

Biochemical markers for diagnosis of diseases and follow up

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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

aminotransferase

ALT*: alanine

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)

α -Fetoprotein:

- It is produced by the fetal liver, and falls until term → in newborn babies α -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)

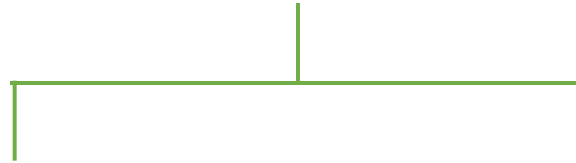
- A peptide secreted mainly in the cardiac ventricles in response to cardiac expansion and pressure overload
- High serum levels are observed in congestive heart failure
- It can be used to differentiate patients whose symptoms are due to heart failure from those whose symptoms are due to other causes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

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