

The tropics encompass almost one third of earth's landmass and are characterized by a hot and humid climate, usually throughout the year. The tropics display a vast number of health problems, which are related to the warm climate, overcrowding and socioeconomic factors. Kidney Injury in the tropical areas has been always an important health related concern. Acute kidney injury (AKI) in tropics is influenced by number of factors like infections, use of unsafe drinking water, exposure to environmental toxins, poverty and inadequate sanitation. Tropical AKI is also influenced by a relative state of hypovolemia due to excess sweating and peripheral vasodilatation due to hot and humid climate. Heavy rainfall creates a favourable environment for survival of organisms causing and transmitting infections like malaria, dengue etc.

The main causes of kidney injury in tropics are due to bacterial, viral or parasitic infections like malaria, dengue, leptospirosis, scrub typhus, acute gastroenteritis etc. Though these infections have been typically considered as a cause of AKI, the residual damage which may be subclinical can lead to chronic kidney disease. In a recent study from a large tertiary care hospital in South India, AKI was seen in 41.1% of patients with tropical infections, the most common causes being scrub typhus, malaria, salmonellosis, dengue and leptospirosis. Various infections causing tropical nephropathy are as under.

MALARIA

Malaria is a protozoal disease of extreme epidemiological concern because of its greater prevalence in tropical areas. Renal involvement is more frequently associated with infection by *P. falciparum* and *P. malariae*. AKI is a very devastating manifestation of malaria reported in about 3% cases of malaria. The incidence is particularly high in cases of severe *P. falciparum* malaria where it can be seen in up to 60% patients.

The parasite inhabitates red blood cells (RBC) and alters their morphology and metabolism. It induces formation of membrane protuberances or "knobs" on the erythrocyte surface. *P. falciparum* infected cells adhere to the vascular endothelium and uninfected RBCs to form rosettes. This promotes cytoadherence between RBCs, platelets and endothelium leading on to microcirculatory failure and organ dysfunction. Immune system activation also leads to endothelial injury and immune complex deposition. Proinflammatory cytokines, reactive oxygen species and vasoactive mediators lead to haemodynamic changes causing decreased renal blood flow and glomerular filtration rate. The most common manifestation of

kidney injury in malaria is acute tubular necrosis (ATN). Acute tubulointerstitial nephritis, diffuse proliferative glomerulonephritis and mesangioproliferative glomerulonephritis are other important manifestations.

Acute malarial nephropathy and chronic malarial nephropathy are two major clinical syndromes associated with kidney involvement in malaria. Acute malarial nephropathy presents as AKI seen in falciparum malaria while chronic malarial nephropathy, also known as quartan malarial nephropathy is actually a glomerulopathy usually seen in children. It is mostly caused by *P. malariae*.

AKI in malaria is usually seen by the end of first week and is non-oliguric in 50-75% of cases. The laboratory diagnosis can be established by the demonstration of sexual forms of the parasite in peripheral blood smears. Rapid diagnostic immunological tests are currently available. Urinalysis can reveal microalbuminuria, mild to moderate proteinuria and hyaline & cellular casts. Renal histology shows ATN predominantly affecting the distal tubules. Tubular changes include haemosiderin granular deposits, haemoglobin casts, interstitial oedema and mononuclear cell interstitial infiltrates. Mortality from malarial AKI varies between 15% and 50%. Dialysis when initiated early in the course of treatment has a very good outcome.

DENGUE

Dengue is a viral haemorrhagic fever caused by a dengue flavivirus and transmitted by aedes aegypti mosquitoes. The South East Asia and Western Pacific regions in tropics bear about 70% of the total global burden of this disease. Dengue virus infection may manifest as undifferentiated fever, dengue fever, dengue haemorrhagic fever (DHF), or dengue shock syndrome (DSS). Renal involvement is a well-known complication of dengue fever and can manifest as AKI, proteinuria, glomerulonephritis and haemolytic uraemic syndrome. DHF and DSS are more commonly associated with renal injury and AKI is an independent predictor of mortality. The reported frequency of dengue associated AKI is extremely variable, ranging from 1% to approximately 30%. The main causes of AKI include shock secondary to haemorrhage or dengue shock syndrome and rhabdomyolysis leading to acute tubular necrosis. Renal failure can also occur due to the direct involvement of the kidneys without shock and rhabdomyolysis. Diagnosis mainly depends upon the serological tests available. There is no specific treatment and drugs available for dengue fever. Therefore prompt

LEPTOSPIROSIS

Leptospirosis is a worldwide distributed zoonotic disease caused by spirochetes of the genus *Leptospira*. Human infection occurs through contact of abraded skin or mucous membrane with infected tissue or urine of animal host or indirectly through contaminated water, soil or vegetation.

Leptospirosis has a wide spectrum of clinical presentation ranging from asymptomatic condition to a severe multisystem disease. Its clinical presentation may occur as: (i) a non-jaundice, febrile, auto-limited disease (ii) Weil's syndrome with triad of jaundice, AKI and haemorrhages. The acute leptospiremic phase is characterized by fever of 3-10 days and the immune phase occurs after a relative asymptomatic period of 1-3 days during which nephropathy occurs. AKI associated with leptospirosis is non oliguric. Incidence of renal involvement in severe leptospirosis varies from 40% to 60%.

There are various factors responsible for AKI seen in severe leptospirosis. The pathogenic mechanisms suggested include bacterial invasion, inflammatory processes, hemodynamic alterations, and the direct toxicity of bacterial products. Tubulointerstitial nephritis due to direct infection of the kidneys is the predominant mechanism of renal involvement.

The diagnosis is possible during the initial febrile period by visualizing leptospira by direct examination of blood, or by its culture. During the immune phase serological tests may be helpful. Renal biopsy reveals interstitial oedema and infiltration with mononuclear cells and few eosinophils. Acute tubular necrosis primarily affecting the proximal tubules is present and glomeruli are usually spared.

The treatment of severe leptospirosis mainly involves the use of antibiotics and haemodialysis. Early dialysis and treatment of leptospira associated renal injury seems to be helpful in reducing mortality.

SCRUB TYPHUS

Scrub typhus is an acute febrile illness and zoonosis caused by orientia *Tsutsugamushi*, transmitted to humans by the bite of the larva of trombiculid mites. The disease is widely spread all over India and has been reported in several parts of the country.

Scrub typhus is mostly seen during and after the rainy season, mainly affects people who work outside and are exposed to shrubs and vegetation, on which the vector thrives. Presence of a primary papular lesion which enlarges undergoes central necrosis, and crusts to form a flat black eschar is a classical presentation of the disease. This is associated with regional and later generalized lymphadenopathy. The reported incidence of renal failure caused by scrub typhus varies from 10.5% to 42.6%. In the Indian subcontinent AKI has been reported in about 30 to 60% of the patients of scrub typhus.

There are various explanations behind the pathophysiology of AKI in scrub typhus. Vasculitis of the small blood vessels, DIC, hypovolemia and shock causing renal hypoperfusion, injury to vascular endothelium are main mechanisms of renal involvement. Diagnosis of scrub typhus can be made by a number of tests like Weil Felix test, ELISA, western blot along with renal biopsy. Indirect Immunofluorescence remains the golden standard. Renal failure caused by scrub typhus is commonly known to be reversible with the appropriate antibiotic therapy, and rarely requires maintenance haemodialysis.

DIARRHOEAL DISEASES

Diarrhoeal diseases are widely prevalent in the tropical developing countries due to factors like poor socio-economic conditions and lack of clean water supply. Causative organisms include bacterias including *Escherichia coli*, *Campylobacter*, *Salmonella*, *Shigella* & *Vibrio Cholera*, viruses like Rotavirus, Norovirus, Adenovirus & Astrovirus and parasites like *Giardia lamblia*, *Entamoeba histolytica* & *Cryptosporidium*. Diarrhoeal diseases account for most cases of AKI in children in India. Acute tubular necrosis is the commonest cause of renal injury mainly due to hypovolemia and shock. AKI is usually of oliguric type and have metabolic acidosis out of proportion to renal injury. Management approach includes adequate hydration and correction for intra and extravascular volume deficit produced by fluid losses in diarrhoeas.

OTHER INFECTIONS

Some other bacterial, fungal, parasitic and viral infectious diseases are needed to be mentioned which are associated with significant renal involvement. Renal injury in HIV infected patients in the form of acute tubular necrosis is usually secondary to sepsis, hypotension, dehydration and nephrotoxins. Clinically renal involvement may manifest as acute kidney injury, HIV associated nephropathy, HIV related immune complex diseases, nephropathy secondary to ART and diseases related to common comorbidities.

Kidney involvement has been demonstrated with chronic diseases like leprosy and tuberculosis. Renal injury in these diseases can lead to AKI and further progress to CKD and manifests as proteinuria, haematuria, urinary concentration and acidification defects, acute tubular necrosis, diffuse proliferative lesion and amyloidosis. Haemolytic uraemic syndrome (HUS) is another common cause of kidney injury in children in most tropical countries. In India, HUS is responsible for 35-41% of all cases of AKI in children. Schistosomiasis is another important tropical parasitic infection that can involve the kidneys in the form of immune complex glomerulonephritis, also known as schistosomal nephropathy. Fungal infections like renal mucormycosis caused by zygomycetes fungi can lead to kidney injury. It produces organ involvement through vascular invasion and thrombosis resulting in infarction and necrosis of the affected organ. Mostly it involves bilateral kidneys and present with anuric AKI and the outcome is usually fatal.

Visceral leishmaniasis also known as kala azar is a chronic lethal parasitic disease, caused by Leishmania parasite. Kidney involvement in chronic leishmaniasis is frequent, and associated with increased mortality. Patients usually present with proteinuria, microscopic haematuria and leukocyturia. Renal involvement manifests in various forms like AKI, urinary concentration and acidification defect, nephritic syndrome or nephrotic syndrome.

CONCLUSION

Kidney involvement in tropical countries is a challenging problem. The late presentation of patients to health care facilities and the lack of resources in developing countries further make the situation worse. Coordinated and integrated approach from the primary to tertiary health care facilities is very crucial and can reduce the disease burden. Monitoring to assess renal injury, control of preventable risk factors and timely intervention with appropriate antibiotics & early use of renal replacement therapy once kidney injury have proven effective in preventing the long term complications.

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