INFECTIOUS DISEASES AND THE KIDNEY

By Mayuri Trivedi and Itunu Owoyemi

Infectious diseases have been known to be the cause and effect of kidney diseases for a long time. Kidney damage occurs through direct invasion or via immune-mediated injury. Patients with underlying kidney diseases, including kidney transplant recipients, are known to have a greater chance of serious and atypical infections. Interestingly, the spectrum of infections and kidney diseases varies widely across the world. Kidney diseases depend on local epidemiological, environmental, and socioeconomic factors. Immune diseases caused by infections are still rampant in many parts of the world with very little data directing their treatment protocols.

The development of highly effective therapies for treating infections has also led to increased utilization of organs from donors with infections such as hepatitis B and C.

In this special issue of *Kidney News*, we highlight the interesting spectrum of infections and kidney diseases around the world. ■

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Plasmodium Vivax and the Kidney: The Not-So-Benign Parasite

By Sayali B. Thakare

Despite consistent public health efforts for over half a century for mitigation of its spread, malaria—caused by five species of plasmodium—remains a widely prevalent disease affecting 84 countries as of today (1). Newer challenges continue to plague malaria control programs, with a recent example being disruption of services due to the COVID-19 pandemic. An undeniable rise in the incidence, morbidity, and mortality attributable to *Plasmodium vivax* in the last decade has led to a renewed interest in its pathogenicity and an acute need of realistic estimates of its global disease burden (2, 3).

P. vivax is the most geographically spread of malarial parasites. Although the World Health Organization (WHO) captures a decline in case proportions of *P. vivax* (1), an increasing body of evidence emphasizes the not-so-benign nature of vivax malaria. *P. vivax* has broken the evolutionary barrier and is increasingly reported from Duffy blood group-negative sub-Saharan Africa (4, 5). The WHO's global technical strategy for malaria operates under a highly ambitious target of eliminating malaria from 35 countries by 2030 and reducing incidence and mortality rates worldwide by 90%. *P. vivax* has been recognized as a major epidemiological challenge to achieving these targets, chiefly due to key differences in parasite and vector biology (3) (Table 1).

Likewise, host factors contribute to enhanced pathogenicity in vivax malaria. Pronounced inflammatory response despite low parasitemia (6); higher cytokine production (interferon-γ/interleukin-10 ratio and C-reactive protein) (7); endothelial stimulation (8); capillary sequestration (8); and persistent hepatic, splenic, and bone marrow reservoir formation lead to severe disease with multi-organ dysfunction not unlike that with *Plasmodium falciparum*. *P. vivax* disproportionately affects other high-risk groups, such as pregnant women and children, in areas of high transmission (3, 9–11).

Cytoadherence leading to formation of rosettes and clumps is implicated in impaired microcirculation and organ damage in vivax malaria. Coupled with hypovolemia and shock, this contributes to acute kidney injury (AKI) (Figure 1). Malarial kidney biopsies show acute tubular necrosis, acute cortical necrosis, thrombotic microangiopathy, glomerulonephritis, or tubulo-interstitial nephritis (12–17). Postinfectious glomerulonephritis (18) and crescentic glomerulonephritis (19) have also been reported. Recent studies have demonstrated the presence of *P. vivax* DNA in kidney biopsies (14). Sequestrated parasites in donor organs can lead to symptomatic disease in transplant recipients (20–23). Curiously, one of the early reports describes synchronous, high-grade fever in two kidney transplant recipients attributed to *P. vivax* acquired from the same deceased donor (24).

Multiple large case series of malarial AKI from the Indian subcontinent report the proportion of *P. vivax* as 15.2% (25), 20.4% (26), 41.79% (27), and 54.4% (28). Renal replacement therapy was required in 33.3%–76.6% of these cases. Mortality was observed to be 15%–20%. Predictive factors for mortality var-

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