



Clinical Chemistry and Biochemistry: The Role of Biomarkers and Biomolecules

Haseeb Ahsan^{1*}

¹Faculty of Dentistry, Department of Biochemistry, Jamia Millia Islamia, New Delhi–India

*Corresponding email: drhahsan@gmail.com

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ABSTRACT

Biochemistry is a branch of biosciences which deals with the study of chemical reactions that occur in living cells and organisms. It is a subject in which biological phenomenon is analyzed in terms of chemical reactions or metabolic pathways. Biochemistry has been previously named as biological chemistry, chemical biology, clinical chemistry, chemical pathology, physiological chemistry, including medical biochemistry and clinical biochemistry. Medical biochemistry studies the chemical composition and physiological reactions in the human body. Clinical biochemistry is the measurement of chemicals or analytes in body fluids for the diagnosis, monitoring and management of patients with various diseases such as diabetes, cardiovascular diseases, etc. An increase in the number and availability of laboratory diagnostics has helped in the solution of clinical problems. Particularly important is the contribution of clinical chemistry to the diagnosis and monitoring of diabetes. The importance of lipids and lipoproteins for public health has increased with clinical studies showing the benefit of lipid lowering in cardiovascular diseases. An understanding of clinical chemistry and biochemistry would be useful in the study of medical and allied sciences for the advancement of knowledge in academic and professional courses. This review article is an attempt to understand the scope and significance of basic and applied aspects of biochemistry.

Keywords: Medical Biochemistry, Chemical Biology, Clinical Biochemistry, Chemical pathology, Clinical Chemistry, Biomarkers

INTRODUCTION

Biochemistry is a branch of biosciences which deals with the study of chemical reactions that occur in living cells and organisms. It is a discipline in which biological phenomena are analyzed in terms of chemistry and is therefore, also known as “biological chemistry”, “chemical biology”, “chemical physiology”, “chemical pathology”. The term “biochemistry”, includes “physiological chemistry” and “biological chemistry”, the aspects of biochemistry that deal with the chemistry and function of large molecules (e.g., proteins and nucleic acids). Biochemistry is the study of chemical reactions at the cellular and molecular level particularly biological molecules or biomolecules (Ahsan, H., 2021). Biochemistry is the study of the chemical substances and processes that occur in plants,

animals, and microorganisms and the changes during development and life of an organism. Therefore, it is concerned with the chemistry of life and the molecular basis of metabolic and physiological processes (Fig. 1). All chemical changes within the organism such as the degradation of substances (catabolism) to produce energy, or the building of complex molecules necessary for life processes (anabolism) are collectively termed metabolic reactions or metabolism. In fact, biochemistry originated as an offspring/offshoot of human biology or physiology when it was realized that the chemical analysis of urine, blood and other body fluids may help in diagnosis of diseases. The advancement in biochemistry has led to an understanding of chemical structures and processes in health and disease and their underlying mechanisms. The objective of biochemistry is to understand the fundamental unit of life, the living cell, and the various function and properties of its individual chemical constituents (Dominiczak, M.H., 2011).

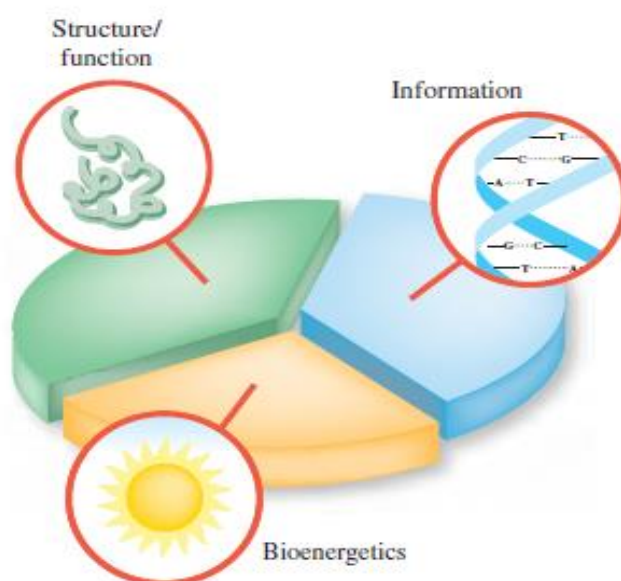


Figure 1. The various aspects of general biochemistry(adapted and reprinted from Biochemistry: from atoms to molecules to cells; web.thu.edu.tw/hclu/www/biochem/chap01.pdf).

Problem of Research

Biochemistry has emerged as a distinct discipline around the beginning of the 20th century when scientists combined chemistry, physiology and biology to investigate the chemistry of living systems. Biochemistry is involved in the investigation of chemical changes in diseases, drug action and other aspects of medicine, nutrition, genetics and agriculture. It was initially referred to as “biological chemistry”, “physiological chemistry”, “biochemiemedicale”, “medical biochemistry”, “biochemialekarska” (Dominiczak, M.H., 2011). Many scientists consider the in vitro synthesis of urea by Friedrich Wöhler, a German chemist, as the beginning of modern biochemistry. Linus Pauling, in the 20th century,

used the basic laws of physics and chemistry to study the structure of proteins through X-ray crystallography. The term “Biochemistry” was first introduced by the German chemist Carl A. Neuberg in 1903. Perhaps the most important and significant advancement in the field was the elucidation of the double helical structure for deoxyribonucleic acid (DNA) by James D. Watson and Francis H. C. Crick in 1953. Modern biochemistry originated when biologists, microbiologists, chemists, physiologists and geneticists characterized the structure and function of cellular components (Fig. 2).

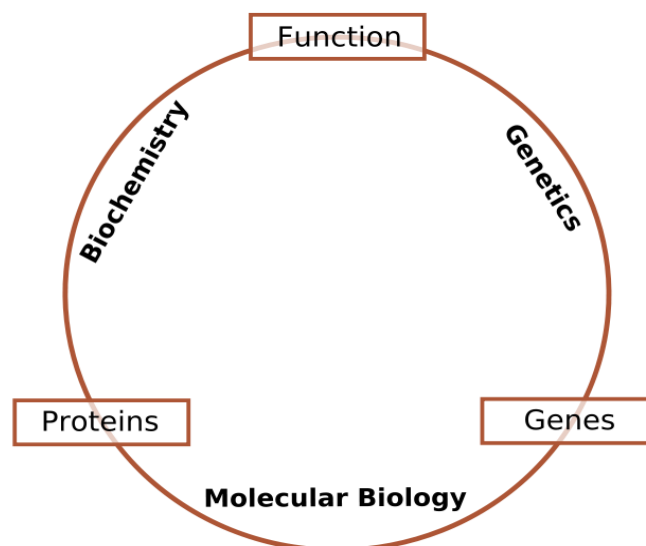


Figure 2. The relationship between biochemistry, genetics and molecular biology through their function, proteins and genes (reprinted from Wikimedia Commons, the free media repository. Copyright: This file is licensed under the Creative Commons Attribution).

Research Focus

All living beings are composed of molecules and atoms known as biomolecules and their biochemical reactions and interactions sustains life of organisms. If a change is observed at an anatomical or a physiological level, it is due to the result of a change at the biomolecular or biochemical level (Beeley, J.A., 1974).. The major objective of biochemistry is to understand the chemical processes associated with living organisms at the cellular and molecular level. The biochemical study of diseases has opened up new therapeutic approaches such as the determination of the function and action of biomolecules in diseases, inborn errors of metabolism, oncogenes in cancer cells, etc. (Fig. 3). Biochemical studies have already led to the molecular understanding of diseases such as diabetes, sickle-cell anemia, phenylketonuria, cystic fibrosis, hypercholesterolemia, neurodegenerative diseases, autoimmune diseases and cancers. The sequencing of the human genome, hailed as one of the greatest scientific advancement and achievement of the 20th century, will help in understanding diseases and search for a cure various diseases such as viral diseases, Alzheimer's, Parkinson's, influenza, Covid-19/SARS-CoV-2, etc. Genetic engineering or recombinant DNA technology will play an important role in the diagnosis and treatment of

diseases through the identification of cellular components and chromosomal regions for genetic mutations (Garcia, W.P., 1985). Therefore, medical biochemistry has a profound impact on our understanding of medicine, health and nutrition.

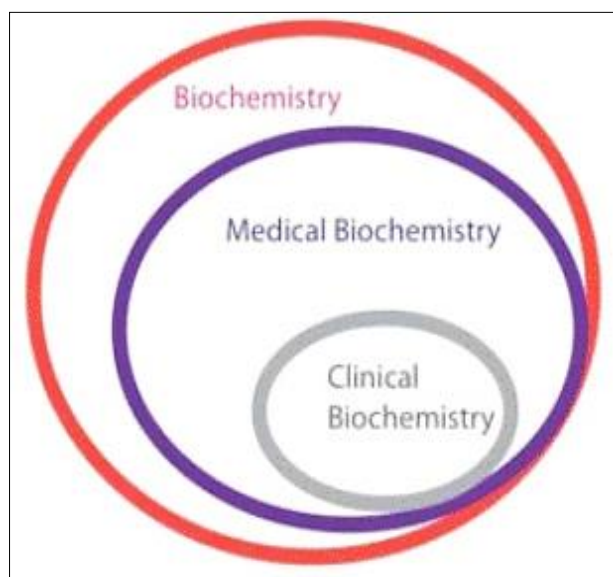


Figure 3. The relationship between biochemistry, medical biochemistry and clinical biochemistry (reprinted from Dominiczak, 2011. copyright Encyclopedia of Life Support Systems, EOLSS).

METHODOLOGY OF RESEARCH

This study is a qualitative research that will discuss clinical and molecular biochemistry in applied medicine studies through various literatures. The study of biological catalysts (enzymes) and cellular metabolism is useful for understanding the requirements of diet and nutrition in wellbeing and health. Metabolism consists of biochemical reactions taking place in a living organism and is a highly coordinated and purposeful activity for the production of energy and synthesis and degradation of cell components such as macromolecules (proteins, lipids and carbohydrates). These various biochemical reactions are catalyzed by enzymes and are classified into anabolism (energy requiring biosynthetic pathways) and catabolism (degradation of large biomolecules and the production of energy for cellular function). Some metabolic reactions may be amphibolic consisting of both anabolic and catabolic components. The primary functions of metabolism is the generation and utilization of energy, synthesis of molecules required for cellular structure and function (i.e. proteins, nucleic acids, lipids, carbohydrates) and the removal of waste products. The metabolic changes associated with specific diseases and pathological conditions give rise to a change in the biochemical profile of a particular body fluid, e.g. increased blood glucose in diabetes mellitus and a decreased glucose levels in the cerebrospinal fluid in bacterial meningitis (Luthra, K., 2004).

Hence, clinical biochemistry has become an important part of the clinical laboratory investigation for the chemical analysis of substances in body fluids (serum, urine, saliva) in the diagnosis and management of patients such as electrolytes, glycated hemoglobin (HbA1c), lipids and lipoproteins profile (cardiovascular diseases), inborn errors of metabolism, etc.

The functional components of clinical laboratory sciences are clinical pathology, hematology, clinical biochemistry, clinical microbiology, serology, blood bank, histology and cytology. The function of clinical laboratory is to perform qualitative and quantitative analysis of body fluids such as blood (serum or plasma), urine, feces, cerebrospinal fluid (CSF). The various body fluids such as blood, urine, feces, cerebrospinal fluid and other body fluids are examined in clinical chemistry and biochemistry. Clinical biochemistry deals with the laboratory analysis of chemical and biochemical parameters of various organs and organ systems such as liver, stomach, heart, kidneys, brain, endocrine system, etc. Some biochemical investigations are done routinely for most patients e.g. blood glucose, serum creatinine and urea, lipid profile, analysis of liver enzymes and analysis of urine (Lopez, J., et al, 2015; Ahsan, H., 2014; Maldonado, F.S., 2013; Varley, H & Bell, M., 1980; Hastings, A.B, 19972). Endocrinology-related tests include the thyroid function and various hormones (including assessment of the gonadal, fetoplacental and pregnancy). Before the introduction of radioimmunoassay (RIA), which allowed measurement of picogram concentrations of analytes, the hormones were measured indirectly (e.g. thyroid hormones were estimated as protein-bound iodine, and steroids, as their urinary metabolites) (Dominiczak, M.H., 2011). Therefore, an increase in the number and availability of clinical chemistry and biochemistry laboratory investigations is significant in the diagnosis and prognosis of pathological condition.

RESULTS AND DISCUSSION

Clinical biochemistry deals with the methodology and interpretation of biochemical investigations on body fluids and tissues for the diagnosis, treatment and monitoring of diseases (Dominiczak, M.H., 2011). Diagnostic biochemistry has made exponential progress in the last 50 years with the development of advanced automation and detection systems. Moreover, with the availability of analytical kits and autoanalyzers, it is now possible to perform rapid and large scale diagnostic tests and analysis. The progress and advancement in the analysis of the genetic materials such as single nucleotide polymorphism (SNP), DNA fingerprinting (genotyping), polymerase chain reaction (PCR) technology has revolutionized various tests in clinical biochemistry (Ahsan, H., 2021), due to the integration of molecular diagnostics with pathological and microbiological laboratory investigations (Rosenfeld, L., 2002). The clinical biochemistry laboratories providing molecular diagnostics services are performed through the utilization of PCR with high capacity instrumentation using mass spectrometry (MS). For example, gene polymorphism, pharmacogenomics and PCR based molecular tests are performed in the central laboratory facility by integrating molecular

diagnostic services with the clinical biochemistry laboratory. Hence, there is an increased demand to provide high throughput and dedicated services by the diagnostic laboratories for advanced procedures and investigations in clinical microbiology and pathology (Rosenfeld, L., 2002). The issues in clinical biochemistry are associated with high volume testing namely laboratory automation and workflow management and computational issues. The last decades have witnessed a noticeable advancement in the identification of biomarkers through molecular techniques and technology known as systems biology such as genomics, epigenomics, proteomics, metabolomics and bioinformatics (Ahsan, H., 2021; Dominiczak, M.H., 2011). Proteomic approach may be divided into conventional protein biomarker detection and multiplex proteomics. Epigenomics is a recently emerging area of molecular diagnostics for the exploration of epigenetic markers in tumor diagnosis and monitoring. The rapid progress in systems biology has significantly improved the discovery of biomarkers for their usefulness in academic and pharmaceutical environment ((Rosenfeld, L., 2002)). Thus, with increasing number of diagnostic applications, the scope of clinical biochemistry is becoming increasingly significant in applied and basic medical sciences (Dominiczak, M.H., 2011; Aroor, A.R., 2011; Kogut, M., 1974).

The role of clinical biochemistry through the use of biomarkers for diagnosis and monitoring of diseases and the discovery of epigenetic biomarkers has been the major development in clinical translational science. Comprehensive molecular investigation requires the analysis of genomics (microarray, epigenomics, and specific genes) and proteomics. Moreover, recent studies have demonstrated the ability of epigenetic biomarkers such as DNA methylation, histone modifications and changes in microRNA (miRNA) expression using human fluid and tissue samples. The protein arrays or protein chips are becoming a valuable tool which offers a promising approach for the detection and progression of diseases. The functional proteomics and liquid chromatography (LC) coupled to tandem mass spectrometry (MS) (LC/MS) based metabolomics has provided novel insights into the molecular biochemistry of diseases (Beeley, J.A., 1974; Rosenfeld, L., 2002). The diagnostic laboratories provide investigations such as genetic polymorphism in relation to cancer risk, pharmacogenomics and genetic disorders for inherited disorders of metabolism, toxicology (Garcia, W.P., 1985; Luthra, K., 2004; Lopez, J., et al., 2015; Lopez, J., et al., 2012). Large referral laboratories in medical institutes may offer additional molecular diagnostic services such as proteomics, transcriptomics and epigenomic investigations (Devli, T.M., 2010; Maldonado, F.S., 2013; Rosenfeld, L., 2002).

CONCLUSIONS

Medical biochemistry includes all aspects of clinical chemistry, laboratory hematology with coagulation, immunochemistry, and laboratory endocrinology. Clinical chemistry and biochemistry is an important applied sub-discipline of medical biochemistry, also known as clinical chemistry, pathological biochemistry or chemical pathology. Clinical biochemistry is one of the most rapidly advancing areas of laboratory and clinical medicine. The marked increase in the number and availability of laboratory diagnostic procedures is important in

making clinical and therapeutic decisions. Clinical chemistry and biochemistry is concerned with methodology and interpretation of biochemical tests performed on body fluids and tissues, to support diagnosis, treatment and monitoring of disease. Clinical biochemistry is the measurement of chemicals or analytes in body fluids to provide data for the diagnosis and management of patients. Hence, an understanding of clinical and molecular biochemistry would be useful in the study of medicine in diagnosis of pathologies through advanced methodologies and technological advancements.

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