Laboratory Diagnostic Link to Infections: An Update

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Abstract- This review article highlights the various organs affected due to infection by a host of microorganisms resulting in the elevation of Liver Function Tests particularly liver enzymes due to infections by falciparum malaria, parasites, viral infections, dengue, measles, tuberculosis, anaplasmosis etc. Kidney function progressively decrease in infections due to measles, tetanus, staphylococcus, malaria, MRSA viruses and cardiac function tests are elevated in pneumonia. In bacterial meningitis CSF analytes are altered, while HIV, HCV, HbsAG infections are said to affect every organ. We have used recent reach findings during the last 13 years and hence this review article will certainly serve as a platform for exploring new avenues for research in this interesting field.

Index Terms- Malaria, LFT, HIV, AST, ALT, CKD, CSF.

I. INTRODUCTION

Microorganism are excellent models for understanding cell function in higher organisms including humans and the six features associated with living organisms are metabolism, reproduction, differentiation, communication, involvement and evolution. All these above are associated with chemical reactions and microbes change the clinical and physical properties of their habitats. Harmful microorganisms cause infection which in turn affect chemical reactions. Although microbiology tests identify the type of infections but it does not pinpoint the alterations in biochemical analytes and the organs which are affected. This paper is therefore an attempt to identify the alterations in biochemical analytes organ wise and the role of measured blood analytes to the degree of infection. This will help to evaluate the incubation period of microorganism infections in humans, its survival rate based on analytes change there by bringing biochemical investigation to assess the infectious status.

Malaria

The mean level of most of the biochemical liver function test parameters were below the normal reference ranges, and a highly significant difference was observed between pregnant women with malaria, and their controls, in the level of aspartate aminotransferase (AST), Alanine transaminase (ALT), total protein, albumin and globulin, but not in the levels of bilirubin fractions.¹¹ Hepatic dysfunction in acute Plasmodium falciparum malaria ranged from mild elevation of liver enzymes to acute hepatitis (ALT>10 times of normal level). It indicates severe illness with high frequency of complication and mortality rates.² Children with cerebral malaria had a higher rate and more severe course of acute renal failure than children with mild malaria. Today, there is no evidence of a dominant role of steroid-resistant and chronic "malarial glomerulopathies" in children with a nephrotic syndrome in Africa. Acute Renal Failure (ARF) was a frequent and serious complication of falciparum malaria in non-immune adults. However, recently it has been reported more often in semi-immune African children with associated morbidity and mortality.³

Exchange transfusion is helpful in patients with heavy parasitemia, those with severe jaundice, and those with the Systemic Inflammatory Response syndrome with an overall reduction of mortality by 20%. Apheresis has been reported to successfully support anuric patients with cerebral and pulmonary complications.⁴ Falciparum malaria associated with ARF is a life threatening condition, but early presentation and intervention with appropriate anti-malarial and dialysis therapy is associated with improved survival and recovery of renal function. Early dialysis treatment in patients with severe falciparum malaria and signs of deteriorating renal function is recommended.⁵ P. vivax malaria can cause ARF, which occurs more commonly in P. falciparum malaria. Renal ischemia is the dominant pathogenic mechanism that results in acute tubular necrosis. The prognosis of ARF in P. vivax malaria is favorable.⁶ Malaria is associated with ARF, which occurs most commonly in plasmodium falciparum infected patients. Early diagnosis and prompt dialysis with supportive management can reduce mortality and enhance recovery of renal function.⁷

Parasite levels had a significant influence on metabolic acidosis but not on CI. Alterations related to cardiac function, hemoglobin levels and metabolic acidosis were most prominent in children younger than 2 years.⁸ Hypovolemia is as a major underlying cause of lactic acidosis and hypoglycemia in African children with severe falciparum malaria. These deleterious metabolic conditions contribute to myocardial affection which was evident but not predictive per se of fatal outcome. Suggesting impaired cardiac function contributing to clinical manifestations in P. falciparum malaria.⁹ Findings may be relevant for fluid management and should be further explored in endemic regions.¹⁰ Increased CI reflecting high output status is associated with low hemoglobin levels while metabolic acidosis is linked to parasite levels.¹¹ Cardiovascular manifestations in severe falciparum malaria include mainly hypotension and acute pulmonary oedema.In addition to severe falciparum parasitaemia
and sequestration, secondary infections, severe anemia, hyperpyrexia, dehydration/fluid overload, metabolic acidosis, hypoxia, and disseminated intravascular coagulation can also contribute to the cardiovascular problems in malaria. Malaria can also complicate pre-existing cardiac decompensation and may even prove fatal for patients with compromised heart.

Liver enzymes increase in malaria parasitaemia to a level dependent on the degree of parasitaemia and also suggest that the liver is involved in the pathophysiology of malaria.

Patients with Plasmodium falciparum malaria have high incidence of subclinical haemorrhagical disorders which do not amount to overt DIC but adversely affect renal function contributing to acute renal failure. There is strong evidence of hepatocyte dysfunction and hepatic encephalopathy in some of these patients, with no obvious non-malarial explanation. Current guidelines may need to be revised. Liver enzymes AST, ALT and ALP significantly increases in malaria patients as compared to control subjects. Therefore these enzymes may be useful in diagnosis of malaria subjects.

**Viral Infections**

There was a reverse correlation between liver enzyme levels and renal allograft function when analysed with univariate and linear regression analyses. This correlation increased over time. There was also a significant relation between cyclosporine blood levels and liver enzyme values in the univariate analysis. However, this relationship was attenuated over time. Elevated liver enzymes also correlated with anemia. The Liver enzyme elevation is a common finding among kidney transplant recipients. Serial monitoring of aminotransferases, particularly ALT, should be performed in all patients after kidney transplantation.

In clinical practice of rheumatoid arthritis (RA), various kinds of laboratory tests are required for diagnosis, assessment of the disease activity, assessment of complications and risk factors before starting therapy, and assessment of adverse effects during the therapy. Anemia, thrombocytopenia, and leukocytosis are common in active RA. Reactivation of hepatitis B virus (HBV) after immunosuppressive therapies is a potentially serious complication. Hbc and/or HBs antibodies should be measured before starting the therapies even if HBs antigen is negative, and appropriate interventions including measurement of HBV-DNA and starting prophylaxis (entecavir is recommended) should be performed. HBV infection with elevated ALT, rather than HBV infection alone, was associated with reduced renal function.

Reduced eGFR and albuminuria are associated with increased risk for infection-related mortality. Efforts are needed to reduce its incidence and mitigate the effects of infections among individuals with CKD. The risk of hospitalization and death with pneumonia is greater at lower eGFRs, especially in younger adults. This association may contribute to excess mortality in people with CKD. Creatinine peak was inversely correlated to GA in preterm infants born less than 32 weeks of gestational age. Neonatal rather than maternal morbidity affected Creatinine peak. In hsPDA, creatinine increase preceded ibuprofen administration. Using more sensitive and specific markers of myocardial injury, the prevalence of myocarditis during acute influenza infection is substantially lower than previously thought, whereas skeletal muscle injury is relatively common and it seems likely that this complication is rare. Patients with SARS are prone to have mild non-specific hepatitis. It seldom causes the typical symptoms of hepatitis and it is easy to be ignored in clinic.

FPG on admission could be an independent predictor for the severity of H1N1 pneumonia. Elevated FPG induced by H1N1 pneumonia is not a result of direct damage to pancreatic β-cells, but arises from various factors’ combinations caused by H1N1 virus infection.

Myocarditis can be a rare but severe complication of infectious disease and should be considered as a diagnosis in patients presenting with chest pain and elevated cardiac enzymes in the absence of underlying coronary disease. It can lead to cardiomyopathy and congestive heart failure. There are only a few reported cases of myocarditis associated with Campylobacter infection.

**Dengue**

Thrombocytopenia and elevated transaminases were observed in patients with classic dengue fever. The main laboratory abnormalities found in dengue hemorrhagic fever were thrombocytopenia, hemoconcentration and elevated transaminases, similar to severe dengue with the exception of hemoconcentration. Most laboratory abnormalities started on the 3rd day but were more evident on the 5th day with restoration of values by the 11th day; this was more prominent in under 15-year-olds and with the more severe clinical forms. These results are relevant in assessing the disease because they can be used as markers for more severe forms and can help by enabling the adaptation of the therapeutic conduct to the needs of individual patients.

Marmosets are susceptible to dengue virus (DENV) infection. However, blood parameter data and clinical signs of DENV-infected marmosets are limited. Five DENV-inoculated marmosets demonstrated thrombocytopenia, nine demonstrated leukocytopenia, and five demonstrated an increase in the levels of AST, ALT, LDH, and BUN. Additionally, seven DENV-inoculated marmosets demonstrated clinical signs including fever and decreases in activity. None of the four mock-inoculated marmosets demonstrated changes in either hematomatological or biochemical parameters. Marmosets inoculated with DENV exhibited clinical signs and changes in hematological and biochemical parameters. The results suggest that blood parameter data and clinical signs could potentially be useful markers for understanding the progress of DENV infection in studies using marmosets. There is no specific treatment for dengue-associated fulminant liver failure. After administration of intravenous N-acetylcysteine, a rapid decrease in liver transaminases and normalization of coagulation profile was observed followed by clinical improvement and favourable outcome despite factors associated with poor prognosis. The use of intravenous N-acetylcysteine is safe and efficient in the treatment of dengue-associated fulminant liver failure, especially in centres when liver transplantation is not readily available.

Transaminase levels increased in virtually all dengue patients and correlated with other markers of disease severity. However, peak enzyme values usually occurred later than other complications. Clinically severe liver involvement was infrequent and idiosyncratic, but usually resulted in severe bleeding. Chronic co-
infection with hepatitis B was associated with modestly but significantly increased levels of ALT, but did not otherwise impact the clinical picture. The frequency of dual dengue and malaria infection was 23.21%. The serology of the dengue and malaria showed negative results in 30.35%. The diagnosis of dual infections could be made on the basis of history, clinical examination supported by hematological results. It is recommended that all the patients suspected for dual infections should be treated concomitantly for dengue and malaria in malaria endemic areas.

The clinical and biochemical profile of dengue haemorrhagic fever (DHF) varies from epidemic to epidemic. Clinical features of DHF varied from the previous epidemic. Hepatic dysfunction with increased levels of liver enzymes was common in DHF. Liver damage is a common complication of dengue infection and aminotransferase levels are a valuable marker for monitoring these cases. The incidence of dengue fever (DF) is estimated to have increased 30-fold in the past 50 years. Dengue viruses were shown to cause cardiac disease with clinical manifestations ranging from mild elevation of biomarkers to myocarditis and/or pericarditis. Patients with severe dengue had worse cardiac function compared with dengue in the form of left ventricular systolic dysfunction with increased left myocardial performance. Septal myocardial systolic velocities were reduced as well as right ventricular systolic. Patients with severe dengue have evidence of systolic and diastolic cardiac impairment with septal and right ventricular wall being predominantly affected.

Measles a & Tetanus

Tetanus is a disease caused by Clostridium tetani. Acute renal failure (ARF) can occur in patients with tetanus and a number of mechanisms may contribute to this, including rhabdomyolysis and autonomic nervous system overactivity. ARF is an important complication of tetanus, which was not associated with death. Hyperglycemia, hyperkalemia, and thrombocytopenia seem to increase mortality.

Staphylococcus

Complete eradication of MRSA is necessary to treat MRSA-associated glomerulonephritis, and if this is not attained, a permanent loss of renal function occurs.

Tuberculosis

Urea breath testing may provide a useful diagnostic and biomarker assay for tuberculosis and for treatment response. Future work will test specificity for M. tuberculosis using lung-targeted dry powder inhalation formulations, combined with co-administering oral urease inhibitors together with a saturating oral dose of unlabeled urea, which would prevent the delta signal from urease-positive gastrointestinal organisms and the rate of LFT abnormalities was higher when patients were exposed to INH, and significant abnormalities were more frequent than reported in the INH literature. It is prudent to closely follow the LFTs of these patients. The results have shown the importance of estimating some LFT parameters, prior to the start of Antitubercular Drugs (ATD) and Antiretroviral Therapy (ART) in these cases. Hence, a mandatory performance of LFT is recommended, as it is simple and cost effective. TNF-alpha and IL-1 released from activated Kupffer cells (KCs) were involved in BCG plus LPS induced liver injury. FR167653 significantly attenuated hepatocyte injury via inhibition of TNF-alpha and IL-1 released from activated KCs.

Meningitis

Increased CSF lactate is a useful post neurological bacterial meningitis (PNBM) marker, with better predictive value than CSF hypoglycorrachia or pleocytosis. Lactate levels ≥ 4 mmol/L showed 97% sensitivity and 78% specificity, with a 97% negative predictive value. There have been relatively few attempts to focus on poor prognostic markers associated with AIDS related Cryptococcalmeningitis in Asian patients. Simple bedside clinical tools like ophthalmoscopy and CSF manometry can help in risk stratification in this group of patients. A logistic regression analysis, taking into account age, gender, length of hospital days, sepsis definition, presence of meningitis, creatinine kinase MB isoenzymes, and cTnI serum levels, demonstrated that severity of septic disease was the only variable significantly associated with the death. Evaluation of serum levels of cTnI within the first 24 hrs of diagnosis of sepsis or septic shock in children was not better than creatine kinase MB isoenzyme or clinical evaluation, to predict the outcome (death or discharge from hospital) of septic process. The mean CSF and serum cortisol levels were higher in patients with bacterial meningitis than patients with aseptic meningitis and control group and the difference was highly statistically significant. Also, there was positive correlation between CSF cortisol level and severity of bacterial meningitis using Glasgow outcome score. Serum and CSF cortisol levels were elevated in patients with meningitis and can be used as a marker for differentiating bacterial from aseptic meningitis.

HIV

Tenofovir is associated with greater effect on decline in renal function and a higher risk of proximal tubular dysfunction in antiretroviral naive patients initiating antiretroviral therapy (ART). PLHIV are at increased risk of renal disease, with greater risk at later stages of infection and at older ages. ART prolongs survival and decreases the risk of renal disease. However, less reduction in renal disease risk occurs for Tenofovir-containing ART than for other regimens. The risk of kidney disease associated with the widely used agent tenofovir continues to be studied, although its incidence in reported clinical trials and observational studies remains quite low. Future studies about the relationship between black race and kidney disease, as well as strategies for early detection and intervention of kidney disease, hold promise for meaningful reductions in morbidity and mortality associated with kidney disease.

Galactose elimination capacity as a parameter of cytosolic liver function and indocyanine green clearance as a parameter of liver perfusion were not affected by ART. Antiretroviral drugs may have significant effect on liver function. It is therefore recommended that liver function of HIV patients on ART should be determined regularly to monitor progress of ART therapy. Liver biopsy accompanied by liver function test provides a clearer picture of macroinflammation. Such co-infected individuals also face increased risk of hepatotoxicity from ART. Individuals with HIV-HBV coinfection should have both the
infections completely assessed in order to decide on the best therapeutic option for both viruses. HAART has a duration and drug dependent effects on the liver cells integrity and functions. This effect is lesser with NRTIs as compared with NNRTIs and PI. It is therefore recommended that routine liver function tests be instituted in HIV patients on HAART regimen. There was a small but statistically significant elevation in ALT and SAP at 2 weeks and AST at 6 weeks after ART initiation. The proportion of patients with rate-limiting toxicity of liver enzymes was small. None had treatment terminated because of hepatotoxicity.

A significant lipid profile change occurs in AIDS patients compared to HIV infection and healthy subjects. There were no significant differences in total TT4 concentrations among the AIDS patients when compared to HIV infection and normal healthy subjects. A measured FT4 concentration was slightly but significantly decreased in HIV /AIDS patients. Total T3 concentrations were normal in HIV infected patients, but slightly decreased in AIDS; more important, T3 level was decreased in AIDS patients. The level of FT3 concentration was slightly but significantly increased in HIV infected and significantly decreased in AIDS patients. Thyroid dysfunction is frequent in HIV infection and with progression of disease there is a primary hypothyroid like state that occurs in patients with HIV infection. TT3, FT3, FT4 and serum TSH can be used as a surrogate marker of the progression of the disease. Although 1 in 10 patients on raltegravir therapy developed significant creatine kinase elevation as defined, symptoms were uncommon, not severe and occurred in patients with easily identifiable risk factors. Virucidal agents designed for topical vaginal use block HIV infection of genital tissue. Such agents have major implications for world health, as they will provide women with a mechanism of personal and covert protection from HIV infection.

HBs Ag and HCV

Adefovir dipivoxil (ADV) is an independent predictor for significant deterioration of renal function. Patients on ADV should be monitored, especially patients who are older, have baseline renal insufficiency, or have hypertension and/or diabetes mellitus. Recent studies with extended follow-up of renal transplant recipients suggest that HCV infection may affect patient and graft survival during the second decade. Further studies are required to identify the mechanisms of infection of patients with end-stage renal disease and to define better treatment strategies for these patients before and after kidney transplantation and all patients with CRF should be immunized against hepatitis B as early as possible in the development of their disease, to ensure maximum response, and to minimize the effects of elevated serum creatinine and increasing age. A significant number of patients have been infected with hepatitis B and C viruses; laboratory analysis in patients with a chronic course did not always correlate with the evolution of the disease; the clinical course is mostly mild. Total antioxidant activity was significantly decreased in both hepatitis B and C. Among the enzymes analyzed, ALP, ALT, LDH and AST were all significantly increased in both patients with hepatitis B and C whereas CK was significantly decreased in patients with hepatitis B and remained unchanged in patients with hepatitis C.

Liver function test parameters were elevated compared with control subjects (P < 0.001). The increase in serum alpha-fetoprotein was higher (P < 0.001) in HCV than HBsAg positive patients. Serum alpha-fetoprotein level was highest in HCV compared to HBsAg positive and hepatitis negative patients with CLD. HRW significantly attenuates oxidative stress in CHB patients, but further study with long-term treatment is required to confirm the effect of HRW on liver function and HBV DNA level. More than 170 million people worldwide are chronically infected with the HCV, which is responsible for over 1 million deaths from cirrhosis and primary liver cancers. Beside chronic liver disease, relevant extrahepatic manifestations of HCV infection include cryoglobulinemia, lymphoproliferative disorders, and renal diseases. hs-CRP and fibrinogen may be considered as a CHC progression prognostic factor. Evidence indicates that HCV have a key role in coronary heart disease. Hepatic transaminase tests such as ALT and AST often are part of standard laboratory panels in asymptomatic outpatients, similar to screening tests for blood donors and for life insurance applicants. The evaluation of an abnormal ALT or AST level in an asymptomatic patient therefore is a common challenge encountered by primary care physicians.

The Red Cell Distribution Width(RDW) was elevated in chronic hepatitis B (CHB) patients and patients with HBV related liver cirrhosis and was positively correlated with the severity of HBV-related liver cirrhosis. RDW is a potential index to assess the severity of HBV-related liver diseases. Independent of IL-28B polymorphisms, blood IP-10 is a promising biomarker for predicting therapy response in chronic hepatitis C virus HCV infection. Urine IP-10 has been proposed as a biomarker in tuberculosis, but to date, no urine biomarkers for HCV infection have been evaluated. IP-10 is detected and increased in the urine of HCV-viremic patients compared to healthy donors and cured-HCV subjects. Recent studies on liposomal formulation of chemotherapeutic and bioactive agents and their targeted delivery show liposomal antibiotics potential in the treatment of microbial infections. The frequency of anti-HCV treatment approximately doubled between 1995 and 2001. Although adherence to consensus recommendations regarding pre-therapeutic evaluation is not ideal, a substantial improvement has occurred since 1995. Nevertheless, means of increasing the availability of antiviral therapies, particularly for patients with HIV co-infection or injecting drug use, require further study.

Bacterial Infection

Procalcitonin (PCT) levels are not significantly affected by loss of renal function, immunosuppressive agents or autoimmune disorders. Thus, significantly elevated PCT concentrations offer good sensitivity and specificity for the early diagnosis of systemic bacterial infection in patients with CRF or patients with ESRD treated by HD. CRP concentration may be an useful indicator for inflammation in patients with renal diseases, but have low specificity for the diagnosis of bacterial infection. The absolute number of WBCs or red blood cells in the urine and the presence of casts, proteinuria, and leukocyte esterase were not associated with positive culture or urinary tract infection. Neither pyuria nor a positive culture was related to temperature, systemic WBC count, or serum albumin, urea, or creatinine.
Differences in the average plasma glucose values, urea, creatinine, bilirubin and ALT between the patients diagnosed with bacteraemia and sepsis are not statistically significant. The results have shown that even in the course of a bacteraemia, there is a significant increase in the non-specific inflammatory parameters indicating the gravity of bacteraemia as well, with a constant risk of developing sepsis and septic shock. The importance of running and following-up the laboratory parameters herewith is emphasised for the purpose of detecting sepsis in a timely manner and administering an adequate therapy.\(^{(73)}\)

Severity of liver dysfunction and severity of renal dysfunction are both important determinants of short-term mortality among liver cirrhosis patients with bacteraemia and spontaneous bacterial peritonitis in Japan.\(^{(74)}\) Helicobacter pylori infection in gastric mucosa may cause systemic inflammatory reaction. Study did not demonstrate nutritional benefits after H pylori eradication treatment, as the level of nutritional markers reduced. This relationship needs to be confirmed by further prospective studies.\(^{(75)}\) Aggressive fluid rehydration remains the cornerstone of management of cholera. Instead of presenting with a classical BUN/Creatinine ratio of >20:1, patients with pre-renal failure in cholera may present with a BUN/Creatinine ratio of <15:1.\(^{(76)}\) Infection with cytotoxin associated gene A (Cag-A) positive H. pylori strain may play a role as a risk factor in development of ischemic heart diseases through provocation of high inflammatory response or through other mechanism. Therefore eradication of this infection is important as it is much less expensive than long term treatment of the other risk factors.\(^{(77)}\)

During cardiac surgery (mitral valve replacement) Prostoglaslin E1 (PGE1) may suppressed the production of IL-6, IL-8 but not IL-10, which may be related to its myocardial protection effect.\(^{(78)}\) Abnormalities in liver enzyme levels are frequent during severe enterocolitis due to S. enteritidis in adult patients. These abnormalities are moderate and self-limited.\(^{(79)}\) Hyperbilirubinemia and liver enzyme abnormalities are commonly observed in sepsis. However, the frequency in premature neonates and the specific relation to gram-negative bacteria are not known. Gram-negative bacteraemia is commonly associated with cholestasis in premature neonates. Liver enzyme abnormalities are more common than elevated conjugated bilirubin, not all gram-negative bacteria have the same effect and the lack of enteral feeding seems to play a more significant role than the administration of parenteral nutrition.\(^{(80)}\)

**Anaplamosis**

A significant increase in WBC is observed as a result of significant increase and decrease in lymphocytes and neutrophiles, respectively. The biochemical changes revealed significant increase in AST, ALT, total bilirubin, BUN and icteric index, however significant decrease in total protein values were encountered in infected camels.\(^{(81)}\)

**Human T Lymphotropic Virus**

Markers of Human T Lymphotropic Virus infection (infection status, antibody titer, and provirus load) are associated with hematologic and biochemical alterations, such as lymphocyte abnormalities, anemia, decreased eosinophils, and elevated LDH levels.\(^{(82)}\)

**Babesiosis**

Results indicated that the percentage of the infection with Babesiosis was 15.42% and the percentage of parasitaemia ranged between 3.5-10.4% with a mean 6.95%. Infected goats showed signs of loss of appetite, weakness, pale mucous membranes, jaundice, fever, coughing, nasal discharge, recumbency, diarrhea and haemoglobulinuria. A statistically significant decrease were recorded in total RBC, Hb, PCV and platelets counts.\(^{(83)}\) A gradual decrease in Hb value was observed at various stages of parasitaemia and there was a sharp fall when parasitaemia reached more than 50%. Examination of blood smears showed phagocytosis of both healthy and infected erythrocytes.\(^{(84)}\) Chronic canine babesiosis caused by B. gibsoni is highly pathogenic associated with anaemia and haematobiochemical alterations.\(^{(85)}\) A significant reduction was observed in the number of RBC, Hb concentration and PCV values (p < 0.05). In histopathological examination, hepatocellular degeneration and necrosis, fibrosis, mucus gland and biliary hyperplasia, mild lymphocytic hepatitis, granuloma and telangiectasia were observed. It seems that the increased and reduction of significant blood parameters, may be due to liver failure and pathological changes following larval migration and stimulating of immune responses.\(^{(86)}\) In Trypanosoma evansi, infection the main changes in the erythrocytes were macrocytes, hypochromic cells, Howell–Jolly bodies, target cells, stomatocytes and burr cells. Serum chemistry revealed hypoproteinaemia, hypocholesterolaemia, hypoglycemia, hyperbilirubinemia, elevated creatinine, BUN, increased AST and ALT.\(^{(87)}\) T. annulata infection in cattle is associated with hematological and biochemical, and ECG changes.\(^{(88)}\)

There was parasite resistance to ivermectin. Famacha data showed negative correlation with packed cell volume, leukocytes, hemoglobin, albumin, total protein, globulin and albumin/globulin ratio. The packed cell volume showed a strong and positive correlation with hemoglobin, albumin and total protein. Treatment with ivermectin and closantel were not responsible for considerable changes in hematological and biochemical parameters evaluated.\(^{(89)}\) The average activity of the enzymes studied in chagasic patients, except LDH and CPK, are significantly altered (p < 0.05) in the majority of the arterial and venous blood samples. The finding of released AST, ALT, ALP, acid maltase and alpha-HBDH in groups IA and IB is an indication of early myocardial damage in chronic chagasic patients without clinical evidence of cardiac disease. It is suggested that the possible evaluative pattern for myocardial damage could be established by the increment in coronary sinus blood of the enzymes AST, acid maltase and alpha-HBDH.\(^{(90)}\)

**Leishmaniasis**

Animals with the clinical form of the disease demonstrate hematological and biochemical changes consistent with anemia, uremia, hyperproteinaemia, and hyperglobulinemia, which present themselves as strong clinical markers of visceral leishmaniasis associated with the signs previously reported.\(^{(91)}\)
II. CONCLUSION

This review article has given an update of all possible human infections and the organs and the associated analytes which are affected. If it has highlighted the biochemical changes in main organs of humans such as liver, heart and kidney. Persistent infections may lead to damage to the above organs. Based on all the updates given in this paper, reach activities may be focussed on the role biochemistry in infectious diseases as a broad research topic and selecting a particular organ which are prone to infections and studying the changes in analytes concentration. This will make biochemistry as an integral part of clinical microbiology.

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