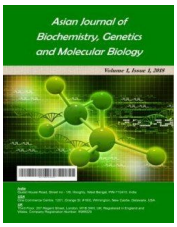

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Clinical Diagnosis of Disease States Using Enzymes and Proteins (Review)

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Authors' contributions

This work was carried out in collaboration between all authors. Authors NE, SC and POJ designed the study. Authors OAD, OO and CCI wrote the first draft of the manuscript. Authors SC, DO and OAD managed the literature searches. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Disease states which are abnormal conditions that negatively affects the structure or function of parts or all of an organism usually lead to moderate or extensive tissue damage depending on the time of onset and severity of the disease. Such tissue damages are usually associated with the release of enzymes (specific to the diseased organ or tissue) into circulation which results in an increase in activity of such enzymes in body fluids. The measurement of these changes in enzymatic activity is usually employed as an important clinical assessment tool for detecting, diagnosing, screening and monitoring diseases and pathological processes. Some of the enzymes used in diagnosis include transaminases (in liver diseases), creatine kinase (in myocardial infarction), amylase (in pancreatitis), acid phosphatase (in malignant diseases), and alkaline phosphatase (in bone diseases). Some other enzymes are used as diagnostic reagents in

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detecting the presence of compounds of clinical importance. These include glucose oxidase (for detecting the presence of glucose), urate oxidase (for testing the presence of uric acid) and cholesterol oxidase (for testing the presence of cholesterol) in diabetes, kidney stones and arteriosclerosis respectively. Various body fluids also contain proteins other than enzymes that are of diagnostic importance especially the plasma proteins. The plasma proteins are broadly divided into two namely; albumin and globulin. The globulins include gamma-globulins, beta-globulins, alpha-1 globulins and alpha-2 globulin. Many physiological and/or disease conditions produce changes in these individual plasma protein concentrations, and measurements of these changes can provide diagnostic information. Some of such enzymes and proteins of diagnostic importance are discussed in this review.

Keywords: Phosphatase; transaminases; arteriosclrosis; albumin; oxidase.

1. INTRODUCTION

Enzymes are soluble, colloidal organic catalysts synthesized by living cells [1]. The large numbers of enzymes present in the human body are synthesized intracellular, and for most, their functions are also exercised within the cells that produced them. Some are however; secreted into the intracellular fluids (e.g blood) and they can be further divided into two classes namely; I. Functional plasma enzymes and II. Non-functional plasma enzymes [2]. Functional plasma enzymes also known as plasma specific enzymes are present at all times in the circulation of normal individuals and perform specific physiologic functions in the blood. The functional enzymes include lipoprotein lipase, pseudocholinesterase and pro-enzymes of blood coagulation and fibrinolysis [3]. The second class known as non-functional plasma enzymes (cell-derived enzymes) perform no function as such in the blood but are present in the circulation as a result of the normal wear and tear processes of the cells. The non-functional enzymes include the transaminases (Alanine aminotransferase and Aspartate aminotransferase), lactate dehydrogenase enzyme and alkaline phosphatase [3].

Disease states usually lead to moderate or extensive tissue damage (depending on the time of onset and severity of the disease) which eventually leads to the release of enzymes (non-functional enzymes specific to the diseased organ or tissue) into circulation resulting in an increase in the activity of these enzymes in body fluids [4]. The basic principle of using enzyme levels for diagnosing disease is based on comparing the changes in activity in serum or plasma of these enzymes which are usually present in the serum in very low active amounts under normal circumstances [5]. A sensitive analysis would give insight into the pathological changes and nature of the disease. However, as the enzymes and their isoforms may belong to varied tissue types, it is of significant relevance to have a detailed knowledge of isoenzymes of the enzymes understudy and their enzymatic properties like kinetics, effect of factors like temperature and pH, rate of release from the cells of origin and rate of clearance from circulation [5].

Various body fluids also contain proteins other than enzymes that are of diagnostic importance especially the plasma proteins. The plasma proteins are numerous and are varied in their origin and functions. Albumin is regarded as the single most important quantitative plasma protein. Many physiological and/or disease conditions produce changes in individual plasma protein concentrations, and measurements of these changes often provides diagnostic information [2].

The relevance of enzymes and plasma proteins in clinical diagnosis of diseases cannot be over emphasized. Thus, this write up highlights some of such useful enzymes and proteins.

2. ENZYMES IN HEPATO-BILIARY DISEASES

2.1 Alanine Transaminase (ALT)

ALT was formally known as Glutamic Pyruvate Transaminase (SGPT). It catalyses the reversible transamination of L- alanine and 2- oxoglutarate to pyruvate and glutamate in the cytoplasm of the cell, it can be found in the liver, skeletal muscle and heart. ALT Increased serum level of ALT indicates a severe liver disease, usually viral hepatitis and toxic liver necrosis. Kim et al. [6] reported that ALT is a common serum marker of liver disease. Even a minor elevation of ALT is a good indicator of severity in liver disease.

2.2 Aspartate Transaminase (AST)

AST, also known as serum glutamate oxaloacetate transaminase (SGOT), is a pyridoxal phosphate (PLP) dependent enzyme that catalyses the reversible transamination of L-aspartate and 2- oxoglutarate to oxaloacetate and glutamate. Significant increase in the serum level (10- 100 times the normal (0- 40 IU/L) of AST indicates severe damage to liver (viral hepatitis or toxic liver necrosis) or heart cells (MI) [7]. AST could be a useful marker to screen liver fibrosis.

2.3 Alkaline Phosphatase (ALP)

The increase in the level of serum ALP indicates an increased hepatocytic activity in hepatobiliary disease. Higher ALP levels in serum are observed when bile ducts are blocked as in the case of cholestasis [8].

2.4 Gamma Glutamyl Transferase (GGT)

Gamma-glutamyltransferase (GGT) is an enzyme that transports amino acids; it is present in the cell membrane of nearly all human cells. This enzyme is sometimes referred to as a "transpeptidase". Specifically, it catalyzes the transfer of a gamma glutamyl group to another acceptor. It is most abundant in the kidney, liver, pancreas and intestine, but the majority of the GGT detected in serum derives from the liver. GGT is the most sensitive biomarker of hepatobiliary disease [9]. Increases occur earlier and persist longer than ALP in cholestatic disorders [10].

3. ENZYMES IN MYOCARDIAL INFARCTION

3.1 Creatine Kinase- MB (CK- MB)

The death of the heart muscle due to myocardial infarction (MI) prompts the release of several molecules such as creatine kinase (CK) into the circulation. Khan et al. [11] reported in an experiment that serum CK levels are significantly higher in patients with acute infarction than that of control (normal range: 10- 50 IU/L). Three isoforms of CK exists namely: MM, MB and BB isoforms. CK-MB which is the isoform present in the heart is the most specific and accurate means of detecting MI than total CK estimation [12].

Other useful markers in MI are myoglobin, troponins Aspartate transaminase (AST) and Lactate dehydrogenase (LDH) [8,13].

4. ENZYMES IN MALIGNANT DISEASES

4.1 Acid Phosphatase (ACP)

Five important isoforms of ACPs exists. They are the lysosomal, prostatic, erythrocytic, macrophage and osteoclastic forms [5]. They differ widely with tissue and chromosomal origin, molecular weight, amino acid homology, sequence length, and resistance to L (+) tartrate and fluoride [14]. ACP level in male prostate gland is 100 times more than in any other body tissue. Kirschenbaum et al. [15] have reported that prostatic acid phosphatase (PAP) is strongly expressed by prostate cancer cells, especially in bone metastases.

5. ENZYMES IN MUSCULAR DISEASES

The most commonly measured and most reliable and sensitive biochemical index of muscle diseases is creatine kinase (CK) measurement. Both AST and Aldolase are also useful indices but are less sensitive. CK is high in muscular dystrophies, polymyositis as well as toxic myopathies [16].

6. ENZYMES AS DIAGNOSTIC REAGENTS

Some enzymes are used as reagents to detect the presence of compounds of clinical importance. Below are examples of such enzymes.

Enzymes	Compounds detected	Disorder	References
Urease	Urea	Renal diseases	De Melo et al. [17]
Oxalate oxidase	oxalate	Kidney stones	Reddy and Vadgama [18]
Glucose oxidase	Glucose	Diabetes	Wang et al. [19]
Cholesterol oxidase	Cholesterol	Arteriosclerosis	Marazuela et al. [20]
Glutamate	Glutamate oxidase	Neuropathy	McLamore et al. [21]
Acetylcholinesterase	Acetylcholine	Neurological problems	Horiuchi et al. [22]
Lactate oxidase	Lactate	Ischaemic myocardium	Marzouk et al. [23]

Enzymes	Compounds detected	Disorder	References
β -glucocerebrosidase	Sphingolipid	Gaucher's Disease	Grabowski [24]
Dopamine-b-hydroxylase	Dopamine	Schizophrenia	Di Natale et al. [25]
Serum aspartate and alanine aminotransferase	Cholesterol	Intracerebral hemorrhage	Kim et al. [26]
Lysosomal serine protease	Collagen	Rheumatoid arthritis	Sohar et al. [27]

7. PLASMA PROTEINS IN DIAGNOSIS

Proteins are the most abundant compounds in human serum. The major measured serum proteins are divided into two groups namely: Albumin and Globulins.

A typical blood panel will provide four different measurements namely: (i) Total protein (TP) (ii) Albumin (iii) Globulins and iv) Albumin- Globulin Ratio [28].

7.1 Total Protein (TP)

The total protein represents the sum of albumin and globulins. Ideally, the total protein is approximately 7.5 g/dl and optimal range of about 7.2- 8.0 g/100 ml. The total protein may be elevated due to chronic infection, adrenal cortical hypofunction, liver dysfunction, collagen vascular disease, hypersensitivity states, dehydration and respiratory distress while it could be decreased due to malnutrition and malabsorbtion, liver diseases, diarrheoa, pregnancy etc [29].

7.2 Albumin

Albumin is synthesized in the liver. Its presence in the plasma creates an osmotic force that maintains fluid volume within the vascular space. A very strong predictor of health; low albumin is a sign of poor health. Its optimal range is 4.5- 5.0 g/100 ml. albumin levels may be elevated in dehydration, poor protein utilization, congestive heart failure and may be decreased in malnutrition, polydipsia, and liver dysfunction [30].

7.3 Globulins

Globulins are proteins that include gamma globulins (antibodies) and a variety of enzymes and carrier/transport proteins. The specific profile of the globulins is determined by protein electrophoresis, which separates the proteins according to size and charge [31].

There are four major groups that can be identified: gamma globulins, beta globulins, alpha-2 globulins and alpha-1 globulins. Once the abnormal one has been identified, further studies can determine the specific protein excess or deficit [32].

7.4 Albumin/ Globulin Ratio

The liver can function adequately on 20% of liver tissue, thus early diagnosis by laboratory methods is difficult. A reversed A/G ratio may be a helpful indicator. The optimal range is 1.7- 2.2. The AG ratio may be elevated in hypothyroidism, hypogammaglobulinemia and could be decreased in liver dysfunction [31].

8. CONCLUSION

Enzymes and plasma proteins play a pivotal role in clinical diagnosis. Enzymes have a wide range of applicability from diagnostic markers to diagnostic reagents as a result of their high specificity. Though there are a large number of enzymes and proteins in diagnostic use already, more research has to be focused on elucidating the potentials of more enzymes to aid the diagnosis of the numerous diseases of man.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Joshi AR, Marks V. Guide to biochemistry. 4th Edn. B. Jain publishers. 2004;258-300.
2. Nduka N. Clinical biochemistry for students of pathology. 1st Edn, Longmann Nigeria PLC, Ikeja, Lagos. 1999;119-137.
3. Tapasya S, Kunzang C. Clinical enzymology and its applications. India Institute of Medical Sciences Publications. 2007;1:28-35.
4. Gatsing D, Aliyu R, Kuiate JR, Garba IH, Jaryum KH, Tedongmo N, Tchouanguep FM, Adoga G. Toxicological evaluation of the aqueous extract of *Allium sativum* bulbs on laboratory mice and rats. Cameroon Journal of Experimental Biology. 2005;1:39- 40.
5. Burtis CA, Ashwood ER. Tietz fundamentals of clinical chemistry. 4th Edn.

WB Saunders Company: U.S.A. 1996;122-128.

6. Kim HC, Nam CM, Jee SH, Han KH, Oh DK, Suh I. Normal serum aminotransferase concentration and risk of mortality from liver diseases: Prospective cohort study. British Medical Journal. 2004;328:983-986.
7. Lesmana CR, Salim S, Huasan I, Sulaiman AS, Gani RA, Pakasi LS, Lesmana LA, Krisnuhoni E. Diagnostic accuracy of transient elastography (Fibro Scan) versus the aspartate transaminase to platelet ratio index in assessing liver fibrosis in chronic hepatitis B: the role in primary care setting, Journal of Clinical Pathology. 2011;64:916-919.
8. Corathers SD. The alkaline phosphatase level: Nuances of a familiar test. Pediatric Reviews. 2006;27:382-390.
9. Pratt DS, Kaplan MM. Evaluation of abnormal liver enzyme results in asymptomatic patients. New England Journal of Medicine. 2000;342:1266-1268.
10. Vroon DH, Israili Z. Alkaline phosphatase and gamma glutamyltransferase, in clinical methods: The history, physical, and laboratory examinations. 3rd edtn (Boston, Butterworths). 1990;42-350.
11. Khan HA, Alhomida AS, Sobki SH, Moghairi AA, Koronki H. Blood cell counts and their correlation with creatine kinase and C-reactive protein in patients with acute myocardial infarction. International Journal of Clinical Experimental Medicine. 2012;5:50-53.
12. Rosalki SB, Roberts R, Katus HA, Giannitsis E, Ladenson JH. Cardiac biomarkers for detection of myocardial infarction: Perspectives from past to present. Clinical Chemistry. 2004;50:2205-2209.
13. Iqbal SJ. Persistently raised serum acid phosphatase activity in a patient with hypophosphatasia: Electrophoretic and molecular weight characterization as type 5. Clinica Chimica Acta. 1998;271:213-215.
14. Bull H, Murray PG, Thomas D, Fraser AM, Nelson PN. Acid phosphatases. Molecular Pathology. 2002;55:65-67.
15. Kirschenbaum A, Liu XH, Yao S, Leiter A, Levine AC. Prostatic acid phosphatase is expressed in human prostate cancer bone metastases and promotes osteoblast differentiation. Annuals of New York Academy of Science. 2011;1237:64-68.
16. Goldberg DM, Werner M, Zaidman JL. Enzymes and isoenzymes in pathogenesis and diagnosis advances in clinical enzymology. Bassel: Karger. 1987;5:89-112.
17. De Melo JV, Cosnier S, Mousty C, Martelet C, Jaffrezic-Renault N. Urea biosensors based on immobilization of urease into two oppositely charged clays (Laponite and Zn-Al layereddouble hydroxides). Analytical Chemistry. 2002;74:4037-3409.
18. Reddy SM, Vadgama PM. Ion exchanger modified PVC membranes−selectivity studies and response amplification of oxalate and lactate enzyme electrodes. Biosensors and Bioelectronics. 1997;12: 1003-1005.
19. Wang X, Zhang Y, Cheng C, Dong R, Hao J. Glucose in human serum determined by capillary electrophoresis with glucose micro-biosensor. Analyst. 2011;136:53-58.
20. Marazuela MD, Cuesta B, Moreno Bondi MC, Quejido A. Free cholesterol fiber-optic biosensor for serum samples with simplex optimization. Biosensors and Bio-electronics. 1997;12:233-235.
21. McLamore ES, Mohanty S, Shi J, Claussen J, Jedlicka SS, Rickus JL, Porterfield DM. A self-referencing glutamate biosensor for measuring real time neuronal glutamate flux. Journal of Neuroscientific Methods. 2010;189:14-16.
22. Horiuchi T, Torimitsu K, Yamamoto K. On-line flow sensor for measuring acetyl-choline combined with microdialysis sampling probe. Electroanalysis. 1997;9: 912- 916.
23. Marzouk SAM, Cosofret VV, Buck RP, Yang H, Cascio WE, Hassan SSM. A conducting salt-based amperometric biosensor for measurement of extracellular lactate accumulation in ischemic myocardium. Analytical Biochemistry. 1997;69:2646-2648.
24. Grabowski GA. Gaucher disease and other storage disorders hematology. American Society of Hematology. Education Program. 2012;13–8.
DOI: 10.1182/asheducation-2012.1.13
PMID 23233555
25. Di Natale C, Macagnano A, Martinelli E, et al. Lung cancer identifi cation by the analysis of breath by means of an array of non-selective gas sensors. Biosensors and Bioelectronics. 2003;18:1209–18.
26. Kim HC, Kang DR, Nam CM, Hur NW, Shim JS, Jee SH, Suh I. Elevated serum aminotransferase level as a predictor of intracerebral hemorrhage, Korea medical

insurance corporation study. Stroke. 2005; 36:1642.
27. Sohar N, Hammer H, Sohar I. Lysosomal peptidases and glycosidases in rheumatoid arthritis. Biol Chem. 2002;383: 865.
28. Whicher JT. Abnormalities of plasma proteins. In Biochemistry of Clinical Practice. Williams DL, Marks V. eds. London: Heinemann. 1983;280-289.
29. Estridge HB, Reynolds PA, Walters J. Basic medical laboratory techniques. 4th edn, Thompson learning: USA. 2000;223-235.
30. Hemat RAS. Principles of Ortho-molecularism. Urotex. 2004;20:206- 217.
31. Marshall WJ. Illustrated textbook of clinical chemistry. 2nd Edn, Gower Medical Publishing. 1992;356-359.
32. Roitt IM, Brostoff Male DK. Immunology. Edinburgh: Churchill Livingstone. 1985; 554-558.

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