Vector-Borne Parasitic Diseases: Climate Change, Non-Climate drivers and Immunity

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Abstract

Despite efforts by monitoring and public health systems to reduce vector-borne diseases, they remain a global concern, which causes more than one billion individuals are infected each year, with over one million people deaths. Among these infections, those diseases caused by parasites such as malaria, leishmaniasis and schistosomiasis are public health issues. Climate directly influences the probability of a vector-borne diseases outbreak. climatic conditions is one structural determinant of vector population, evolution , survival rates , disease transmission and infection patterns. additional to non-Climate drivers such as ecological , socio-economic and public health systems are important contributors to

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the establishment and transmission of vector-borne epidemic diseases. Today, despite available drugs , regrettably, many parasites develop resistance , thereby frustrating, the effectiveness of therapeutic strategies. To prevent and control disease, understanding the processes through which parasite development in host. In addition to the mechanisms by host respond to parasite exposure (co-evolution) and the ability of the parasite to suppress (or avoid) the immune response of its host. The aim of this review is highlight on vector-borne parasitic diseases infect human in terms the influence of climate change and other non-climatic drivers on the transmission of these diseases, in addition to knowing, (co-evolution) between mechanisms used by parasites within the host and host defense against parasitic infection.

Keywords: *Vector-borne parasitic diseases, malaria, leishmaniasis, schistosomiasis*

الملخص

على الرغم من الجهود التي تبذلها أنظمة المراقبة والصحة العامة للحد من الأمراض المنقولة بالنواقل ، إلا أنها تظل مصدر قلق عالمي ، مما يتسبب في إصابة أكثر من مليار شخص كل عام ، مع وفاة أكثر من مليون شخص. من بين هذه الإصابات ، الأمراض التي تسببها الطفيليات مثل الملاريا وداء الليشمانيات والبلهارسيا هي من قضايا الصحة العامة. يؤثر المناخ بشكل مباشر على احتمال تفشي الأمراض المنقولة بالنواقل. الظروف المناخية هي أحد المحددات الهيكلية لنواقل الأمراض والتطور ومعدلات البقاء على قيد الحياة وانتقال المرض وأنماط العدوى. بالإضافة إلى الدوافع غير المناخية ، مثل النظم البيئية والاجتماعية والاقتصادية وأنظمة الصحة العامة ، فهي مساهمات مهمة في إنشاء ونقل الأمراض الوبائية المنقولة بالنواقل. اليوم ، على الرغم من الأدوية المتاحة ، للأسف ، فإن العديد من الطفيليات تطور المقاومة ، وبالتالي تحبط فعالية الاستراتيجيات العلاجية. للوقاية من المرض ومكافحته ، فهم العمليات التي يتم من خلالها تطور الطفيلي في المضيف. بالإضافة إلى آليات استجابة المضيف للتعرض للطفيلي (التطور المشترك) وقدرة الطفيل على قمع (أو تجنب) الاستجابة المناعية لمضيفه.

تهدف هذه المراجعة إلى تسليط الضوء على الأمراض الطفيلية المنقولة بالنواقل التي تصيب الإنسان من حيث تأثير تغير المناخ والدوافع غير المناخية الأخرى على انتقال هذه الأمراض ، بالإضافة إلى معرفة (التطور المشترك) بين الآليات المستخدمة من قبل الطفيليات داخل المضيف والدفاع المضيف ضد العدوى الطفيلية.

Introduction

Vector-borne diseases are illnesses caused by pathogens and parasites in human populations. .More than half of the world's population is at danger of vector-borne diseases (VBDs); each year, over a billion people are infected and one million people die as a result of these infections (WHO, 2014). Mosquitoes are one of the best known disease vector. Others include certain species of ticks, flies, sandflies, fleas, bugs and freshwater snails. that transmitted viruses, parasites, and bacteria to humans. One sixth of the illness and disability suffered worldwide is due to vector-borne diseases(WHO, 2004 & 2018). One of the most pressing public health concerns is parasitic illnesses. Disease causing parasites affect more than 20 million individuals worldwide, including malaria, Chagas disease , African trypanosomiasis, leishmaniasis, Schistosomiasis and Filariasis (WHO, 2010). .

Ecosystem change encompasses climatic change, environmental change, and its interconnections, and is thought to be linked to a many emerging diseases (Hanson *et al*, 2008). Climate change is affecting many infectious disease agents, particularly those transmitted via an ectotherm of poikilotherm invertebrate vectors or intermediate host whose distribution and development are inextricably linked with climate(CampbellLendrum *et al*, 2015). The changes in temperature and precipitation, either in intensity, mean, minimum and maximum values,

as well as the duration and the variability of the changes, will affect the environment in which the VBDs are transmitted (fouque & Reeder, 2019). When environmental conditions are changing because of climate change, the genetically determined vector competence will not be affected, but the vectorial capacity may dramatically change and provide conditions that are more favorable to outbreak transmission (Oo *etal*,2011).

Climate and weather impact transmission cycles of vector-borne pathogens directly by effects of temperature on the duration of the extrinsic incubation period of pathogens in insect vectors (Cable *et al*, 2017). The development and replication of pathogens transferred through vectors (the extrinsic incubation period or EIP) or in the environment also occurs more quickly at high temperatures (Reisen *et al*,2014).

Other drivers such as changes to the environment through deforestation and urbanization; developments in agriculture and food production; Change in human behavior; changes in medicine, public health and the use of antimicrobials; and the occurrence of "shocks" such as war, migration, poverty (Jones *etal*,2008) are important contributors to the establishment and ultimate transmission of vector borne diseases (Jones *et al*, 2008; Suk & Semenza, 2011; McMichael, 2013; Semenza *et al*, 2016a & 2016c).

Today, despite available treatments, the disease causing parasites affect more than 20 million individuals worldwid (Maizels & Yazdanbakhsh ,2003; WHO, 2010). Given that parasites interact at a close range with the host's immune system, that is, at the level of the molecules involved in defence, it is expected that parasites have evolved ways of interacting with the host at the same level(Moore, 2002).**.** Parasitic infections and the host's immune responses are the result of

dynamic co-evolution of the host and the parasite's complex life-cycle with each life stage resulting in a different interaction with the immune system (Anthony *et al*, 2007; MacDonald *et al*,2002).

Abetter understanding of parasite biology, pathology, immunology, and parasite-host interactions has resulted in better therapeutics and management strategies that have significantly improved patient outcomes. Unfortunately, many parasites develop resistance (Vanaerschot, *et al*, 2014). thereby thwarting the effectiveness of therapeutic strategies (Geiger *et al*,2016) there is still incomplete understanding of the interaction between the host's immune response and these parasites (Brindley *et al*,2009). This review highlights vector-borne parasitic diseases infect human in terms the impact of climate change such as temperature ,rainfall ,humditiy and Other drivers such as urbanization ,migration, developments in agriculture , quality of public health services; and drug resistance, Human behavior and conflicts ect...on ultimate transmission of vector borne diseases . as well as understanding the processes through which parasite development in host. In addition to the mechanisms by host respond to parasite exposure (co-evolution) and the ability of the parasite to suppress (or avoid) the immune response of its host. .

Vector-borne parasitic disease

1- Malaria

Malaria is a mosquito-borne infectious disease caused by the parasitic protozoans of the genus Plasmodium *(P. vivax, P. falciparum*, *P. ovale*, *P. malariae*, *P. knowlesi*, *P. cynomolgi*, and *P. simium*) and transmitted by female mosquito vectors of the Anopheles genus . (Greenwood *et al*, 2008; Brasil *et al*, 2017). According to the World

Health Organization's (WHO) World Malaria Report 2019, there were 228 million cases of malaria worldwide in 2018, resulting in 405 000 deaths. Malaria is found in more than 90 countries and affects over 40% of the world's population (Garcia ,2010).

Malaria transmission occurs mainly in tropical and sub-tropical countries in Africa, Central and South America, Asia and Oceania (Courtenay *et al*, 2019). The burden is greatest in the WHO African Region, which accounts for an estimated 90% of all malaria deaths, and in children under the age of five, who account for 78 % of all deaths (WHO, 2014). Recent modelled descriptions of parasite prevalence in Africa predict the contemporary intensity of *P falciparum*. (Hay *et al*, 2009 ; Gething *et al*, 2011). *Plasmodium. falciparum* accounts for most of malaria deaths. *Plasmodium vivax* (*P. vivax*), the second most common species of malaria parasite, differs *to P. falciparum* in that it survives in the liver for long periods, causing relapse several months to years after infection. *P. vivax* has the widest geographical distribution of all human malarias, and accounts for about half of all malaria cases outside sub-Saharan Africa(WHO, 2018).

Attempts to track the changing burden of malaria in Africa have focused on modelled predictions of clinical and fatal outcomes (Snow *etal*,1999 ; Cibulskis *etal* ,2011). Malaria is an acute febrile disease with a 7-day or longer incubation period following the initial infective mosquito bite Initial symptoms may be mild, such as headache, fever, and vomiting or chills, but these symptoms are difficult to distinguish as malaria. Of the five parasite species that cause malaria in humans, *P. falciparum*, is the most severe, and thus most deadly. As a result, a correct diagnosis of infection caused by *P. falciparum* is critical. Severe anemia, cerebral malaria, renal failure, acute respiratory distress

syndrome, acidosis, and cardiopulmonary complications are among the clinical manifestations of severe malaria ((Gay, *et al*, 2012).

Africa has been identified as one of the parts of the world most vulnerable to the impacts of climate change (Field, *etal*, 2014; McCarthy *et al*, 2001). Environmental variables such as temperature, humidity, rainfall, and wind speed affect the incidence of malaria, either through changes in parasite life cycles and the duration of mosquito or influences on human, parasite , or vector behavior (Gubler *et al*, 2001; Koenraadt *et al*, 2004). Overall, Anopheles mosquitos require sufficient rainfall to establish breeding sites that do not dry out or wash away over a 9–12 day period. Replication of the parasite within the mosquito vector requires a minimum air temperature of about 16°C for *P.vivax* and19–20°C for *P.falciparum* (Detinova, 1962; Marten *et al*, 1997). Increased temperatures that are close to the upper limit for vector and pathogen survival (roughly about35–37°C) tend to reduce transmission, but increasing daily temperature variation towards the lower limit tends to increase transmission. (Marten *et al*, 1997; Paaijmans *et al* ,2010; Craig *et al*,1999).

. Malaria is rarely in the desert areas, but Libya has documented of Malaria outbreaks and concerned about an invasion of mosquitoes carrying the deadly disease. Libya is a dry North African country that stretches from the Mediterranean to the Sahara Desert. Annual precipitation reaches 350 mm at along the coast and about 500 mm on the northeastern Jebel Akhtar; elsewhere, it is sparse, rarely exceeding 25 mm (Ramsdale, 1990). Many Libyan oasis, like those in other Saharan regions, have a history of malaria outbreaks caused by *Plasmodium vivax* and *Plasmodium farcipamm*. "The latter malaria parasite has been exterminated from the Mediterranean basin, but it still reigns supreme in

Africa south of the Sahara. (Ramsdale, 1990). *Plasmodium. vivax* is not found in West Africa. Though transmission persists in several Middle Eastern and North African countries, it has been removed from Europe since 1975 (Bruce-Chwatt & Zulueta de,1980) and is almost completely eradicated from the Mediterranean region (Hamid *et al*, 2018).

The shifting distribution of malaria vectors, as well as fluctuations in malaria prevalence, are complicating vector control efforts and posing a threat to some countries' malaria elimination targets. Evidence of altering patterns in malaria-affected areas is difficult to link to climate change alone since they occur in a changing environment, with changes in land use, water management, and human activities exposing different populations to different transmission patterns (Kibret *et al*,2016).In Libya, a steady stream of migrant workers, many of whom are from highly malarious parts of the world, ensures the maintenance existence of a parasite reservoir that is likely larger than it has ever been. Furthermore, improved air and road communications increasingly facilitate population movement within, as well as into the country. As a result, current data on the prevalence of anopheline mosquitoes, some of which are vectors of human malaria parasites in Libya, is still important for public health. (Ramsdale, 1990).

Humans with no previous experience of malaria almost invariably become ill on their first exposure to the parasite. The picture that emerges from human studies is that immunity to malaria infection is relatively slow to develop and incomplete, although immunity to death is acquired more quickly and may be important after a single episode (Gupta *et al*,1999). Immune attack could theoretically be directed at any point in the life cycle from the time of entry of the sporozoite . However, longitudinal studies in exposed populations suggest that immune responses to the pre-

erythrocytic stages probably have limited involvement. (Owusu-Agyei *et al*,2001)

The mechanism by which vaccines may act is indicated by studies in mice in which elimination of pre-erythrocytic parasites requires mainly CD8+ effector cells producing interferon-γ (IFN-γ) that kill parasites in infected hepatocytes (Schofield *et al*,1987).

Antibodies to the sporozoites are thought to have a lesser function. For erythrocytic stages, potential targets for an immune response are free merozoites or intraerythrocytic parasites. Given that HLA class I or II molecules are absent from the surface of the parasite or the infected red blood cell (RBC), it is usually assumed that humoral responses are key in blood-stage immunity. In mouse models, B cells and antibodies are important in eliminating parasites (Langhorne *et al*,1998),the mechanisms by which antibody is effective include blockade of the invasion of RBCs by merozoites (Blackman *et a*1990), antibody-dependent cellular killing mediated by cytophilic antibodies (Bouharoun *et al*,1995) and binding of antibody to parasite-induced molecules on the RBC surface, leading to greater clearance of infected RBCs (Bull *et al*,*1998*).

studies in humans and mice indicate an important role for mononuclear phagocytes in innate immunity to malaria due to their ability to phagocytose infected erythrocytes in the absence of cytophilic or opsonizing malaria-specific antibody (Serghides *et al*,2003).

Additionally, previous studies demonstrate that mouse DC subsets differentially produce cytokines to malaria parasites. Bone-marrow-derived DCs, macrophages and B cells isolated from immune mice have all been shown to have the capacity to present malaria antigens to T cells (Quin *et al*,2001). Interestingly, in *Plasmodium chabaudi* malaria

infection, both CD8α†DCs and CD8α¯ DCs promote Th1 by inducing IFN- y production in CD4 T cells at the early stages of infection (Sponaas *et al*, 2006). However, only CD8α¯ DCs induce CD4 T cells to produce IL-4 and IL-10, promoting Th1 to Th2 switching at the acute phase of infection (Sponaas *et al*,2006). Thus, the differential cytokine responses by DC subsets observed here appear to be related to the modulation of Th1 and Th2 development during the course of malaria infection.

2-Leishmaniasis

Leishmaniasis is a vector-borne infection caused by parasitic protozoans of the genus Leishmania that are transmitted to humans through the bite of an infected female phlebotomine sand fly. Among over 800 species of sand fly, 98 are proven or suspected vectors of human leishmaniases; these include 42 Phlebotomus species in the Old World and 56 Lutzomyia species in the New World (Maroli *et al,* 2013). Leishmania parasites cause three forms of leishmaniases according to the localization of the parasites in mammalian tissues, notably visceral, cutaneous, and mucosal leishmaniasis. The outcome of infection depends on the species of Leishmania parasites and the host's immune responses (Roberts, 2006). CL is the most widespread form and establishes as skin lesions that can recover spontaneously. VL is the most acute form of the disease and, left untreated, is typically fatal(Thakur& Kumar,1992). According to the world health organization (WHO) reports, leishmaniasis affects 12 million people worldwide and is approximately to cause 20,000-40,000 deaths annually (Alvar *et al*, 2006-2012). The disease is widespread in the tropical and subtropical areas and found in 98 countries in Europe, Africa, Asia and America (Alvar *et al*,2012) .

In the Eastern Mediterranean Region (EMR) of the World Health Organization (WHO), leishmaniasis is a major public health problem. Cutaneous and visceral leishmaniasis mainly appears in 14 out of 22 countries of the area (Postigo, 2010). Cutaneous and visceral leishmaniases are a significant human health risk for many of coastal and interior Libya. Visceral leishmaniasis appear sporadically in Tripoli and eastern parts of the country, with newly identified foci increasing south near the border with Chad (El-Buni *et al*, 1993). In addition, at least 13,000 cases were reported during the early 1970s through the 1990s, transmission of the disease from development projects and cutaneous leishmaniasis cultivation projects to villages. The most important agent of leishmaniasis in Libya is *L. major* MON-25 (Annajar, 1999).

Regarding of infection, there are two common types of CL; Zoonotic cutaneous leishmaniasis (ZCL) caused by *L. major* and *L. infantum*, and anthroponotic cutaneous leishmaniasis (ACL) caused by *L. tropica* in urban areas (Postigo, 2010). In Libya, cutaneous leishmaniasis is almost exclusively prevalent in the northwest regions where *L Major* is the dominant causative species followed by *L.tropica* (Amro *et al*, 2012). *L.infantum* is hypo-endemic and limited to young persons under 20 years old (Belal *et al*, 2012) . The reservoirs host of *L.major* in Libya *Meriones spp* (gerbils jirds and *Psammomys obesus* (sand rat) with *Phlebotomus papatasi* as the transmitting vector (Alvar *et al*, 2012; Ashford *et al*, 1977). Molecular identification studies have recently reported that cases caused by *L. tropica* and *L. infantum* were common in certain regions of northwest Libya, such as Misurata, Al Jabal Al Gharbi, Nalut and Tarhuna (Amro *et al*, 2012 ; Amro *et al*, 2017; Belal *et al*, 2012; Abdellatif *et al*, 2013).

Climate variability may have different impact in the transmission of leishmaniasis depending on the particular vectors and the various Leishmania species in different regions of the world (Cárdenas *et al*,2004; Rodriguez-Morales, 2005; Cross *et al*, 1996). The spreading of the vector depends on the environmental situations. Temperature is one of the most important factors in the survival, activity, development and behavior (Kasap, 2005). The optimal temperature for the development of sand flies and Leishmania parasites is approximately 25 °C (Killick-Kendrick & Killick-Kendrick, 1987 ; Rioux *et al*, 1985). Seasonal distribution of cutaneous leishmaniasis was notarized ,and has exposed a peak during November-February (Amro *et al*, 2012; Belal *et al*, 2012).

Totally cases of cutaneous leishmaniasis in Libya found exclusively from the northwestern area of the country. These areas have a typical Mediterranean coastal climate in the higher northern regions such as Tripoli, and a semi-arid and dry climate in Al Jabal Al Gharbi and Wadi al-Hayat in the south. Like several other countries about the Mediterranean Sea, climatic and environmental situations and expansion of agricultural activities in these regions may be appropriate, for transmission of Leishmania (Bousslimi e*tal*, 2010; Ben-Ahmed *etal.*, 2009)

Leishmaniases are known as dynamic diseases influenced by various factors (Antoniou *et al*, 2013). it is suspected that risk factors for this infectious illness, have increased due to armed and political conflicts since 2011 as well as discontinuation of the national Leishmania control program aimed at preventing theprevalence, of cutaneous leishmaniasis to non-endemic regions. (Amro *et al*, 2012; Amro *et al*, 2017) Additionally, other factors like socio-economic situation,, lifestyle, persons behaviour through the illness transmission months during summer, existence of new

agriculture developments, building work, and waste collection may also have a role in trasmission of cutaneous leishmaniasis (Bounoua *et al*,2013; Alvar *et al,* 2012; Salam *et al,2014*). Cutaneous leishmaniasis affects all age groups with sligh thigher ratio in males than females this could be related to the outdoor activities of men (working duties and leisure Amro *et al,* 2012; Mostafa *et al*,2016).

Leishmania sp. have a digenetic lifecycle in which the parasite exists in two stages. One is the amastigote form, which is an intracellular non-motile form found in the phagocytes and circulatory systems of the mammalian hosts. The other stage, the promastigote, is an elongated extracellular flagellated form that is found in the alimentary tract of infected female sand flies. All parasite species undergo important changes in their morphology while residing in their invertebrate host and this influences their virulence and partially circumvents the protective immune response of the host. Compared with some other parasites, Leishmania uses an intracellular replication strategy to avoid being killed by the host's immune system; i.e., it hides inside a host cell and thereby influences the progression of the lesions (Vannier *et al*, 2002).

Infection and immune evasion mechanism macrophage is a primary phagocyte that plays host for Leishmania (Reiner & Locksley,1995). Activation of macrophage is a primary mechanism to eliminate the Leishmania parasite presumably mediated by toxicmetabolites of oxygen, which may include super oxide anion (O2), hydrogen peroxide (H2O2) and nitric oxide (Assreuy *et al*,1994). Activated macrophages produce different cytokines like TNFα (Reimann *et al*,1994), IL-6 (Hirohashi & Morrison,1996), IL-18 (Kim *et al*,2000) IL-12 (Kato *et al*,1997) and IFN-γ (Munder *et al*,1998). IL-12 is an effective adjuvant and a

prerequisite for Th1 type of immune response in most of intracellular parasitic infections (Afonso *et al*,1994).

The main producers of IL-12 are antigen presenting cells for example macrophages and dendritic cells, which produce IL-12 through CD40 and CD40L interactions (Kato *et al*,1996). CD40L present on the surface activated. IL-18 is another proinflammatory cytokine that helped in evoking Th1 immune response particularly in collaboration with IL-12 most effectively (Tsuji *et al*,1999). IL-12 and IL-18 both induced IFN-γ from murine macrophage in combination but either one alone was not sufficed to induce IFN-γ from the peritoneal macrophages (Munder *et al*,1998). . The most completely studied anti-leishmanial cytokine is TNF-α . TNF-α synergizes with IFN-γ in the induction of iNOS and NO production by macrophages in vitro(Deng *et al*,1993). Additional cytokines that, with IFN-γ, synergistically mediate activation of macrophage to clear *L. major* include IL-2 (Belosevic *et al*,1990), IL-4 (Bogdan *et al*, 1991), and IL-7 (Gessner *et al*,1993).

Neutrophils or polymorphonuclear neutrophils (PMNs), the first cells to migrate to the site of infection or injured tissue (Woodman *et al*,1998), function as a primary effector or phagocytic cells, phogocytosing Leishmania (Pearson & Steigbigel, 1981). Leishmania phagocytosed neutrophils start secreting the chemokines like IL-8 (Laufs *et al*, 2002) essential to bring the more neutrophils at the site of infection. Two to three days later, the second wave of cells, monocytes /macrophages, enters the site of infection (MuÈller *et al*, 2001). It has been shown that Leishmania promastigotes can induce the migration of human PMNs by releasing a factor (Leishmania chemotactic factor, LCF) with potent chemotactic activity on neutrophils (van Zandbergen *et al*, 2002). It was shown that co-incubation of Leishmania with PMNs

inhibits the CXC-chemokine interferon gamma (IFN-γ)- inducible protein-10 (IP-10) (van Zandbergen *et al*, 2002) suggesting that Leishmania inhibited the Th1 or NK cell activity.

Dendritic cells as an efficient antigen presenting cells (APCs) and Leishmania infection Incubation of Leishmania promastigotes with dendritic cells induced early IL-12 production in vitro, which might be contributed from the pre existing pool of IL-12 p70 which was secreted soon after ligation of any microbial product (Quinones *et al*, 2000), suggesting the role of DCs in the initiation of T cell immune response in Leishmania infection. It is also reported that uptake of Leishmania amastigotes by skin derived DCs induces IL-12 p70, (Kelsall.*et.al*, 2002).

Since T cells come later during infection, it is possible that parasite modulates its host in terms of signaling or antigen presentation for its own benefit and induces factors that provide disease progressive environment and prime T cells for Th2 differentiation. It is also possible that parasites starts modulating the macrophages at the time of entry and later on modulated parasitized macrophages interact with T cells and may induce IL-4 and disease inducing factors from T cells that help in disease progression and parasite survival in susceptible host. (Mathur *et al*, 2004) . This suggests the crucial role of IL-10 in disease initiation independent of T cells and in disease progression later on in CD40 combination with IL-4. (Mathur *et al*, 2004). T cells (Renard *et al*, 1994) interacts with on the macrophages and induces IL-12 expression and production (Yamane *et al*,1999). CD40 ligation induces IL-12, which in turn activates the T cell to produce IFN-γ and leishmanicidal function.

3-Schistosomiasis

Schistosomiasis, also known as bilharzia, happens to be one of the groups of neglected tropical diseases(NTDs), ranked second most prevalent among NTDs (Oyinloye *etal,*2014; Adenowo *etal,* 2015). Schistosomiasis is a parasitic infection caused by blood flukes of the genus Schistosoma. Transmission occurs through skin penetration of infective cercariae on exposure to snail-infested waters (Colley *etal,*1998).The life cycles of all the Schistosoma spp. are all similar yet very complex as the parasite alternates between two hosts: the intermediate (snail) and the definitive (such as human, bovines and domestic cattle) host(Oyinloye.*etal,* 2014; https://www.cdc.gov/parasites/schistosomiasis/gen_info/faqs.htm). In the early phase schistosomiasis may be completely asymptomatic, while hepatic, intestinal, and genito-urinary complications have been reported in chronic patients (Alirol *etal,* 2015). Schistosoma infection has been estimated to affect over 218 million people who are in need of preventive treatment and over 800 million people are at high risk infection in not less than of the 78countries of the world Over the years; most of the secountries fall with in Africa, Eastern Asia and South America (WHO, 2017).

There are six types of *schistosomes* that affect humans all over the world (Drudge-Coates& Turner, 2013) *Schistosoma intercalatum*, *Schistosoma mekongi*, *Schistosoma japonicum* and *Schistosoma guineesis* are localized to specific settings whilst, *Schistosoma haematobium* and *Schistosoma mansoni* are wide spread (Kulinkina, 2017). Most African countries and some countries in the Middle East are endemic for *Schistosoma haematobium*, *S mansoni*, *S intercalatum* has been reported in ten countries in Africa (Chitsulo *etal,* 2000). In poor rural areas, the

disease is spread, in agricultural and living communities and among those who engage in daily domestic, occupational, and recreational activities within waterbodies Children are especially at risk of illness when swimming or playing in contaminated water (Gundamaraju, 2014).

Libya has an ancient history of Schistosomiasis infections. The first case was reported in 1925 in the Ghat region, followed by another report in 1932 from Wadi al-Shati in the Fezzan region in the southern part of Libya (El-Gíndy & El- Edríssy, 1975). Recently, Darnah has been specific as a localized area of risk for *S. haematobium* (IAMAT,2012). The snail intermediate hosts for *S. haematobium* in Libya are *Bulinus truncatus* and *Bulinus globosus*., was first recognized in the Ghat region in 1957, for many years no human infection was registered, However the snail intermediate host *B. truncatus* is known to be endemic in one remaining region, in Alfogaha and *S. mansoni*, transmitted by *Biomphalaria alexandrina* snails, is currently locally endemic at the Taourga region (Jones, 2015;WHO,2007). Addition to Infections of S.haematobium are occurring in Sebha, and more attention should be paid to the diagnosis, prevalence of snail host, and people must be advised on the public health of the importance of urinary Schistosomiasis in Libya (Abdulrahman *etal*, 2007). Prevalence in the Taourga oasis society was as rise as 39.8% in school-aged children in 1999 (WHO,2007). *Schistosoma haematobium* and *S. mansoni* are focally endemic in Libya, and prevalence has been evaluated at 5% since 2003(Rollinson *et al*, 2013).

Like numerous other parasitic helminthes, the distribution and intensity of schistosomiasis are changing by area,, mainly due to the carefully limited ecological conditions for the habitat of the vector snails and variable conditions of habitat in connection to annual rainfall , unforeseen drought, irrigation schemes and other water development

venture, (Kaneko *et al*, 1991). In climate change scenarios, especially when environmental warming is observed, the epidemiology of schistosomiasis will be directly affected. (Githeko *et al*, 2000). previous studies concerning the relationship between temperature with the development of the Schistosoma on the mollusc indicate as optimal threshold temperatures between 23 °C and 28 °C (Standen, 1951; Stirewalt, 1954). The country is predominate, by large areas of hot, dry and sandy regions with high-salinity water. These conditions are not conducive, for widespread colonization of the snail intermediate host, so their distribution is intermittent (Doumenge & Mott ,1984).

The spread and transmission of the different types of schistosomiasis is usually associated with poor environmental and sanitary conditions, usually affecting people living in unfavorable socio-economic conditions. (Calasans*et al*, 2018; WHO,2006). The burden of the disease is felt considerably by school-aged (SAC) and pre-school-aged children. National control campaigns offering mass drug administration (MDA) of praziquantel for children aged 5–15 often struggle with logistical challenges due to the remoteness of some endemic regions (Sheehy *etal*,2021).

1990 In Libya, a control program was started that included screening and treatment of the entire population with praziquantel chemotherapy, snail control, and health education, and as of 2007, the prevalence of the disease in the community had decreased to 3%. Comprehensive treatment and biological control of snails are planned on an annual basis until the disease is eradicated (Jones, 2015;WHO,2007) Data is scant and inconsistent on overall schistosomiasis trends in Libya. However, as of 2013, Libya did not require the use of preventative chemotherapy to treat schistosomiasis (saadawi *etal*, 2021).

Immune responses during schistosomiasis can be thought of in terms of three topics: immunopathogenesis, resistance to reinfection, and immunodiagnostics. All three are affected by the development and establishment of chronic infection in the presence of chronic antigenic exposure. Faced with multiple antibody and cellular immune responses, adult schistosome worms persist in the bloodstream for decades, seemingly impervious to attack from immune effector mechanisms.

The immunopathology and immunoregulation associated with morbidity of schistosomiasis has been studied extensively. However, the immune mechanisms related to resistance, to reinfection, or in response to candidate vaccines are much less defined. Although adult worms are refractory to immune attack, immature, developing worms (skin-stage and lung-stage schistosomulae) are the probable targets of protective immunity.(Wilson,2009) .

This immune evasion by adult schistosomes is a result of several mechanisms (Keating, 2006) and leads to a stalemate: the worms thrive and the host survives. Indeed, morbidity seems to be associated with immunopathology against only eggs that remain trapped in tissues. That immune responses are essential for effective treatment (Doenhoff *et al*,1991) and that many anti-worm and anti-egg antibody responses are detected by serodiagnostic assays shows that adult worm antigens are readily detected by the host immune system, although intact worms effectively evade immune attack. Although the responsible antigens and host immune responses are not fully defined, resistance to reinfection is consistently associated with IgE antibodies against worm antigens,(Fitzsimmons *et al*,2012) low concentrations of IgG4 antibodies to worm antigens, and high blood eosinophilia.(Mitchell *et al*, 2012) During acute illness, which is less well studied than chronic disease , there is a

measurable level of tumour-necrosis factor (TNF) in the plasma, and peripheral-blood mononuclear cells (PBMCs) produce large quantities of TNF, interleukin-1 (IL-1) and IL-6 (de Jesus *et al* ,2002). Notably, cytokine production by PBMCs after stimulation with parasite antigen reflects a dominant TH1 (TH1), rather than TH2, response (de Jesus *et al*,2002) . Presumably, in the natural progression of the disease, the developing egg-antigen induced TH2 response down regulates the production and effector functions of these pro-inflammatory mediators ; the production of IL-10 during this period might have a crucial role in this process (Montenegro *et al* ,1999) . The main TH2 cytokine .that is responsible for fibrosis is IL-13. Mediators that are associated with TH1 responses, such as interferon-γ (IFN-γ),IL-12, TNF and NO can prevent IL-13-mediated fibrosis (Hesse *et al*,2001). Infection intensity is one factor that can affect the severity of chronic schistosomatic disease, perhaps particularly in children (Mohamed *et al*,1999) . However, it seems to be more important whether an infected individual is genetically predisposed to disease (Mohamed *et al*,1999). Patients with hepatosplenomegaly owing to *S. mansoni* infection were found to have a TH1-like response and high plasma levels of TNF receptor I (TNFRI) and TNFRII, whereas individuals who had less severe disease but similarly intense infections (as assessed by counting the number of eggs in faecal samples) had TH2 responses and low plasma levels of soluble TNFR (Mwatha *et al* ,1998). So, an important function of the TH2 response during infection is to produce cytokines that can prevent or dampen the production or effector functions of potentially dangerous inflammatory mediators. whereas IL-10 might have an important regulatory role in schistosomiasis, preventing the development of excessive TH1- and TH2-

mediated pathologies. B cells were shown to be essential for the induction of a TH2 response during infection ((Hernandez *et al*, 1997). .

Conclusions

Vector-borne parasites represent one of the most important issues in public health and are among the vector-borne diseases that continue to contribute significantly to the global burden of disease. These parasitic diseases such as malaria, leishmaniasis and schistosomiasis that people suffer from these diseases occur as a result of their contact with infection through Abite arthropods which include mosquitoes and sandflies. As well as exposure to infected aquatic snails. Climate change are particular likely to affect vector borne parasitic diseases . The impact of climate on vector borne parasitic diseases can be explained by the fact that the arthropod vectors of these diseases are ectothermic (cold-blooded) and, therefore, that are closely related with climate as well as effects on the pathogen, transmission cycles and re-emergence of vector-borne parasitic diseases. climate change has been a primary driver thus far on a local and global scale. additional to other drivers such as ecological , socio-economic and public health systems are important contributors to transmission of vector-borne epidemic diseases. The most urgent need today is to ensure enhanced vector -borne parasitic disease control efforts that integrate the management of risks posed by climate change. The development of policies and programmes that decrease the influence of vector-borne parasitic diseases by diagnosing and treating diseases early , vector control, vaccinating, the re-design of national healthcare system components (human resources, facilities, health information systems , technology and health policies. The need to espouse, mechanisms that will expedite and facilitate collaborations between health and

environment ministries and empowering public health practitioners,researchers to cooperate in casting integrated strategies .

Despite available drugs , unfortunately, many parasites develop resistance , thereby frustrating, the effectiveness of therapeutic strategies. Understanding the immune mechanism of host-parasite interactions will advance knowledge of the mechanisms of VBPD to track relevant immune and parasite molecules that ensure protection or lead to disease. therefore, this is a much-needed and important field of research to improvement and development of treatments and which may flatten the way for vector control .

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