# Plasma Proteins

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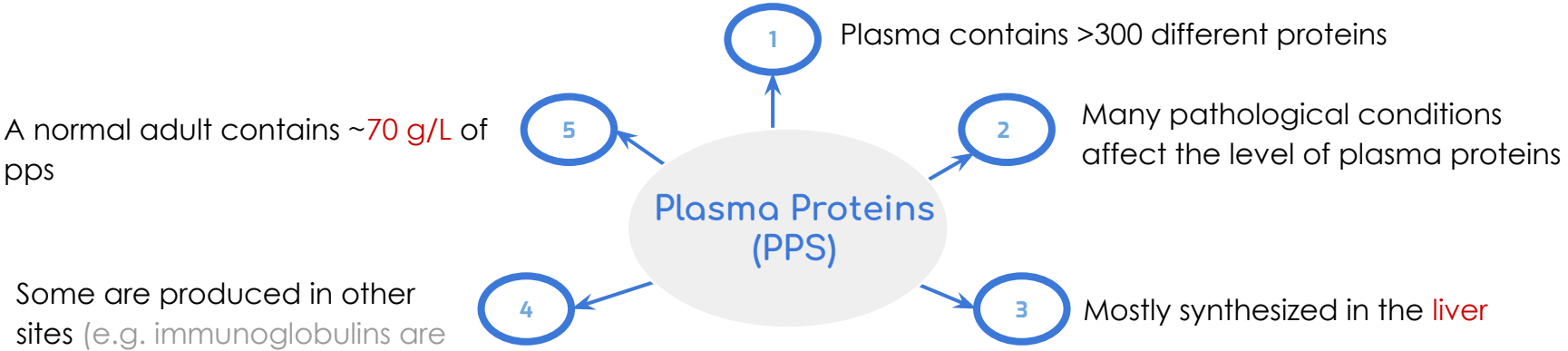
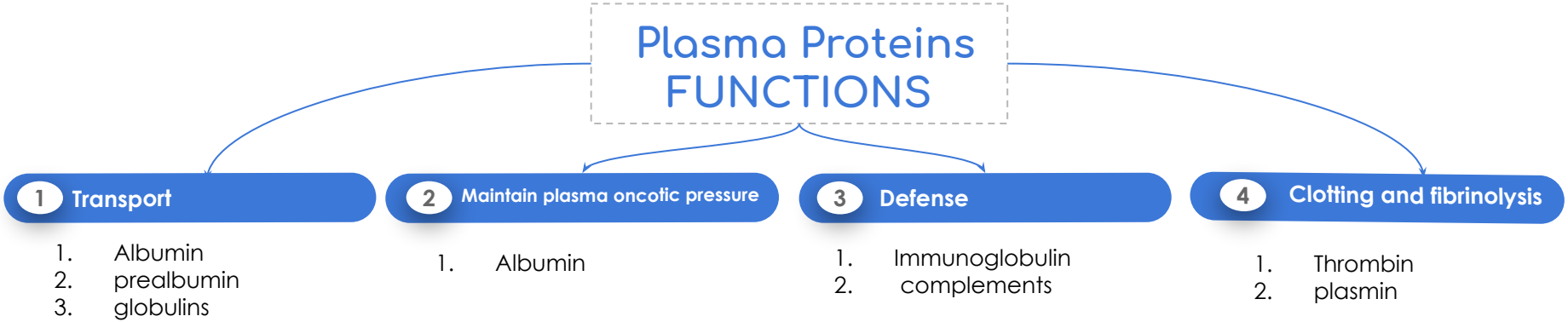
## Objectives:

- Identify types and various functions of plasma proteins.
- Discuss the role of plasma proteins in the diagnosis of diseases and conditions.
- Interpret the normal and abnormal electrophoretic patterns of plasma proteins.
- Identify the role positive and negative acute phase proteins in various diseases.

## Overview:

- Functions and characteristics of plasma proteins
- Measurement of plasma proteins and diagnosis of diseases
- Electrophoretic patterns of plasma proteins
- Acute phase proteins


Plasma Proteins (PPS)
1
Plasma contains >300 different proteins
2
Many pathological conditions affect the level of plasma proteins
3
Mostly synthesized in the liver
4
Some are produced in other sites (e.g. immunoglobulins are produced by plasma B cells)
5
A normal adult contains ~70 g/L of pps


Plasma Proteins FUNCTIONS
1 Transport
1. Albumin
2. prealbumin
3. globulins
2 Maintain plasma oncotic pressure
1. Albumin
3 Defense
1. Immunoglobulin
2. complements
4 Clotting and fibrinolysis
1. Thrombin
2. plasmin

# Measurement of Plasma Proteins

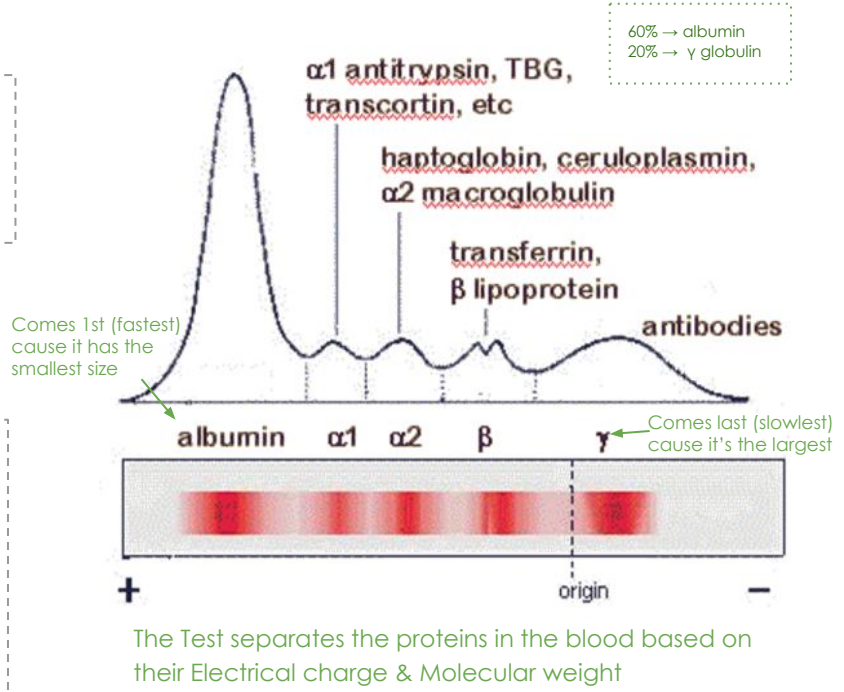
1- Quantitative measurement of a specific protein:

- **Chemical or immunological reactions**

2- Semiquantitative measurement by electrophoresis:

- Proteins are separated by their electrical charge in electrophoresis
- **Five separate bands of proteins are observed**
- These bands change in disease

Normal Pattern of Plasma Protein Electrophoresis




The Test separates the proteins in the blood based on their Electrical charge & Molecular weight

# Types of Plasma Proteins

1. Prealbumin
2. Albumin
3. γ- Globulins
4. $\alpha_1$-Globulins:
   1. $\alpha_1$-Antitrypsin
   2. α-fetoprotein
5. $\alpha_2$-Globulins:
   1. Ceruloplasmin
   2. Haptoglobin
6. β-Globulins:
   1. CRP
   2. Transferrin
   3. β2-microglobulin

# Prealbumin (Transthyretin):

## Information

- Migrates faster than albumin in electrophoresis
- Separated by immunoelectrophoresis
- Short half-life (2 days)

It is NOT an albumin precursor, it's a completely different protein that doesn't show bands in electrophoresis because it's small

## Function

A transport protein for:

1- Thyroid hormone

2- Retinol (vitamin A)

## Lowered levels in:

1. liver disease,
2. nephrotic syndrome,
3. acute phase inflammatory response
4. malnutrition

# Albumin

1- Most abundant plasma protein (~40 g/L) in normal adult.

2- Synthesized in the liver as **preproalbumin** and secreted as albumin.

3- Half-life in plasma: 20 days

4- Decreases rapidly in injury, infection and surgery.

## Functions

1- Maintains oncotic pressure:

–The osmotic pressure exerted by plasma proteins that pulls water into the circulatory system.

–Maintains fluid distribution in and outside cells and plasma volume.

2- 80% of plasma oncotic pressure is maintained by albumin.

3- A non-specific carrier of: hormones, calcium, free fatty acids, drugs, etc.

4- Tissue cells can take up albumin by pinocytosis where it is hydrolyzed to amino acids.

5- Useful in treatment of liver diseases, hemorrhage, shock and burns.

## Abnormalities

**1- Hypoalbuminemia:**

Causes:

1- Decreased albumin synthesis (liver cirrhosis, malnutrition)

2- Increased losses of albumin:

-Increased catabolism in infections

-Excessive excretion by the kidneys (nephrotic syndrome)

-Excessive loss in bowel (bleeding)

-Severe burns (plasma loss in the absence of skin barrier

Effects:

1- Edema due to low oncotic pressure

-Albumin level drops in liver disease causing low oncotic pressure

-Fluid moves into the interstitial spaces causing edema

2- Reduced transport of drugs and other substances in plasma

3- Reduced protein-bound calcium

- Total plasma calcium level drops

- Ionized calcium level may remain normal

**2-Hyperalbuminemia:**

1- No clinical conditions are known that cause the liver to produce large amounts of albumin.

2- The only cause of hyperalbuminemia is dehydration.

# $a_1$-Antitrypsin

## Information

1. Synthesized by the liver and macrophages.
2. Over 30 types are known.
3. The most common is **M type.**

## Function

1- An acute-phase protein that inhibits **proteases**.

2- Proteases are produced endogenously and from leukocytes and bacteria.

- **Digestive enzymes** (trypsin, chymotrypsin)
- **Other proteases** (elastase, thrombin)

3- Infection leads to protease release from bacteria and from leukocytes.

## Genetic definciny

1- Synthesis of the defective $a_1$-Antitrypsin occurs in the liver but it cannot secrete the protein.

2- $a_1$-Antitrypsin accumulates in hepatocytes and is deficient in plasma.

## Laboratory Diagnosis:

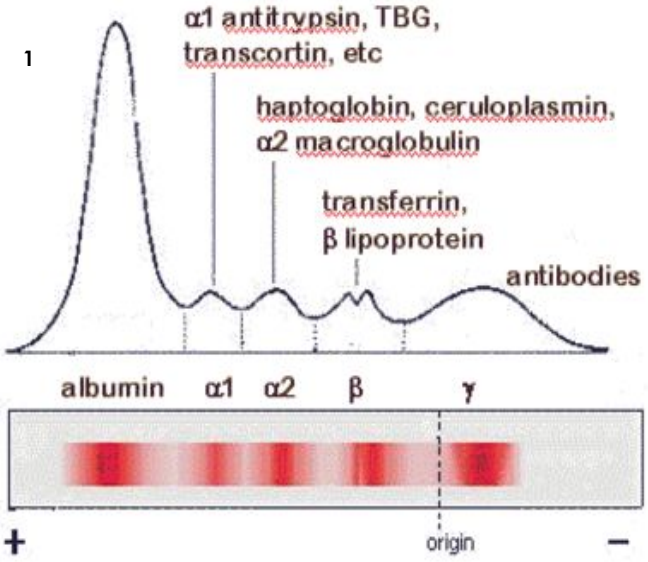
1. Lack of $a_1$-globulin band in protein electrophoresis.
2. Quantitative measurement of $a_1$-Antitrypsin by:

   Radial immunodiffusion, isoelectric focusing or nephelometry

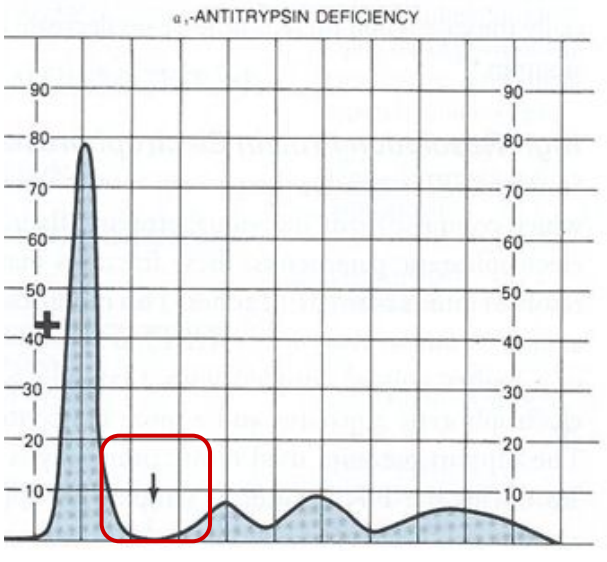
## Clinical Consequences of $a_1$-Antitrypsin Deficiency:

1. Neonatal jaundice with evidence of cholestasis
2. Childhood liver cirrhosis
3. Pulmonary emphysema in young adults

1




2



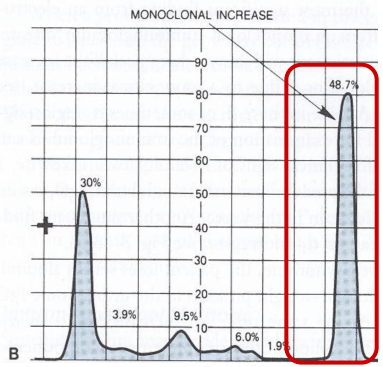

- Picture 1 shows a normal Serum Electrophoresis Pattern
- Pictures 2 shows **$\alpha_1$-Antitrypsin\$\alpha_1$-globulin** is gone. which means the patient has no **$\alpha_1$-Antitrypsin**

| Plasma protein | Information/Function | Abnormality |
|---|---|---|
| **α-Fetoprotein (AFP)** | -Synthesized in the developing embryo and fetus by the parenchymal cells of the liver.<br>-AFP levels decrease gradually during intra-uterine life and reach adult levels at birth.<br>-Function is unknown but it may protect fetus from immunologic attack by the mother & no known physiological function in adult. | -Elevated maternal AFP levels are associated with: **Neural tube defect, anencephaly**<br>-Decreased maternal AFP levels areassociated with: **Increased risk of Down's syndrome**<br>-AFP is a tumor marker for: **Hepatoma and testicular cancer.** |
| **Ceruloplasmin** | -Synthesized by the liver & **contains >90% of serum copper.**<br>-An **oxidoreductase** that inactivates ROS causing tissue damage in acute phase response.<br>-Important for iron absorption from the intestine. | -**Wilson's disease**:<br>Due to low plasma levels of ceruloplasmin, **copper** is accumulated in the liver and brain. |
| **Haptoglobin** | -Synthesized by the liver & binds to free hemoglobin to form complexes that are metabolized in the reticuloendothelial system (RES).<br>-Limits iron loss by preventing Hb loss from kidneys (recycling) | -Plasma level decreases during **hemolysis**. |
| **Transferrin** | -A major **iron-transport** protein in plasma 30% saturated with iron & Iron deficiency results in increased hepatic synthesis.<br>-A ***negative*** acute phase protein[1]. | -Plasma level **drops** in: Malnutrition, liver disease, inflammation, malignancy. |
| **β2–Microglobulin** | -A component of human leukocyte antigen (**HLA**) & present on the surface of lymphocytes and most nucleated cells.<br>-Filtered by the renal glomeruli due to its small size but most (>99%) is reabsorbed. | -Elevated serum levels are found in: severe inflammation (infections, SLE, and rheumatoid arthritis)<br>-May be a tumor marker for: **Leukemia, lymphomas, multiple myeloma.** |
| **C-Reactive Protein (CRP)** | -A ***Positive*** acute-phase protein synthesized by the liver & Important for **phagocytosis**.<br> | -High plasma levels are found in many inflammatory conditions such as **rheumatoid arthritis.**<br>-A marker for **ischemic heart disease.** it's ultra sensitive CRP |

1.Acute phase proteins will be discussed in the next slides

# Hypergammaglobulinemia

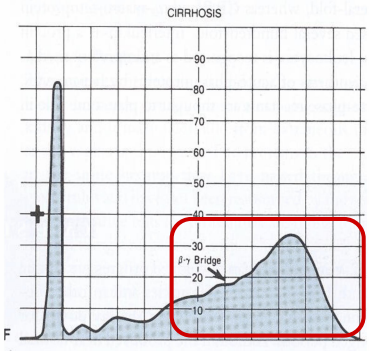
## 01 Monoclonal Hypergammaglobulinemia




- Proliferation of a **single** B-cell clone produces a single type of Ig□.
- Appears as a separate dense band (paraprotein or **M band**) in electrophoresis.
- Paraproteins are characteristic of malignant B-cell proliferation.
- Clinical condition: **multiple myeloma.**

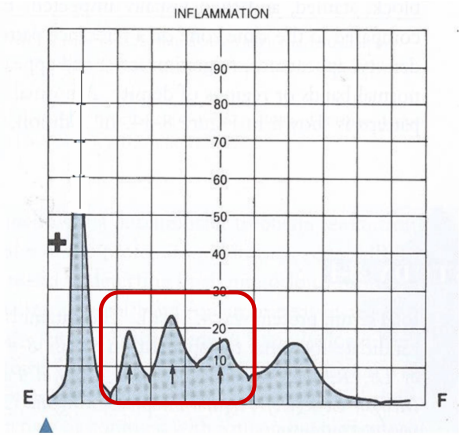
**3M**: **M**onoclonal - **M** band - **M**ultiple myeloma

## 02 Polyclonal Hypergammaglobulinemia




- Stimulation of **many** clones of B cells produce a wide range of antibodies.
- □**γ-globulin band** appears large in electophoresis.
- Clinical conditions: **acute and chronic infections, autoimmune diseases, chronic liver diseases.**

# Positive acute phase proteins




-Plasma protein levels increase in: Infection, inflammation, malignancy, trauma, surgery.
-These proteins are called acute phase reactants & synthesized due to body's response to injury.

-**Examples**: **a1-Antitypsin, haptoglobin, ceruloplasmin, fibrinogen, C-reactive protein.**

**Mediators that cause these proteins to increase after injury are:**
Cytokines (IL-1, IL-6), tumor necrosis factors a and β, interferons, platelet activating factor.

**Mediators functions:**
1. Bind to polysaccharides in bacterial walls.
2. Activate complement system.
3. Stimulate phagocytosis.

# Negative acute phase proteins

-These are proteins which decrease in inflammation: **Albumin, prealbumin, transferrin**
-They're mediated by inflammatory response via cytokines and hormones.
-Reason for the decrease in synthesis of these proteins is:
**to save amino acids for positive acute phase proteins.**

Dr's note: Acute phase inflammatory response is the first response that you will have within 24 hours of an acute insult/infection. Your body will try to fight the insult by synthesizing certain proteins in increased amounts (positive proteins), while decreasing the amounts of other proteins (negative proteins).

# Take Home Messages

- **Plasma proteins play essential roles in a number of cellular functions.**
- **They possess diagnostic significance in identifying various pathological conditions.**

# Summary

| Plasma proteins | | |
|---|---|---|
| **Functions** | **Abnormal levels of proteins** | **Proteins used as markers** |
| **1.transport**: (albumin/prealbumin/globulin)<br>**2.maintain plasma oncotic pressure:** (albumin)<br>**3.Defense:** (Immunoglobulins and complement)<br>**4.Clotting and fibrinolysis**: (Thrombin and plasmin) | **1. Prealbumin:** decreased level in liver disease, nephrotic syndrome, acute phase inflammatory response, malnutrition.<br>**2. Albumin:** Decreased in liver cirrhosis, malnutrition, Increased losses of albumin (such as severe burn/bleeding). While it's increased in dehydration.<br>**3. α1-Antitrypsin:** decreased levels lead to neonatal jaundice / childhood liver cirrhosis / pulmonary emphysema.<br>**4. α-fetoprotein:** increased level associates with neural tube defect and anencephaly while decreased level associates with Down syndrome.<br>**5. Ceruloplasmin:** decreased level in Wilson's disease.<br>**6. Haptoglobin:** decreased during hemolysis.<br>**7. CRP:** increased in inflammatory conditions such as rheumatoid arthritis<br>**8. Transferrin:** decreased in Malnutrition, liver disease, inflammation, malignancy.<br>**9. β2-microglobulin:** increased levels / overproduction in inflammatory diseases.<br>**10. γ- Globulins:** increased level result in hypergammaglobulinemia. | **1. AFP is a tumor marker for Hepatoma and testicular cancer.**<br><br>**2. β2-microglobulin may be a tumor marker for Leukemia, lymphomas, multiple myeloma.**<br><br>**3. CRP is a marker for ischemic heart disease.** |

# Quiz

## MCQs :

**Q1: Which of the following is a tumor marker for hepatoma:**
**a)** C-Reactive protein **b)** a-fetoprotein **c)** β2–Microglobulin **d)** Haptoglobin

**Q2: Which of the following is a negative acute phase protein:**
**a)** Transferrin **b)** Haptoglobin **c)** C-Reactive protein **d)** Fibrinogen

**Q3: Decreased maternal AFP is associated with:**
**a)** Lymphoma **b)** Anencephaly **c)** Wilson's disease **d)** Down syndrome

**Q4: Which of the following is a clinical consequences of $a_1$-Antitrypsin Deficiency:**
**a)** Adulthood liver cirrhosis **b)** Pulmonary emphysema **c)** Renal failure **d)** ischemic heart disease

**Q5: Which of the following causes Hyperalbuminemia:**
**a)** Increase kidney secretion **b)** Severe burns **c)** Dehydration **d)** Increase catabolism in infection

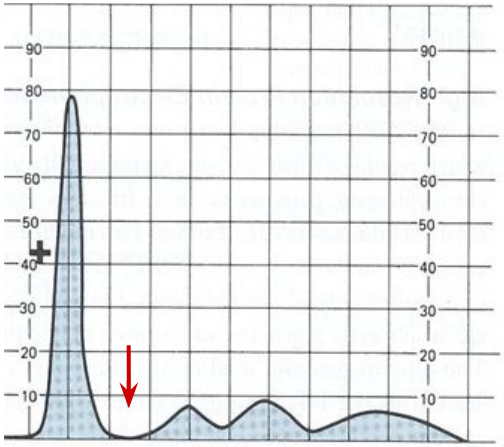
**Q6: Which of the following is true regarding CRP?**
**a)** Important for phagocytosis **b)** Synthesized by kidney **c)** Marker for heart failure **d)** All of them

★ **MCQs Answer key:**

1) B 2) A 3) D 4) B 5) C 6) A

# Quiz

## SAQs :




**Q1: What kind of measurement does this graph indicates?**

**Q2: What kind of abnormality does the RED arrow indicates? Explain.**

**Q3: List TWO clinical consequences of this abnormality.**

**Q4: List THREE negative acute phase proteins.**

**Q5: List THREE mediators that cause positive acute phase proteins to increase after injury.**

★ **SAQs Answer key:**

1) Semiquantitative measurement by plasma protein electrophoresis.
2) Indicate $a_1$-antitrypsin deficiency, because there's lack of $a_1$-globulin band in the graph.
3) Childhood liver cirrhosis - Pulmonary emphysema in young adults.
4) Albumin, prealbumin, transferrin.
5) Cytokines (IL-1, IL-6), tumor necrosis factors a and β , interferons, platelet activating factor.

# Team members

**Girls Team:**

- **Ajeed Al-Rashoud**
- Alwateen Albalawi
- Amira AlDakhilallah
- Arwa Al Emam
- Deema Almaziad
- Ghaliah Alnufaei
- Haifa Alwaily
- Leena Alnassar
- Lama Aldakhil
- **Lamiss Alzahrani**
- Nouf Alhumaidhi
- Noura Alturki
- Sarah Alkhalife
- Shahd Alsalamah
- Taif Alotaibi

**Boys Team:**

- Abdulrahman Bedaiwi
- Alkassem Binobaid
- Khayyal Alderaan
- Mashal Abaalkhail
- Naif Alsolais
- Omar Alyabis
- Omar Saeed
- Omar Odeh
- Rayyan Almousa
- Yazen Bajeaifer

# Team Leaders

Lina Alosaimi

Mohannad Alqarni

★ You Will Never Have This Day Again, So Make It Count


We hear you