

# Biochemical markers for diagnosis of diseases and follow up

Foundation Block

Dr. Usman Ghani

# Lecture objectives

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

- Comprehend the importance and diagnostic qualities of various biomarkers
- Understand the importance of different biomarkers in the diagnosis, treatment and follow up of a disease.
- Recognize the types of biomarkers and their use in specific diseases such as heart, cancer, liver, kidney and pancreatic diseases

# Overview

- What is a biomarker?
- Diagnosis and prognosis
- Plasma and tissue-specific biomarkers
- Qualities of a good biomarker
- Types: Enzymes, proteins, hormones
- Enzymes: Amylase, lipase, trypsinogen, ALT, AST
- Proteins: Cystatin C, BNP,  $\alpha$ -fetoprotein, PSA
- Hormones: Anti-Mullerian hormone

# 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
- A biomarker is measured to follow up a disease or treatment

# diagnosis and prognosis

## Diagnosis:

- Identification of a disease from its signs and symptoms

## Prognosis:

- The future outcome of a disease



Most common body fluids for measurement of biomarkers are:

- Serum
- Plasma
- Urine

Some biomarkers are either:

- Plasma-specific or
- Tissue-specific

## Plasma-specific biomarkers



- Normally present in plasma
- Perform their functions in blood
- High level of activity in plasma than in tissue cells
- Examples: blood clotting enzymes (thrombin), cholinesterase, etc.



## Tissue-specific biomarkers

- Present inside the cell
- Conc. is lower in plasma
- Released into the body fluids in high conc. due to:
  - cell damage
  - defective cell membrane





Cell damage can be due to:

- Tissue inflammation
  - Examples: Alanine aminotransferase in liver disease (e.g. acute hepatitis)
  - Amylase in acute pancreatitis
- Ischemia → hypoxia → infarction →  
↑ plasma [Troponins] in myocardial infarction

# Qualities of a good biomarker

A good biomarker should be:

- Able to accurately diagnose a disease
- Able to accurately predict prognosis of a disease
- Compliant with treatment follow up
- Easily obtainable from blood, urine, etc.

# Qualities of a good biomarker assay

- A good biomarker assay should be rapid to deliver results faster
- **Sensitive**
  - Ability of an assay to detect small quantities of a marker
- **Specific**
  - Ability of an assay to detect only the marker of interest



# Types of biomarkers

- Enzymes
- Hormones
- Proteins



# Enzymes as biomarkers

- Enzymes are clinically used for the diagnosis and prognosis of various diseases

Examples include:

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

# Amylase and Lipase

## 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 serum amylase level is also present in other diseases
- Amylase appears in the serum within 2-12 hours after abdominal pain and returns to normal within 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 of flu-like illness for two days with symptoms of fever, vomiting and abdominal tenderness in the right upper quadrant. On examination she was found to have jaundice with enlarged liver and tenderness. Her liver enzymes enzymes such as **ALT (alanine aminotransferase)** and **AST (aspartate aminotransferase)** were elevated.

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

- Cystatin C
- B-type natriuretic peptide (BNP)

## Tumor markers

- $\alpha$ -Fetoprotein
- Prostate Specific Antigen (PSA)

# 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 and failure
- Unlike creatinine, its serum conc. is independent of gender, age or muscle mass
- Abnormally high serum levels of cystatin C indicates kidney failure
- Clinically useful 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

# Tumor markers

- A molecule secreted by a tumor that is measured for diagnosis and management of a tumor
- $\alpha$ -fetoprotein
- Prostate specific antigen (PSA)

# $\alpha$ -Fetoprotein

- Produced by fetal liver
- In newborn babies  $\alpha$ -fetoprotein levels are very low
- High conc. are observed in:
  - Hepatocellular carcinomas (hepatoma)
  - Testicular carcinomas
  - GI tract carcinomas
- However, high serum levels are also found in benign (non-cancerous) conditions e.g. hepatitis
- High conc. are not always suggestive of a tumor

# Prostate Specific Antigen (PSA)

- Produced by prostate gland
- High serum PSA levels are observed in prostate cancer
- Less specific in diagnosis
- High serum levels are also observed in:
  - Benign prostatic hyperplasia (BPH)
  - Prostatic inflammation/infection

# Anti-Mullerian Hormone

- Produced by ovaries in females
- 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 messages

- Biomarkers are used for diagnosis, prognosis and follow up of diseases
- A biomarker should exhibit good diagnostic and prognostic values
- Examples of biomarkers used in different disease will help understand their qualities and limitations

# References

- What are biomarkers? Kyle Strimbu and Jorge A. Tavel, *Curr Opin HIV AIDS*. 2010 November ; 5 (6): 463–466
- Biomarkers: Potential uses and limitations. Richard Mayeux. *J. Amer. Soc. Exp. Neuro Therap.* Vol. 1, 182–188, April 2004