MedCrave
Step into the World of Research
Journal of Analytical & Pharmaceutical Research

Mini Review

Open Access
CrossMark

Biochemical indicators in trypanosomiasis infections

Abstract

Biochemical assessment of the body fluids gives an indication of the functional state of the various body organs and biochemical changes in the fluids which result from trypanosomiasis infections depend on the species of the parasite, its virulence, susceptibility of the host and the period of infection during which the samples are taken. Evaluations of biochemical parameters are usually done on specimen that includes serum or plasma and cerebrospinal fluid (CSF) obtain from infected animals or humans. Abnormal fluctuations are observe in indicators such as marker enzymes, electrolytes, plasma proteins, metabolites, plasma amino acids, hormones, haptoglobin, glucose, glycoproteins among other parameters on specimen collected. As observed from researchers past work, they often make use of few biochemical indicators which may be due to inability to get the appropriate ones to use at the point in time. This review is done to summarize the existing and new biochemical indicators used in trypanosome infection analysis.

Keywords: indicators, biochemicals, trypanosomiasis, infections

Volume 9 Issue 1 - 2020

Olanrewaju Roland Akinseye, Adelabu Mustapha, Aziekwu N. Angela
Nigerian Institute for Trypanosomiasis (& Onchocerciasis) Research, Nigeria

Correspondence: Olanrewaju Roland Akinseye, Nigerian Institute for Trypanosomiasis (& Onchocerciasis) Research, Nigeria, Email akinseyeroland@gmail.com

Received: December 19, 2019 | **Published:** January 24, 2020

Abbreviations: CSF, cerebrospinal fluid; ALT, alanine transaminase; AST, aspartate transaminase; ALP, alkaline phosphatase; GGT, gamma glutamine transaminase

Introduction

Trypanosomiasis is an endemic disease which is invariably fatal if not treated. Antigenic variation a mechanism by which the parasite evades the host immune system, results in the fluctuating parasitaemia that characterizes the disease.[1] This phenomenon underlies the wide spectrum of systemic dysfunction and the infection of multiple organs by the parasite.[1] The biochemical changes observed in trypanosome infections (man or animals) are determined by several factors which include; the virulence of the parasite in acute chronic; the susceptibility of the host; and the period of the infection during which samples are taken, among others.[2] Despite the variations in hosts (man, domestic and experimental animals) and trypanosomes (*T. brucei, T. gambiense, T. rhodesiense, T. evansi, T. vivax*, *T. congolense*), the severity of the biochemical changes associated with various host-parasite combinations is determined by the level of parasitaemia which develops during the early phase of infection.[1]

The three phases of trypanosome infections are recognizable for biochemical perturbation which includes:

Acute phase: Begins with the first appearance of trypanosomes in the blood after incubation period (1week). It is characterized by high parasitaemia with remarkable biochemical instability.

Chronic phase: is characterized by low frequency and intensity of parasitaemia. The surviving subjects are characterized by lower levels of parasitaemia but with reversal of some biochemical changes such as hypoglycaemia and persistence of others such as the plasma protein changes.

Recovery phase: is characterized by aparasitaemia or low very infrequent parasitaemia. This occurs in the subjects that survive the two previous phases, and is characterized by abatement of parasitaemia or even sterilization, accompanied by gradual reversal of abnormalities previously developed.

The abnormalities in enzymes, electrolytes, plasma proteins, metabolites, plasma amino acids, hormones, haptoglobin, glucose, glycoproteins among other parameters induced by trypanosomes arise from their direct and indirect effects via their products, on hosts tissues such as liver, kidney, bone marrow and lymphoid organs, resulting in organ malfunction, as well as from extractions from and additions to host chemistry associated with parasite metabolism.[2] Hence, it is important to identify and familiarize with various biochemical indicators that can be used for analysis during trypanosome infection.

Biochemical indicators

The evaluation of the biochemical indicators such as enzymes, electrolytes, plasma proteins, metabolites etc. in plasma and cerebrospinal fluid samples can be used to measure the functional state of the various body organs and changes in body fluids that result from infections depending on the species of the trypanosome and its virulence.[2]

Enzymes-Alanine transaminase (ALT), Aspartate transaminase (AST), Alkaline phosphatase (ALP) and Gamma glutamine transaminase (GGT)

ALT is found in plasma and various body tissues but most common in the liver and involves in transferring amino group from L-alanine to alpha -ketoglutarate to form pyruvate and L-glutamate. It is used as liver function tests and components of AST/ALT ratio. The elevated level could mean existence of medical problem such as liver damage, diabetes, viral hepatitis, bile duct product etc. and is a commonly use way of screening liver problems.[3] AST is a pyridoxal phosphate-dependent transaminase enzyme which catalyzes the reversible transfer of alpha-amino group between aspartate and glutamate. AST is found in the liver, heart, skeletal muscle, kidney, brain and red blood cells. Both AST and ALT are associated with liver parenchyma cells.[4] The difference is ALT is predominantly in liver and little quantity in other organs. ALT is more specific for liver inflammation while AST may be elevated also in diseases affecting other organs such as myocardial infarction. AST/ALT ratio is commonly measured as biomarkers for liver health.[5]

ALP is a group of iso enzymes found on the outer layer of the cell membrane and catalyzes the hydrolysis of organic phosphate ester present in the extracellular space. It is used to detect liver disease or bone disorders. The damaged liver cells release increased amount of ALP into the blood and ALP is often carried out to detect blocked bile ducts.[6] The condition that can affects bone growth or causes increased activity of bone cells can affect ALP levels in the blood and is a monitor of vitamin D deficiency.

GGT is found in many organs throughout the body with highest concentration in the liver. It is normally present in low levels, but when the liver or bile ducts become obstructed, GGT level can rise. GGT test is not very specific and cannot be used to differentiate various causes of liver damages because it can be elevated with many types of liver diseases – liver cancer as well as non-hepatic conditions.[7] GGT and ALP increased during liver diseases but only ALP will increase with conditions affecting the bone tissues. Consumption of even small amount alcohol can increased the level of GGT.

In an article titled, "The biochemical changes induced by natural human African trypanosomiasis," by Awobode 2006.,[9] he observed that plasma enzymes (ALT, AST and ALP) levels in trypanosome positive subjects were significantly higher than that of control while GGT showed no significant differences. The results suggest probable infiltration of vital body organs and inflammation particularly of liver, muscles and kidney by *Trypanosoma brucei gambiense* at the time of diagnosis. The damaged to the body cells result in the alteration of membrane permeability and consequent release of enzymes into the extracellular fluid. The elevated enzyme levels may also arise from the effect of trypanosome lyses resulting from the host's defense mechanism,[8] hence, the changes in the level of ALT, AST and ALP serves as parameters for measure the functional state of the body organs during infections by trypanosome species.

A. Electrolytes

Sodium (Na+), Potassium (K^+), Chloride (Cl^-), Calcium (Ca^{2+}), bicarbonate, triglycerides and phosphate ions are the major biochemical electrolytes under investigation during trypanosome infection. An experimental study observes that blood Na^+ level is normal in acute *T. rhodesiense* infection of mice while hyponatraemia is reported in human *T. rhodesiense* infection and K^+ decreased as well.[2] Normal electrolyte level in human infected *Trypanosoma brucei gambiense*is observed by Awobode and stated that the body regulates balance and maintains its fluid composition and volume for normal physiological and biochemical events of life.[9] The perturbation observed in the level of electrolytes serves as parameters for measure the functional state of the body organs during infections by trypanosome species.

B. Plasma protein

Total protein (TP), albumin (A), globulin (G) and A-G ratio are commonly estimated during trypanosome infection and they are measured in (g/l). A study of *Trypanosoma brucei* infection of mice/deer shows that most of the consistent changes in plasma protein levels are decreasing albumin levels and elevation of globulin level due to hyper gamma globulinaemia.[2] Another study observed an increase in plasma globulin level which is related to tissue destruction by *Trypanosoma brucei*.[10] The instability seen in the level of plasma proteins during infections by trypanosome species, are used as parameters for measure the functional state of the body.

C. Haptoglobulin

This is a plasma protein which binds to free haemoglobin and is produced from the liver. When red blood cells are actively being destroyed, haptoglobulin disappears faster than it is created.[10] Serum haptoglobulin as reported,[2] decreased in human African trypanosomiasis and completely disappear in *T. vivax* infection of cattle. The variation seen in the haptoglobulin content in trypanosome infections, are used as parameters for measure the functional state of the body.

Metabolites-Urea(mmol/L) and Creatinine (µmol/L)

Urea is a waste product of many living organism and the major organic component of human urine. It is the end product/chain of reactions which breakdown the amino acids that make up proteins.[11] Blood Urea Nitrogen (BUN) test is a measure of the amount of nitrogen in the blood that comes from urea and is used as a marker of renal function.

An elevated urea levels in *T. rhodesiense* infections of monkey and mice at 8–10days of infection were recorded by Anosa 1988.,[2] This suggests that urea levels are elevated at periods with high parasitaemia. The causes of elevated Bun levels include kidney disease such as glomerulo nephritis, urinary tract obstruction and/ fever are common features of trypanosomiasis.

Creatinine is the breakdown product of creatine phosphate in muscle and usually produced at constant rate by the body muscle. It is removed majorly by the kidney through glomerular filtration.[12] The estimation of renal function can be made when interpreting the plasma concentration of creatinine along with urea. BUN-Creatinine ratio can indicate other problems besides those intrinsic to the kidney.

An elevated level of creatinine is observed in results documented by Awobode 2006.,[9] for *T.b.gambiense* infection which agreed with the elevated levels of creatinine in monkey clinically infected with *T.b.rhodesiense* and*T. b. gambiense.*[13,14] The variation seen in the values of urea and creatinine in trypanosome infections, are used as parameters for measure the functional state of the body.

Blood lipids–Triglycerides ad Cholesterol (mmol/L)

The role of blood lipids in the pathogenesis of trypanosomiasis is first reported by Tizard et al.,[15] and Robert 1984.,[16] The observation of decrease in the total plasma lipids in *T. congolense* infection of sheep is known to occur.[17] Trypanosomes are known to cleave sialic acid from glycophorins on erythrocyte membranes with the aids of sialidase; they also use erythrocyte sialoglycoproteins for their proliferation and differentiation,[18] this leads to hypocholesterolaemia. However, a study describes that lipids and cholesterol increased in rabbits infected with *T. b. gambiense*.[2] Blood lipids become increased or decreased during trypanosome infections which affect the functionality of the body.

Plasma amino acid

Tryptophan, threonine, tyrosine, arginine & asparagine, serine, valine, isoleucine and leucine levels usually decreases in *T.b.gambiense* and *T.vivax* infected sheep and cattle as stated by Anosa 1988.,[2] Alanine however shows an increase in value probably due to abnormal carbohydrate metabolism. These abnormalities may be due to non-utilization by the host of some amino acids, utilization of others for trypanosome metabolism and secretion of others by trypanosome. Amino acids content in trypanosome infections are varied which serve as parameters for measure the functional state of the body.[2]

a) Hormone

Serum level of follicle stimulating (FSH) and luteinizing hormones (LH) shows a significant decrease in human *T. b. gambiense* infection.[2] These hormones concentration become unstable in trypanosome infections, which serves as indicator for measuring the functional state of the body.

b) Glucose

Hypoglycaemia observed at the periods with high parasitaemia in cattle with acute *T. congolense*. This condition is therefore precipitated by the presence of large numbers of parasites in circulation presumably because of utilization of the glucose for trypanosome metabolism. Glucose infusions increase the survival time of pigs infected with *T. simiae* from the usual 5-12days to 30days as documented by Anosa 1988.,[2] There are changes in the glucose concentration as described in trypanosome infections, and are used as indicators for measure the functional state of the body.

c) Glycoproteins

Plasma concentrations of glycoproteins such as hexose, hexosamine, sialic acid and sero mucoid fraction increase in cattle infected with *T. b. gambiense* and *T.vivax* during the first week of infection and decline in the tenth week when the parasites become very scanty.[2] The increase is thought to result from release of glycoproteins from organs invaded by the trypanosome. Alteration seen in the concentration of glycoprotein during trypanosome infections, are used as parameters for measure the functional state of the body.

d) Kinins, serotonin and histamine

Bradykinin levels increases in human *T. rhodiesiense* infection, in *T. brucei* infections of cattle and mice and in *T. vivax* infections of goats and cattle. Blood serotonin levels decreases during the early acute phase of *T. vivax* infections of goats and cattle, and the decreases is associated with temperature peaks and parasitaemic peaks as well as with thrombocytopenia, fever and platelet aggregation.[2] Blood histamine levels increases in mice infected with *T. brucei*. The fluctuation seen in the bradykinin, serotonin and histamine content in trypanosome infections, are used as indicator for measure the state of well being of the body (Table 1).

Table 1 Tabular form of the biochemical indicators, subjects, trypanosome species and their effects

Biochemical Indicators	Subjects	Trypanosome species	Effects	Reference range of Indicators	References
ALT (U/L)	Human	*T.b. gambiense*	Increase	20-Aug	Awobode.,[9]
AST (U/L)	Human	*T.b. gambiense*	Increase	20-Aug	Awobode.,[9]
ALP (U/L)	Human	*T.b. gambiense*	Increase	20 -70	Awobode.,[9]
GGT (U/L)	Human	*T.b. gambiense*	No change	Apr-60	Awobode.,[9]
Na^+ (mmol/L)	Mice	*T. rhodesiense*	Normal		Anosa.,[2]
	Human	*T. rhodesiense*	Hyponataemia	135 -147	
K^+(mmol/L	Mice	*T. rhodesiense*	Decrease	3.5 – 5.0	Anosa.,[2]
Electrolytes	Human	*T.b. gambiense*	Normal	Varies	Awobode.,[9]
Albumin (g/L)	Deer/Mice	*T. brucei*	Decrease	Varies	Anosa.,[2]
Globulin (g/L)	Deer/Mice	*T. brucei*	Increase	Varies	Anosa.,[2]
Haptoglobulin (mg/L)	Human	*T. vivax*	Decrease	410 -1650	Anosa.,[2]
Glycoproteins	Cattle	*T. brucei*	Increase/Decline	Varies	Anosa.,[2]
		T. vivax	Increase/Decline		
Kinins	Human	*T. rhodesiense*	Increase	Varies	Anosa.,[2]
	Cattle/Mice	*T. brucei*	Increase		
	Goats/cattle	*T. vivax*	Increase		
Serotonin	Goats/cattle	*T. vivax*	Decrease	Varies	Anosa.,[2]
Histamine	Mice	*T. brucei*	Increase	Varies	Anosa.,[2]
Urea (mmol/L)	Monkey/mice	*T. rhodesiense*	Elevate	Varies	Anosa.,[2]
Creatinine (µmol/L)	Human Monkey	*T. gambiense, T. rhodesiense*	Elevate	Varies	Awobode.,[9]

Citation: Akinseye OR, Mustapha A, Angela AN. Biochemical indicators in trypanosomiasis infections. *J Anal Pharm Res.* 2020;9(1):11–14.
DOI: 10.15406/japlr.2020.09.00346

Table continue

Biochemical Indicators	Subjects	Trypanosome species	Effects	Reference range of Indicators	References
Blood lipids (mmol/L)	Rabbit	*T. gambiense*	Increase	Varies	Anosa.,[2]
Tryptophan, Threonine, Tyrosine	Sheep/Cattle	*T. gambiense*	Decrease	Varies	Anosa.,[2]
Arginine, Asparagine	Sheep/Cattle	*T. gambiense, T. vivax*	Decrease	Varies	Anosa.,[2]
Alanine	Sheep/Cattle	*T. gambiense, T. vivax*	Increase	Varies	Anosa.,[2]
FSH and LH	Human	*T. gambiense*	Decrease	Varies	Anosa.,[2]
Glucose	Cattle	*T. congolense*	Decrease	Varies	Anosa.,[2]

ALT, alanine transaminase; AST, aspartate transaminase; ALP, alkaline phospahatse; GGT, gamma glutamate transaminase; FSH, follicle stimulating hormone; LH, lutenizing hormone

Conclusion

Conclusively, this article gives description of the various biochemical indicators which fluctuates during trypanosome infection that are being used in analysis and it is obvious that the biochemical assessment of the body fluids gives an indication of the functional state of the various body organs. The biochemical changes in the fluids which result from trypanosome infections depend on the species of the parasite, its virulence, susceptibility of the host and the period of infection during which the samples taken.

Acknowledgments

None.

Conflicts of interest

The author declares that there are no conflicts of interest.

Funding

None.

References

1. Horn D. Antigenic variation in African trypanosomes. *Mol Biochem Parasitol*. 2014;195(2):123–129.
2. Anosa VO. Haematological and biochemical in human andanimal trypanosomisis Part II. *Reve Elev Med Vet Pays Trop*. 1988;41(2):151–164.
3. Ghouri N, Preiss D, Sattar N. Liver enzymes, nonalcoholic fatty liver disease, and incident cardiovascular disease: a narrative review and clinical perspective of prospective data. *Hepatology*. 2010;52(3):1156–1161.
4. Berg JM, Tymoczko JL, Stryer L. Biochemistry. *WH Freeman*. 2006;656–660.
5. Nyblom H, Berggren U, Balldin J. High AST/ALT ratio may indicate advanced alcoholic liver disease rather than heavy drinking. *Alcohol.*. 2004;39(4):336–339.
6. Shipman KE, Holt AD, Gama R. Interpreting an isolated raised serum alkaline phosphatase level in an asymptomatic patient. *BMJ*. 2013;346:f976.
7. Kaplan MM. Biochemical basis for serum enzyme abnormalities in alcoholic liver disease. In: Chang NC, Chan NM (editors). *Early identification of alcohol abuse: Research Monograph No 17*. NIAAA. 1985:186.
8. Kennedy PG. Human African trypanosomiasis of the CNS:current issues and challenges. *J Clin Invest*. 2004;113(4):496–504.
9. Awobode HO. The biochemical changes induced by natural human African trypanosomiasis. *African Journal of Biotechnology*. 2006;5(9):738–742.
10. Wassell J. Haptoglobin: function and polymorphism. *Clinical Laboratory*. 2000;46(11–12):547–552.
11. Klein J, Blount MA, Sands JM. Urea Transport in the Kidney. *Compr Physiol*. 2011;1(2):699–729.
12. Allen PJ. Creatine metabolism and psychiatric disorders: Does creatine supplementation have therapeutic value?. *Neuro sciBiobehav Rev*. 2012;36(5):1442–1462.
13. Abenga JN, Anosa VO. Serum total proteins and creatininelevels in experimental Gambian trypanosomosis of vervet monkeys. *Afr J Biotech*. 2005;4(2*)*:187–190.
14. Sadun E, Johnson A, Nagle R, et al. Experimental infections with African Trypanosomiasis V. Preliminary parasitological,clinical haematological, serological and pathological observations in Rhesus monkeys infected with *T rhodesiense*. *Am J Trop Med Hyg*. 1973;22(3):323–330.
15. Tizard IR, Nielsen KH, Seed JR, et al. Biologically active products from African trypanosomes. *Microbial Rev*. 1978;42:661–681.
16. Roberts CJ. Blood lipids of ruminants infected with trypanosomes. *Trans Soc Trop Med Hyg*. 1984;68:155.
17. Katunga-Rwakishaya E, Murray M, Holmes PH. Pathophysiology of *Trypanosoma congolense* infection in two breeds of sheep, Scottish blackface and Finn Dorset. *Vet Parasitol*. 1997;68(3):215–225.
18. Taiwo VO, Olaniyi MO, Ogunsanmi AO. Comparative plasma biochemical changes and susceptibility of erythrocytes to *in vitro* peroxidation during experimental *Trypanosome congolense* and *T.brucei* infections in sheep. *J Isreal Vet Med Ass*. 2003:58(4*)*.