**Alkaline phosphatase (ALP):**

The ALPs are a group of enzymes that hydrolyze organic phosphate at high pH (10). They are present in most tissues but are in particularly high concentration in the osteoblasts of bone and the cells of the hepatobiliary tract (produced in the membranes of cell lining bile duct and canaliculi), intestinal wall, renal tubules and placenta. In adults, plasma ALP is derived mainly from bone and liver in approximately equal proportions; plasma activities rise in cholestatic liver disease because ALP synthesis is increased and the enzyme within the biliary tract is repeated into plasma. A raised ALP concentration in the presence of a raised g-glutamyl transferase (GGT) concentration implies that the ALP is of hepatic origin.

**Causes of raised plasma alkaline phosphatase activity**

* **Physiological:**
* During the last trimester of pregnancy, the plasma total ALP activity rises due to the contribution of the placental isoenzyme. Plasma ALP concentration may increase by up to five times and usually returns to normal levels by 1 month postpartum.
* In preterm infant plasma total ALP activity is up to 10 times the URL in adults, and consists predominantly of the bone isoenzyme.
* In children, the total activity increases by about two to five times during the pubertal bone growth shot.
* In the elderly, the plasma bone isoenzyme activity may increase slightly.
* **Pathological:**
* **Bone disease**
* Rickets and osteomalacia.
* Paget's disease of bone (may be very high).
* Secondary malignant deposits in bone.
* Osteogenic sarcoma (only if very extensive).
* Primary hyperparathyroidism with extensive bone disease (usually normal but may be slightly elevated).
* Secondary hyperparathyroidism.
* Healing fractures, Rheumatoid Arthritis.
* **Liver disease**
* Intrahepatic or extrahepatic cholestasis.
* Space-occupying lesions tumors, granulomas and other causes of hepatic infiltration.
* Inflammatory bowel disease: the gut ALP isoenzymes can be increased in ulcerative colitis.
* Malignancy: bone or liver involvement or direct tumors production.

**Possible causes of low plasma alkaline phosphatase activity**

A low plasma ALP concentration is less usual, but may be cause by the following:

Arrested bone growth: Achondroplasia, Hypothyroidism, Sever vitamin C and vitamin B, Magnesium and zinc deficiency.

The alkaline phosphatase test is often used to help diagnose certain liver disease and bone disorders. A raised ALP concentration in the presence of a raised g-glutamyl transferase (GGT) concentration implies that the ALP is of hepatic origin.

Increase in the activity of ALP in liver disease is not due to hepatic cell disruption, nor to a failure of clearance, but rather to increase synthesis of hepatic ALP.

The stimulus for this increased synthesis in patient with liver disease has been attributed to bile duct obstruction (cholestasis) by stone, tumors, intrahepatically by infiltrative disorders or space-occupying lesions.

It is used for many years in differential diagnosis of **jaundice**. It is increased in both infectious hepatitis (viral hepatitis) and post hepatic jaundice in latter the plasma ALP activity may be up to 10 times the UNL., but the rise is usually much greater in case of obstructive jaundice.

Dividing line which has been suggested in 35 KAU/ml. a value higher than 35 KAU/ml is strongly suggestive of diagnosis of obstructive jaundice, in which very high figures even up to 200 KA units/ ml or more may be found.

Serum ALP is found to be normal in haemolytic jaundice.

In cholestasis (obstructive to the flow of bile) plasma ALP increased about 5-10 times of (ULN).

**How are the isoenzymes of ALP used in diagnosis?**

* Isoenzymes of ALP are used to distinguish between liver and bone disease.
* Isoenzymes are most easily differentiated by heat stability test and by electrophoresis.
* ALP isoenzyme produced in liver (ALP1) is heat stable.
* ALP isoenzyme produced in bone (ALP2) is inactivated by heat.
* Detection of isoenzymes helps differentiate the source of pathologic condition associated with elevated total ALP.
* ALP 1 is expected to be higher in liver.