

Biochemical markers for diagnosis of diseases and follow up

Rana Hasanato

Professor and Consultant

Corporate Director of Medical Laboratories
and Blood bank

Lecture objectives:

Upon completion of this lecture, the students should be able to:

- Define biomarkers and its criteria
- Recognize different types of biochemical markers
- Demonstrate the clinical applications of biomarkers in diagnosis of various diseases

What is a biomarker?

- A biological molecule found in blood, other body fluids, or tissues that indicates a normal or abnormal process such as a disease or a condition

Most common body fluids for the measurement of biomarkers are:

- Blood
- Urine
- Biomarkers are either:
 - Plasma-specific
 - Tissue-specific

Plasma-specific biomarkers:

- Normally present in plasma
- Perform their functions in blood
- High level of activity in plasma than in tissue cells

Tissue-specific biomarkers:

- Present **inside the cell**
- A low concentration can be detected in plasma due to cellular turnover
- If higher concentration is detected in plasma, it indicates **cell damage**.

- Cell damage can be due to:
 - 1- Tissue inflammation, example:
 - ALT* in liver disease (e.g. acute hepatitis)
 - Amylase in acute pancreatitis
 - 2- Ischemia □ hypoxia □ infarction □
↑ plasma [Troponin] in myocardial infarction

ALT*: alanine aminotransferase

diagnosis and prognosis:

Diagnosis: Identification of a disease from its signs and symptoms

Prognosis: The future outcome of a disease

Criteria of a good biomarker assay:

A good biomarker assay should be:

- Sensitive: Sensitivity is the Ability of an assay to detect small quantities of a marker
- Specific: Specificity is the ability of an assay to detect only the marker of interest
- Robust to produce fast results

Examples of biomarkers:

- Enzymes
- Hormones
- Proteins

Enzymes as biomarkers:

Examples include:

- Amylase, Lipase
- Alanine aminotransferase (ALT)
- Aspartate aminotransferase (AST)

Amylase:

- Elevated serum amylase level is a diagnostic indicator of acute pancreatitis
- Amylase level greater than **10 times** the upper limit indicates acute pancreatitis
- The test has low specificity because elevated amylase level is also present in other diseases
- Amylase appears in the serum within 2-12 hours after abdominal pain, and returns to normal in 3-5 days

Lipase:

- Serum lipase has higher specificity than serum amylase (elevated only in acute pancreatitis)
- It appears in plasma within 4-8 hours and remains for 8-14 days

Case:

A GP was called to see a 21-year-old female student who had been complaining a flu-like illness for two days, with symptoms of fever, vomiting and abdominal tenderness in the right upper quadrant. On examination she was jaundiced, moreover; the liver was enlarged and tender. A blood was taken for liver function tests which **showed elevated ALT** (alanine aminotransferase) **and AST** (aspartate aminotransferase)

- What is the most likely diagnosis?

Acute Hepatitis

Aspartate aminotransferase (AST) Alanine aminotransferase (ALT):

	AST	ALT
Produced by:	heart, liver, skeletal muscle, kidney, erythrocytes	liver
Elevated in:	Liver disease, heart disease, skeletal muscle disease, hemolysis	Liver disease

Proteins as biomarkers:

- α -Fetoprotein
- Prostate Specific Antigen (PSA)
- Cystatin C
- B-type Natriuretic Peptide (BNP)

a-Fetoprotein:

- It is produced by the fetal liver, and falls until term
 - in newborn babies a-fetoprotein levels are very low
- It remains low under normal conditions.
- High conc. are observed in:
 - hepatocellular carcinomas (hepatoma)
 - testicular carcinomas
 - GI tract carcinomas
- It is a non specific marker

Prostate Specific Antigen

(PSA):

- Produced by prostate gland
- PSA level is used as a tumor marker to aid diagnosis and for monitoring in patients with **prostatic cancer**.
- High serum levels are also observed in:
 - Benign prostatic hyperplasia (BPH)
 - Prostatic inflammation/infection

Cystatin C:

- A cysteine protease inhibitor mainly produced by all nucleated cells of the body
- Useful biomarker for measuring glomerular filtration rate (GFR) in assessing kidney function
- Unlike creatinine, its serum conc. is independent of gender, age or muscle mass
- High levels of serum cystatin C indicates early renal disease
- Clinically used as a marker for:
 - detecting early kidney disease
 - monitoring kidney transplantation

B-type natriuretic peptide

(BNP)

- A peptide secreted mainly in the cardiac ventricles in response to cardiac expansion and pressure overload
- High serum levels are observed in congestive heart failure
- It can be used to differentiate patients whose symptoms are due to heart failure from those whose symptoms are due to other causes such as pulmonary disease.

Hormones as biomarkers:

Anti-Mullerian hormone (AMH):

- In females it is produced by ovaries
- Appears to be a best marker for estimating egg cell reserve in the ovaries (ovarian reserve testing)
- only growing follicles produce AMH
- Plasma AMH levels strongly correlate with number of growing follicles
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Anti-Mullerian hormone (AMH)



High levels in women
with Polycystic ovarian
syndrome (**PCOS**)

Low levels in women
with **ovarian**
dysfunction

Take home message:

- Biochemical markers are essential accurate and non-invasive laboratory tools offering the treating physicians fast means for better management.
- They could be proteins, enzymes, or hormones.
- Recent development in medicine provides new biomarkers