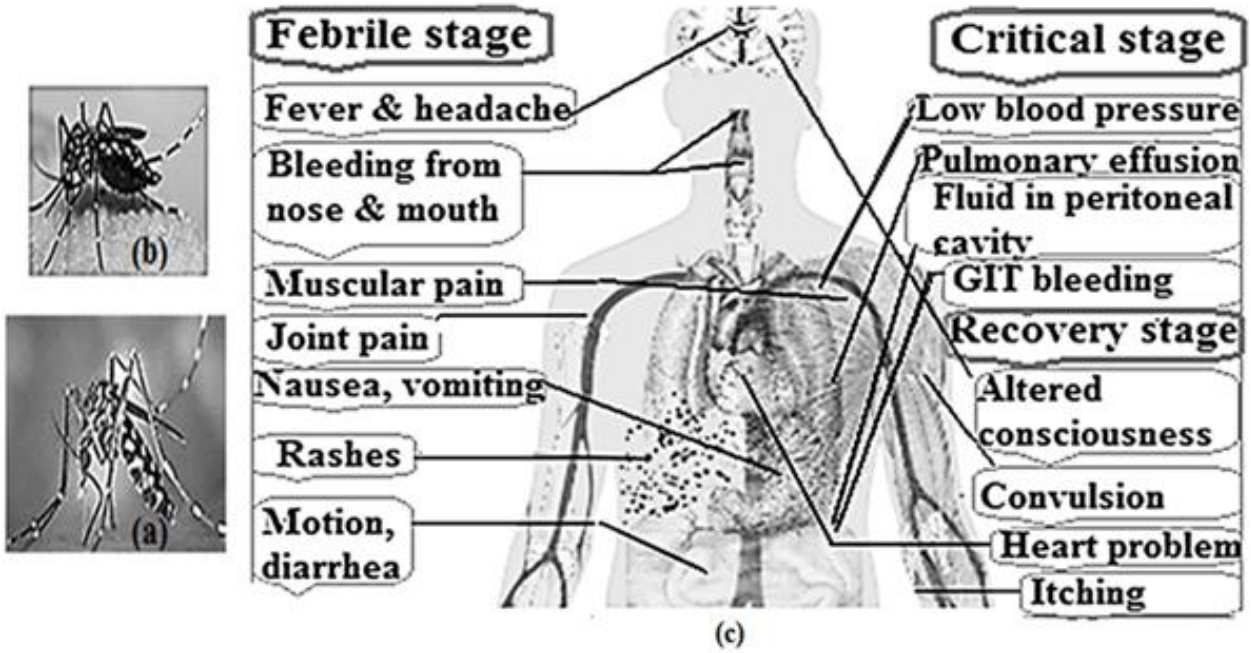


**Fig. 2**: Vectors concerning transmission of dengue: *Aedes albopictus* (a); *Aedes aegypti* (b). Major symptoms concerning dengue illness (c).

were infected from this virus. It was recognized to infect more than 60 countries, like across America, Africa, Asia and Europe, the disease was wide spread in these continents (Dawani *et al*., 2018). The outbreak spreads in Asia, up to the period 1960 to 1980, while in Pakistan it is linked back to the early 1980s (Simon *et al*., 2011). Many infectious diseases are endemic and considered to pose serious health problems in Pakistan. In Pakistan, the chikungunya infection was reported for the first time, its outbreak was once limited to India and to some countries in Africa. The chikungunya outbreak was first reported in Malir district of Karachi. It represents the symptoms that are like dengue, Many Individuals were in hospitals with complaining of severe joint pain, rash and fever. The chikungunya outbreak slowly spread to the surrounding areas. In Sindh province about 803 cases were reported positive in 2016 (Dawani *et al*., 2018). The National Institute of health (NIH) clearly warned about the chikungunya infection, despite this Pakistan experienced its outbreak in Karachi. The Ministry of Health in coordination with WHO initiated several response programs. The prevention from chikungunya includes Public awareness, local transmission acknowledgement, vector control, entomologic investigation, healthcare setup advancement, providing research resources and detection of cases (Dawani *et al*., 2018).

***Socioeconomic impact of malaria***

Malaria is being considered a fundamental hindrance in the development of economy owing to its serious ailment and numerous complications. Malarial parasite(s) causes serious damage to the victims via targeting the cardiac and skeletal muscles besides fluctuation in biomarkers level which poses intervene in the treatment and prevention of disease (Marrelli and Brotto, 2016). Being distressing in nature, often gritted with environmental factors therefore linked with the poverty. It is commonly engrained in developing countries and slackened the economic development via influencing health and economic cost drain. Historically, it was deduced that countries with low fiscal support are more prone to transmit it and to develop economic ingenuity (Arrow *et al.*, 2004). Victims of malaria have to subsist inordinate penury along with incessant impact on social and economic development. It must be eradicated, however, it is important to know the underlying mechanism associated with poverty (Ricci, 2012). The immediate cost burden confers upon providing health services and malaria control programs with community education that affects both economic prospect and domiciliary revenue. Transmission could be tackled with effective antimalarial drugs and via least host vector interaction (Ricci, 2012).

***Socioeconomic impact of dengue***

Historically the dengue pandemics happened rarely, however, recently it has become a tempting ailment in numerous countries. Dengue has reckoned as an emerging disease cause of increase in transmission and advent of dengue complications. At the moment there is no specific treatment and vaccination to prevent this infection (Gallup and Sachs, 2001). The high disease burden has led a need to identify new strategies to control the

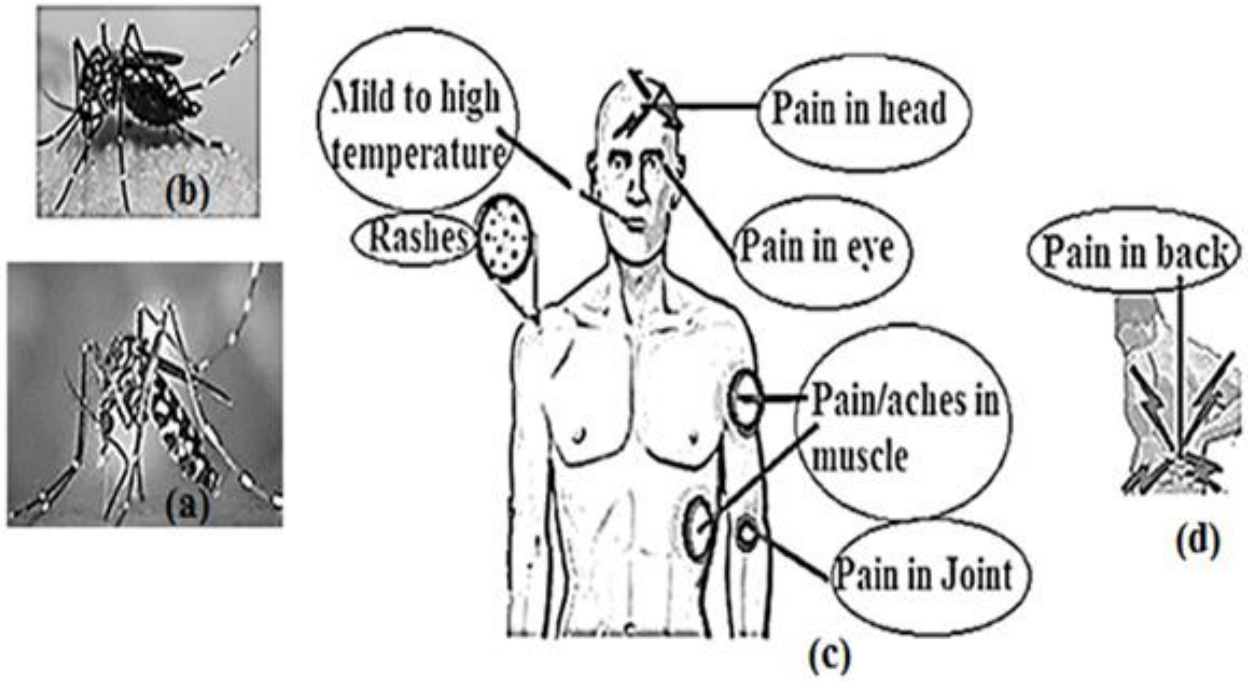


**Fig. 3**: Vectors concerning transmission of chikungunya *Aedes albopictus* (a); *Aedes aegypti* (b). Major symptoms of chikungunya (c & d).

outbreak and for effective management. Dengue endemic countries suffer from low economic development and societal burden because of high cost of integrated system. Its devastating impact has increased economic burden on government and distress among public. The substantial burden of disease requires monitoring of societal impact and development of cost-effective strategy to confine it. Social and environment factors are important in control and prevention of pandemics. Implementation of an effective strategy depends on public discernment and their involvement in different disease control programs. New strategies are inevitable to control the economic burden and distress among community such as initiation of successful immunization programs (Ladner *et al.*, 2017).

***Socioeconomic impact of chikungunya***

Chikungunya is a known extreme crippling ailment; the word chikungunya originates from Bantu dialect of Makonde from Tanzania. It alludes to the bended posture of the patient because of crippling joint agony (Da Cunha and Trinta, 2017). Chikungunya imposes a great impact on daily life, the disease burden remains a major public health delinquent. Chikungunya distresses the quality of life by influencing functional status of the infected individual (Da Rocha *et al.*, 2017). Economic and social factors facilitate chikungunya transmission, both plays an imperative role in disease occurrence and its spread. The emergence of this infectious disease needs to be control and prevented which involves public participation and sustenance. Chikungunya treatment involves no standard regimen, there is no specific vaccine to prevent and control infection. In several countries there is no appropriate detection of the cases because of technical inabilities and inappropriate disease management (WHO, 2007). Chikungunya is a major public health problem, accompanied by acute and chronic phase of illness in infected individual. The chronic phase is more devastating as it is escorted by severe arthralgia that impacts the quality of normal routine life. The disease has caused a high socioeconomic burden that can be tapered by promoting improved health related strategies. The development of effective intervention in the treatment is important to realize the underlying factors involved in transmission of infection (Elsinga *et al.*, 2017). Chikungunya has devastating effects in infected individuals; the disease has increased the economic burden on government. The frequency of clinical indication in infected individuals is prolong and has severely affected the quality of life (Soumahoro *et al.*, 2009).

## MATERIALS AND METHODS

***Data collection***

The key words used for the literature search of this review article were "Mosquito borne infectious diseases, Comparison of malaria, dengue and chikungunya". The Data was collected through internet search on Google scholar, Science Direct and PubMed. The data was carefully selected focusing on clinical features of the respective diseases. The search was also made to identify the rate of prevalence of the disease in Pakistan and the outcomes were rechecked and compared with literature.

## RESULTS

### *Clinical management about malaria (diagnosis and treatment)*

Malaria can cause fever, chills and a flu-like symptom (fig. 1) these symptoms usually appear after an incubation period of seven or more days after being infected with virus (WHO, 2014). Malaria diagnosis is important to prevent from severe malarial complications such as cerebral malaria. Several diagnostic tests are used for the detection of the malaria infection such as immunofluorescence microscopy, PCR, hematological analyzer and immune chromatographic testing. Microscopic identification is used as a gold standard based on erythrocytes morphological changes, but it cannot detect specie at low level such (<1000 parasites/µl) as in case of mixed infection (Ittarat *et al*., 2013). Light microscopy uses thin and thick blood films, blood film test is performed two to three times after the onset of the fever to confirm the infection or until there is a confirmed negative test or if the parasite is too low to be detected (Makhija *et al*., 2015). Molecular diagnosis methods are also used such as PCR technique that mainly differentiate between *Plasmodium vivax* and *Plasmodium falciparum*, but it is also time consuming, expensive and needs expertise. Molecular diagnosis is considered more sensitive as it can detect mixed infections in case two species involvement (Ittarat *et al*., 2013). Rapid diagnostic tests (RDTs) are used for malaria diagnosis, these tests provide results within few minutes (15-20 min), easy to perform and inexpensive but also have limitations like unable to detect low level parasitemia. RDTs are not reliable in detection of *Plasmodium malariae*, *Plasmodium ovale* and less sensitive in case of *Plasmodium vivax*. Several ICT devices are used for malaria detection such as "ICT malaria combo" and "now malaria" these devices can detect all species of Plasmodium another device "OptiMal" is used in case of poor reports of other devices for detection of *Plasmodium ovale* it is more specific and have 100% sensitivity. In febrile patients hemoanalyser is used such as "Cell Dyn" and "Sysmex XE-2100", these two devices are used for diagnosis in febrile patients. In 2007, there were 30,000 deaths reported annually, that was reported by "National statistical survey in Pakistan". Sensitivity of diagnosis is very important because malaria is fatal in non-immune individuals and in children, so it is important to early diagnosis the infection to prevent severe damage (McMorrow *et al*., 2011).

The treatment of uncomplicated *Plasmodium falciparum* malaria includes "artemisinin combination therapy" except for pregnant women in their first trimester. These combinations are dihydroartemisinin plus piperaquine, artemether plus amodiaquine, artemether plus lumefantrine, artemether plus mefloquine and sulfadoxine pyrimethamine plus artesunate, usually recommended for three days. The dose recommendation for dihydroartemisinin plus piperaquine in young children weighing less than 25kg is 2.5 mg/kg/day of dihydroartemisinin and 20 mg/kg/day of piperaquine for three days. In Patients with low transmissibility of *Plasmodium falciparum* infection except in infants less than six months and pregnant women, a single dose of 0.25 mg/kg body weight of primaquine with artemisinin combination therapy is required (WHO, 2015).

The treatment of special risk group like in case of hyper-parasitemia treatment with artemisinin combination therapy is recommended, the patients with HIV should avoid treatment with artemether plus amodiaquine and sulfadoxine pyrimethamine plus artesunate if the patient is treated with co-trimoxazole, zidovudine or efavirenz, during first trimester of pregnancy 7 days treatment with quinine plus clindamycin is recommended. Infants weighing less than 5kg are treatment with the same dose as the children with less than 25 kg weight are treated. The non-immune travelers should treat with artemisinin combination therapy. The treatment of uncomplicated *Plasmodium knowlesi*, *Plasmodium ovale*, *Plasmodium vivax* and *Plasmodium malariae* infection includes the treatment of blood stage infection as treated for *Plasmodium falciparum*. The chloroquine susceptible infection is treated either with chloroquine or with artemisinin combination therapy, but it not recommended in pregnancy in first trimester. The chloroquine resistant infection is treated with artemisinin combination therapy, except pregnant women in their first trimester, pregnant women are treated with quinine (WHO, 2015).

The relapse in patients with non-deficient G6DP is prevented with a 14 days course of primaquine in a dose of 0.25-0.5 mg/kg body weight except in breastfeeding women infants less than 6 months, pregnant women and G6DP deficient patients. While in patients with G6DP deficiency the treatment with weekly dose of 0.75 mg/kg of primaquine for duration of two months with assessment of risks from the primaquine treatment is recommended. The breastfeeding and pregnant women are treated with chloroquine weekly chemoprophylaxis until breastfeeding and delivery are completed then later treated with primaquine based on the status of G6DP (WHO, 2015).

In case of sever malaria the children, adults, pregnant women, breastfeeding women and infants are treated with artesunate injectables for 24 hours. If the patient can tolerate oral therapy after 24 hours of parenteral therapy oral therapy is started with artemisinin combination therapy or with a primaquine in area of low transmission. The young children weighing less than 20kg are recommended with 3 mg/kg dose of artesunate. The alternative treatment in case of un-availability of artesunate includes treatment with artemether, it is a preferred drug as compared to the treatment with quinine in children and adults (WHO, 2015).

**Table 1**: A brief overview about malaria, dengue and chikungunya in Pakistan

| Characteristics | Malaria | Dengue | Chikungunya | References |
|---|---|---|---|---|
| Incubation | 7-30 days | 4-10 days | 2-4 days | (WHO, 2015; WHO, 2009; WHO, 2008; Tolle, 2009) |
| Vector | Anopheles mosquito | *Aedes albopictus*, *Aedes aegypti* | *Aedes albopictus*, *Aedes aegypti* | (WHO, 2015; WHO, 2009; WHO, 2008; Tolle, 2009) |
| Symptoms | Fever, myalgias, shaking chills, headache, fatigue, vomiting, nausea, orthostatic hypotension. | Fever, retroorbital pain, headache myalgias, nausea, weakness, arthralgias, rash, vomiting, gingival bleeding, increased vascular permeability, thrombocytopenia, hemorrhagic manifestation. | Fever, arthralgia, headache, backache, myalgias, rash, hyperpigmentation, oral ulcers, vomiting, stomatitis, photophobia, diarrhea, retro-orbital pain | (WHO, 2015; WHO, 2009; WHO, 2008; Tolle, 2009) |
| Diagnosis | Microscopic Test; Blood Smear, Molecular Test; PCR | Antigen detection, virus isolation, ELISA, RT-PCR. | ELISA, RT-PCR. | (WHO, 2015; WHO, 2009; WHO, 2008; Tolle, 2009) |
| Management | Artemisinin-based combination, primaquine, chloroquine, clindamycin atovaquone, proguanil, quinidine, quinine, doxycycline, | Supportive therapy, hospitalization | Supportive Therapy, hospitalization | (WHO, 2015; WHO, 2009; WHO, 2008; Tolle, 2009) |

***Clinical management about dengue (diagnosis and treatment)***

Dengue can cause flu like symptoms that are self-limiting to serious life-threatening conditions it can also remain asymptomatic (fig. 2). The WHO, in 2009 revised the guideline for more accurate diagnosis and treatment. Still the diagnosis of malaria is challenging as it shows sign and symptoms that are like many other febrile illnesses. There are some diagnostic methods employed for the virus detection such as RNA detection of virus using RT-PCR, Serological test using ELISA technique, virus isolation, Antibody titration and Antigen detection (Cavailler *et al*., 2016). The virus specific antibody detection and virus isolation method are expensive and time consuming and laborious. In acute illness, the Antibodies arises in last stage, it limits the serological diagnosis of infection. After 3-4 days that is after the appearance of the dengue symptoms IgM is then detectable. For Rapid diagnosis of dengue infection more sensitive dipstick system and kits for ELISA test are available (Wichmann *et al*., 2006). A kit used for the extraction of the RNA from positive blood samples that is "QIAGEN QIAamp viral RNA kit". Initial diagnosis is done using ELISA technique, then later the dengue virus serotypes is identified using a technique known as RT-PCR "reverse transcription polymerase chain reaction" extracted RNA is used for this process of identification (Ali *et al*., 2016). According to the new guidelines of WHO in 2009, there are three clinical stages of dengue asymptomatic dengue infection, symptomatic dengue infection and sever dengue infection. The primary dengue is associated with less complication as compared to secondary dengue infection symptoms of dengue includes persistent vomiting, lethargy, rash, retro orbital pain decrease number of platelet count, increasing hematocrit, liver enlargement, abdominal pain, mucosal bleeding, edema, fever, headache, muscle pain and joint pain, while in case of dengue complications severe organ damage or organ failure, severe plasma leakage and bleeding can occur (fig. 2) (Ali *et al*., 2016; WHO, 2009).

Treatment of dengue based on the different group of patients such as group A belongs to patients without warning signs, group B includes patients with warning signs and group C includes patient with severe dengue who need emergency treatment. The warning signs are mucosal bleeding, edema, liver enlargement, lethargy, increased hematocrit, restlessness, vomiting, rapid decrease in platelet number and abdominal pain. Group A, patients do not have any warning sign, tolerate enough fluid intake and can pass urine in every six hours (WHO, 2009).

The patient may be sent home after providing treatment, when the hematocrit level is stable. The patients are advised to take enough bed rest and advised to take adequate fluid, these patients are prescribed with paracetamol, maximum dose of 4000mg/day. Group B patients are treated with intravenous fluid therapy of ringer lactate or 0.9% saline to the patient response. The therapy started with 5-7 ml/kg/hr for first 2 hours then reduce to 3-5 ml/kg per hour for next 2 hours, then further reduce to 2-3ml/kg/hr according to response of patient. Group C includes serious patients, the patient is treated with 5-10 ml/kg/hr intravenous isotonic crystalloid solution, if patient is stable then reduce gradually up to 2-3 ml/kg per hour, if patient is still unstable repeat the second intravenous bolus for one hour, if patient improves reduce gradually. In case of decrease level of Hematocrit, blood transfusion is done (WHO, 2009).

Patients with hemorrhagic complications are given 10-20ml/kg of whole blood or 5-10 ml/kg of packed cells. In case of hypotensive shock the patient is given crystalloid or colloidal solution bolus of 20ml/kg for 15 minutes, if patient is reduce gradually and if the patient is unstable repeat the second bolus for 30 minutes or for one hour and then reduce gradually, before making any assessment the hematocrit level of the patient must be indicated, the decrease hematocrit level indicate bleeding in case of high level of hematocrit intravenous fluid therapy is given that is further increased or decreased according to the patient's response (WHO, 2009).

***Clinical management about chikungunya (diagnosis and treatment)***

Chikungunya infection in an individual is confirmed using different diagnostic tests. These tests include molecular detection and serologic tests (Jacobsen *et al.*, 2016). As the infection can cause symptoms like severe joint pain, muscle pain, nausea, rash, fever, headache and fatigue (fig. 3). It is important to get a proper diagnosis and treatment for the cure of disease (WHO, 2014). The molecular testing involves detection of virus while serological test detects IgM and IgG antibody. There are also some other tests including rapid tests, Immunofluorescence assay and ELISA. PCR methods used for the virus detection are considered more reliable and sensitive then serological assays. Some rare tests used for the virus detection are isolation of virus and culture test, these tests are not used for the routine diagnosis. Differential diagnosis should be done for the detection of virus because the infection can exist with other infectious diseases (Jacobsen *et al.*, 2016).

Chikungunya infection is treated symptomatically as there is no proper treatment for this infection. In acute stage of infection patient is advised for adequate rest at home and to take about 2000ml of water with electrolyte daily as to avoid dehydration. Patient is prescribed with paracetamol 1g twice a day and children prescribed with adjusted divided drug dose that is 50 to 60mg per kg. Another NSAID should be prescribed if the patient is already taking an analgesic. In case of complications the patient is referred to higher health care setup (WHO, 2008). Complications are treated accordingly, in case of severe joint pain prescribe oral daily dose of hydroxychloroquine 200 mg or chloroquine phosphate 300 mg up to four weeks. The chronic stage of Chikungunya infection accompanied with complications like osteoarticular, neurological, dermatological or psychosomatic problems. General guidelines are followed for treating osteoarticular problems, physiotherapy is helpful in this case, NSAIDS are used to relief the pain care must be taken in case of cardiac, gastrointestinal and renal toxicity. For neurological problems antineuralgic drugs in standard doses are prescribed like pregnable, gabapentin, carbamazepine and amitriptyline. Dermatological problems are treated with calamine lotion or zinc oxide cream, antibiotics either systemic or topical and saline compresses may be used to treat skin ulcers. Community support resolves the psychosomatic problems this problem is rare only found in individuals with history of mood disorders (WHO, 2008).

## DISCUSSION

Malaria, dengue and chikungunya are the mosquito-borne infectious diseases responsible for serious health problems to mankind as any of the infection can be life-threatening if ignored. The symptoms are quite similar making it difficult to identify the disease without proper diagnosis (Yaqub, 2017). Malaria is the most common heath problem and the second most prevalent disease in Pakistan. Its diagnosis is important to prevent malaria complications. Several malaria control programs are initiated at government level to control the spread of disease. New effective tools have been presented such as mosquitoes net that are pretreated with insecticides, vaccination, quick diagnostic tests and artemisinin-based combination drug therapy (Kakar *et al*., 2010). Dengue virus causes epidemic cycle after being endemic in most of countries, for two to three years. The mortality rate with dengue is high as compared to the other mosquito borne infections (Dawani *et al*., 2018). Dengue and chikungunya have some similarity as in case of symptoms but difference in interaction pattern between host and mosquito species exists that expresses a substantial dissimilarity. The mortality rate of chikungunya is less in comparison with dengue. After being infected with chikungunya infection the individual gets a lifelong immunity against this infection (Manore *et al*., 2014). A quick over view about malaria, dengue, and chikungunya is summarized in table 1.

## CONCLUSION

This current literature review of malaria, dengue and chikungunya reveals that these mosquitos borne infections

are rapidly spreading with high rate of morbidity and mortality and poses a serious health threats. The symptoms of these three infections are quite similar so are often misdiagnosed. There should be a proper diagnosis to identify the disease and a desired treatment regimen should provide to infected individuals. Prevention and control programs should be implemented in a way to completely eradicate these diseases.

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