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# New Biochemical Parameters That Can Be Used to Diagnose Patients with G6PD Deficiency

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**Abstract** Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an inherited enzyme deficiency that affects millions of people worldwide, particularly in certain regions with high prevalence. Although diagnosis of G6PD deficiency traditionally relies on biochemical assays such as the fluorescent spot test and enzymatic activity tests, there is growing interest in exploring novel biochemical parameters that can aid in the diagnosis of this condition.
In this research we will take (90) sample from serum of glucose-6-phosphate dehydrogenase deficiency patients and control and we will determine level of the glucose-6-phosphate dehydrogenase, albumin, total protein, and other biochemical parameters such as liver function; Alanine transaminase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase (ALP), Bilirubin and compared with new biochemical parameters such as myo-inositol oxidase, hepcidin and haptoglobin. At the end of this research. The results showed that there was a significant decrease ($P<0.05$) in the serum levels of G6PD in patient's group when compared with control group. Also, there were a significant increase ($P<0.05$) in the serum levels of albumin, total protein, ALP, ALT, AST and total bilirubin in patients with (G6PD) deficiency groups when compared with control group. In addition, this research reveals strong positive correlation between some biochemical parameters that we were studied such as total protein with TSB, total protein with albumin, ALT with TSB and Albumin with TSB.

**Keywords:**(G6PD) deficiency , Biochemical Parameters, Serum Biomarkers, Liver Function Tests,and Enzymatic Activity.

## Introduction:

The hereditary condition known as G6PD deficiency is typified by the absence of glucose-6-phosphate dehydrogenase, an enzyme that is essential to the antioxidant defense mechanism of red blood cells [1]. Hemolysis, or the breakdown of red blood cells, can result from a G6PD deficiency when it is brought on by specific oxidative stresses such infections, drugs, and some diets [2]. Because it is X-linked recessive, women may either be carriers or impacted by the disorder, depending on their genetic composition. The condition primarily affects men.

The first stage of the pentose phosphate pathway involves glucose-6-phosphate dehydrogenase (G6PD), which is involved in the conversion of glucose-6-phosphate to 6-phosphogluconolactone and the reduction of nicotinamide adenine dinucleotide phosphate ($NADP^+$) to NADPH. This process is necessary to manage oxygen stress, particularly in individuals with insufficient amounts of G6PD [3]. A deficiency in (G6PD) activity can cause a variety of illnesses, including severe forms of anemia and respiratory distress.

Throughout the body, cytoplasmic enzymes such as glucose-6-phosphite dehydrogenase (Oxidoreductase, EC 1.1.1.49) (G6PD) are present, particularly in red blood cells. In the pentose phosphate pathway (PPP), this enzyme functions as a crucial switch [4].

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The oxidation of glucose-6-phosphate (G6P) to 6-phosophogluconolactone and the reduction of ($NADP^+$) to reduced (NADPH) are catalyzed by glucose-6-phosphate dehydrogenase (G6PD) [5]. In order to supply energy and/or precursors for biomolecule synthesis, glucose-6-phosphate (G6P) enters a variety of metabolic pathways. These pathways are necessary to sustain various activities as well as control cell metabolism and proliferation. First, in the fed and fasting stages, the levels of glucose differ. Maintaining blood glucose levels during fasting requires the liver's capacity to generate glucose. More G6P is lipogenesis-converted to fatty acids in the liver during famine [6]. Secondly, glucose needs to be stored during fasting times in order to supply precursors for the maintenance of biomass, namely cell renewal. Then, ketone bodies provide the majority of the energy for most tissues. The liver is essential for the regulation of glucose synthesis and storage, as well as the redistribution of nutrients, because it is involved in G6P metabolism [7].

Fava beans are a widespread culture in the Mediterranean region that might cause hemolytic anemia in G6PD-deficient people by exacerbating their sickness. Repeated mild or severe hemolysis can lead to long-term complications, particularly in the liver and kidney, the primary organs affected [8]. Therefore, some of the hemolytic process may take place extravascularly, and repeated hepatic hemolytic episodes may result in the production of these increased liver enzymes. Based on biochemical indicators such as albumin, total protein, ALT, AST, ALP, and TSB, which are used to test liver function, it is possible that G6PD deficiency in the liver could be the source of hepatic issues in these individuals. One of the most essential elements of all cells and tissues is protein. They are materials composed of sets of smaller building blocks known as amino acids. More than 125 distinct types of proteins are found in human blood serum; the liver and immune system are the main locations where plasma protein synthesis occurs; the amount of total proteins in the blood is determined by the ratio of synthesis to breakdown [9].

Moreover, albumin is one type of blood protein. It is a single chain of proteins that is mostly produced in the liver and is rapidly released into the extracellular milieu at a daily rate of 9 to 14 grams. The half-life of albumin usually ranges from 12 to 19 days. The human albumin chain is organized in the form of a heart and contains 585 amino acids with a molecular weight of 66.5 kDa [10]. Serum glutamic pyruvic transaminase (SGPT), sometimes referred to as alanine transaminase or ALT, is a transaminase (EC 2.6.1.2). Although it can be found in serum and many different human tissues, ALT is most frequently observed in the liver. Furthermore, blood AST levels are frequently employed as a measure of liver function.

Contrarily, AST is present in more tissues than ALT, and it can be altered by disease or injury in a variety of tissues, including the cardiac and skeletal systems. An enzyme called alkaline phosphatase (ALP) is produced in the bones, liver, and other tissues. In an alkaline pH, it releases phosphate. The reference ranges for alkaline phosphatase (ALP) values vary depending on the patient's age, gender, and medical background. ALP is measured in routine blood tests; elevated serum levels are thought to be markers of bile duct obstruction, liver disease, or bone disease [11]. It also seems to be a significant independent cancer prognostic biomarker. One of the nine stereoisomers of inositol, a physiological substance found in seeds, whole grains, fruits, and human cell membranes, is myo-inositol (also known as myo-Ins). Inositol belongs to the family of sugars. A protein found in cell membranes called Myo-Ins is involved in morphogenesis, lipid synthesis, cell cytogenesis, and proliferation of cells [12].

Myo-inositol has vital biological roles in the tissues and cells of mammals, fungus, higher plants, and some bacteria. It is widely distributed in these environments. Many cell types in tissue culture require myo-inositol to proliferate [13]. A hemoglobin-binding protein called haptoglobin (HP) is made in the liver and carried by the blood. The main function of HP is to

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bind free hemoglobin that has been liberated from lysed erythrocytes, avoiding the formation of superoxide from free radical interactions between the iron in hemoglobin and molecular oxygen [14].

Regarding Hepcidin Increased erythropoiesis and inflammation linked to hemolysis may have contradictory effects on hepcidin and iron status, according to a better understanding of iron metabolism regulation and the role of hepcidin, a 25-amino-acid peptide hormone synthesized by hepatocytes as a key negative feedback regulator of iron status. Hepcidin inhibits the reticuloendothelial membrane's ability to absorb and release iron. Hepcidin is expressed more when there is inflammation, which leads to a hypoferremic state—a critical antimicrobial response. In order to meet the body's increased need for erythrone, erythropoiesis and hypoxia reduce the expression of hepcidin and increase iron intake and release [15].

**The aim**

This research paper aims to review the current understanding of G6PD deficiency, discuss the limitations of existing diagnostic methods, and explore new biochemical parameters that may be useful in diagnosing patients with G6PD deficiency.

**Material and Methods**

Blood samples were taken from (90) people, divided into two groups (60) people with hemolytic anemia (Favzim) who were between the ages from 1 to 15. There were (29) females and (31) males in this group. The samples were taken from Khanaqin General Hospital and Al-Batool Hospital in Diyala Governorate, Iraq country. For the control group, 30 samples were collected from healthy people of the same age, consisting of fifteen females and fifteen males, and they were collected from external labs. The level of enzyme activity in red blood cells was estimated using the diagnostic kit (kit) supplied by (BIOLABO-France), where the principle of action depends on the estimation of the increase in the concentration of NADPH at a wavelength (340 nm) and this represents the activity ratio of the enzyme G6PD in the sample [16].

About other tests is often tested clinically as part of a diagnostic the level of myo-inositol oxidase activity in red blood cells was estimated using the diagnostic kit (kit) supplied by (MYBIOSOURCE-USA), where the principle of action depends on the microplate included in this kit has been pre-coated with an anti-MIOX antibody. Then, standards or samples are added to the relevant microplate wells using an antibody conjugated to biotin that is specific for MIOX [17]. The level of haptoglobin concentration in red blood cells was determined using the diagnostic kit (kit) offered by (MYBIOSOURCE-USA), This kit utilized the sandwich enzyme-linked immune-sorbent assay technique. Antibody for capture was precoated onto 96-well plates. In addition, the biotin-conjugated antibody was utilized as the detection antibody. After washing the wells, the standards, test samples, and biotin-conjugated detection antibody were added to the wells [18]. The HEPC ELISA Kit does a competitive enzyme immunoassay with the help of a polyclonal anti-HEPC antibody and a HEPC-HRP conjugate. The test sample and buffer are treated for one hour on a plate with HEPC-HRP conjugate on it. After the incubation period, the wells are decanted and cleaned five times. The wells are subsequently treated with a substrate for the HRP enzyme. The complex resulting from the enzyme-substrate reaction has a blue tint. Afterwards, a stop solution is applied to halt this process, turning the solution yellow. In a microplate reader, the color intensity is measured spectrophotometrically at 450nm. HEPC from samples and HEPC-HRP conjugate compete for the anti-HEPC antibody binding site, hence the intensity of the color is inversely proportional to the concentration of HEPC [19], [20]. For the liver function test to assess liver health, serum albumin was determined by binding method of Bromocresol green (BCG) where a neutral solution was used

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at pH (4.2), by using (Albumin-Kit BIOLABO-France). Where these dyes are combined with albumin and its color changes from yellow to green, the complex (BCG Albumin) was formed, and its absorbance is measured by spectrophotometer at wavelength (630 nm) (620) which represents the concentration of albumin in the sample [21].

The measurement of total protein by (total Protein-Kit BIOLABO-France). Where total protein concentration is based on the colorimetric method described by (*Gornall and etal*). Where peptide bonds in proteins react with copper (Cu) in alkaline solution to form a colored complex with absorbance, the total protein concentration is measured at the wavelength (550 nm) [22]. For estimate ALT test, it is nearly commonly measured in units per liter (U/L) for diagnostic purposes. We used, (ALT) Activity Assay - Kit GENWAY BIOTECH-USA, ALT catalyzes the transfer of an amino group from alanine to ketoglutarate, with pyruvate and glutamate being the products of this reversible transamination process. and the procedure of detection of ALT was done as described in the manufacturer's instructions, the kit provides a quick, easy, sensitive, and reliable test that is good for high throughput ALT activity assays [23]. (AST) Activity Assay Kit SIGMA-ALDRICH-USA offers a straightforward method for evaluating AST activity in several samples and follow the procedure of detection of AST was done as described in the manufacturer's instructions, The ALP level was determined by (ALP) Activity Assay – Kit Linear Chemicals- Spain, depending on the acceptor of the phosphate group being the alkaline buffer [24]. Finally, by (Total bilirubin Assay - Kit Linear Chemicals- Spain) and diazotizing sulfanilic acid, where bilirubin was transformed into colored azobilirubin, which was then quantified photometrically [25].

## Result and discussion

### The measurement of glucose-6-phosphate dehydrogenase activity.

The G6PD activity in patients with hemolytic anemia (Favzim), as shown in table (1), was substantially lower at the probability level ($p < 0.05$) in patients than in the control group, which had a value (9.017±1.346) IU/g Hb.

**Table (1): The activity of G6PD in the blood of patients with hemolytic anemia compared to control group.**

| Parameters | Mean ± SD | | P - Value |
|---|---|---|---|
| | Patient | Control | |
| G6PD IU/g Hb | 4.869 ± 0.815 | 9.017 ± 1.346 | 0.05 |

The activity of the G6PD enzyme in hemolytic anemia patients of different races was measured; no significant differences were found when comparing the activity of the enzyme in age groups or at the level of probability (P=0.005), with values (4.570 ± 0.782) IU/g Hb in females and (5.149 ± 0.755) IU/g Hb in males. Table 3 illustrates that statistically significant differences were found between the less than 10 years age group's (4.545 ± 0.660) IU/g Hb and the more than 10 years age group's (5.216 ± 0.833) IU/g Hb at the probability level ($P < 0.05$). When hemolytic anemia patients' and the healthy group's G6PD activity results were compared, it was discovered that there were significant differences between the two age groups and male

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and female patients where the probability levels were obtained ($P \leq 0.05$). All of the differences were significant, as indicated in Table (2).

**Table (2) The activity of G6PD in the blood of patients with hemolytic anemia compared with control group in different genders and age groups**

| Parameters | Groups | Mean ± SD | | | |
|---|---|---|---|---|---|
| | | Gender Group | | Age Group | |
| | | Males | Females | Less than 10 years | More than 10 years |
| G6PD IU/g Hb | Patient | 5.149±0.755 | 4.570±0.782 | 4.545±0.660 | 5.216±0.833 |
| | P-Value | P < 0.05 | | P < 0.05 | |
| | Control | 8.556±1.303 | 9.470±1.265 | 8.384±0.998 | 9.701±1.325 |
| | P-Value | P < 0.05 | | P < 0.05 | |

Patients with hemolytic anemia have a problem with red blood cell synthesis, which prevents their bone marrow from making healthy red blood cells. Because this enzyme is more common in red blood cells, it prevents the production of proteins by the cells; thus, the amount of this enzyme diminishes because the distorted red blood cells do not make enough of it. Oxygen radicals, the deoxygenated and oxygenated hemoglobin cycle, and exogenous oxidants all represent a serious risk to red blood cells' ability to withstand oxidative stress [26]. Red blood cells suffer greatly from G6PD deficiency because they are unable to produce nicotinamide adenine dinucleotide in its reduced form [27].

**Levels of Myo Inositol Oxydase Concentrations**

Myo Inositol Oxygenase serum concentrations in the patient and control groups. includes age and gender-based groups, as displayed in tables (3) and (4).

**Table (3) The level of concentration of Myo Inositol Oxydase in the blood of patients with hemolytic anemia compared with control group**

| Parameters | Mean ± SD | | P - Value |
|---|---|---|---|
| | Patient | Control | |
| Myo-inositol Oxidase con. ng/mL | 5.316±1.099 | 3.492±0.501 | P < 0.05 |

When comparing the blood levels of Myo Inositol Oxygenase in the sick group to the control, a significant rise ($P < 0.05$) was seen. Gender-wise, there were no significant differences ($p > 0.05$) between the groups, but age-wise, there was a significant rise ($p < 0.05$). In comparison to the control group, there was a significant rise ($P < 0.05$) in the age group of less than 10, more than 10, and gender group of males and females within the patient group.

**Table (4) The level of concentration of Myo Inositol Oxydase in the blood of patients with hemolytic anemia compared to control group in different gender and age groups**

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**Levels of Haptoglobin Concentrations**

| Groups / Parameters | | Mean ± SD | | | |
|---|---|---|---|---|---|
| | | Gender Group | | Age Group | |
| | | Males | Females | Less than 10 years | More than 10 years |
| Myo-inositol Oxidase con. ng/mL | Patient | 5.441±1.040 | 5.183±1.162 | 5.692±1.223 | 4.914± 0.787 |
| | P-Value | P > 0.05 | | P < 0.05 | |
| | Control | 3.431±0.599 | 3.554±0.390 | 3.674±0.505 | 3.310±0.440 |
| | P-Value | P > 0.05 | | P < 0.05 | |

Concentrations of serum hemoglobin (mean ± SD) in both the patient and control groups. Compared to the control group, the patient group's serum hemoglobin levels rose significantly. Additionally, tables (5) and (6) provide groups based on gender and age. The blood levels of haptoglobin in the patient group showed a significant rise ($P < 0.05$) when compared to the control group, whose value was (48.576±14.033) ng/ml, which was significantly higher at the probability level ($p < 0.05$) than in the healthy group (27.278±6.967) ng/ml.

**Table (5): The concentration of Haptoglobin in the blood of patients with hemolytic anemia compared with control group**

| Parameters | Mean ± SD | | P - Value |
|---|---|---|---|
| | Patient | Control | |
| S. Haptoglobin con. ng/ml | 48.576±14.033 | 27.278±6.967 | P < 0.05 |

According to Table (6), there were no significant differences in the control group ($P > 0.05$) between males and females or between the two age groups when haptoglobin concentration values were compared to those of the hemolytic anemia patients and the healthy group in both gender and age categories.

**Table (6) The concentration of Haptoglobin in the blood of patients with hemolytic anemia compared to control group in different gender and age groups**

| Groups / Parameters | | Mean ± SD | | | |
|---|---|---|---|---|---|
| | | Gender Group | | Age Group | |
| | | Males | Females | Less than 10 years | More than 10 years |
| S. Haptoglobin con. ng/ml | Patient | 54.360±14.052 | 42.392±11.258 | 50.613±16.137 | 46.398±11.245 |
| | P-Value | P < 0.05 | | P > 0.05 | |
| | Control | 27.929±6.128 | 26.627±7.881 | 28.273±6.031 | 26.284±7.878 |
| | P-Value | P > 0.05 | | P > 0.05 | |

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**Hepcidin Concentration**

As indicated in table (7), statistical analysis showed a significant rise ($P < 0.05$) in hepcidin levels (17.693±11.630) ng/ml in hemolytic anemia patients compared to 8.499±3.243 ng/ml in healthy controls.

**Table (7): The concentration of Hepcidin in the blood of patients with hemolytic anemia compared with control group**

| Parameters | Mean ± SD | | P – Value |
|---|---|---|---|
| | Patient | Control | |
| Hepcidin con. ng/ml | 17.693±11.630 | 8.499±3.243 | P < 0.05 |

Table (8) displays the results of a comparison between the patient and healthy control groups of various ages and genders. No significant differences were detected ($P > 0.05$) between the groups' values.

**Table (8): The concentration of Hepcidin in the blood of patients with hemolytic anemia compared to control group in different gender and age groups**

| Parameters | Mean ± SD | | P - Value |
|---|---|---|---|
| | Patient | Control | |
| Total Protein con. g/dL | 8.312±1.026 | 6.556±0.643 | 0.05 |
| Albumin con. g/dL | 5.310±0.286 | 3.975±0.333 | 0.05 |

**Levels of Albumin & Total protein Concentration**

The results showed a significant increase ($P < 0.05$) in the total protein concentration in the blood serum of patients with hemolytic anemia, (8.312±1.026) g/dL compared to the control groups, (6.556±0.643) g/dL, and for albumin, the results showed a significant increase ($P < 0.05$) in the concentration of albumin in hemolytic anemia patients, (5.310±0.286) g/dL compared to the control groups, (3.975±0.333) g/dL, as shown in Table (9).

**Table (9): The concentrations of Total Protein & Albumin in the blood of**

| Groups / Parameters | | Mean ± SD | | | |
|---|---|---|---|---|---|
| | | Gender Group | | Age Group | |
| | | Males | Females | Less than 10 years | More than 10 years |
| Hepcidin con. ng/ml | Patient | 17.104±5.884 | 18.322±15.720 | 21.004±15.467 | 14.154±1.896 |
| | P-Value | P > 0.05 | | P < 0.05 | |
| | Control | 8.032±3.292 | 8.967±3.237 | 7.562±3.324 | 9.437±2.975 |
| | P-Value | P > 0.05 | | P > 0.05 | |

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The albumin concentrations in the patient group were significantly higher than those in the control group. In contrast, earlier studies have shown that individuals with hemolytic anemia have lower plasma albumin concentrations [28]. The main cause of albumin depletion, besides inadequate consumption of macronutrients, is the inflammatory phase of the disease. Those with G6PD deficiency have decreased albumin levels because chronic inflammation reduces albumin synthesis and accelerates the degradation of proteins [29]. There were no statistically significant differences found when the albumin concentrations of patients were compared depending on their age and gender (Table 10).

**Table (10): The concentration of Total Protein & Albumin in the blood of patients with hemolytic anemia compared to control group in different genders and age groups**

| Groups / Parameters | | Mean ± SD | | | |
|---|---|---|---|---|---|
| | | Gender Group | | Age Group | |
| | | Males | Females | Less than 10 years | More than 10 years |
| Total Protein g/dL | Patient | 8.434±0.880 | 8.181±1.163 | 8.332±0.955 | 8.291±1.113 |
| | Control | 6.711±0.515 | 6.401±0.735 | 6.524±0.806 | 6.587±0.452 |
| | P-Value | P < 0.05 | P < 0.05 | P < 0.05 | P < 0.05 |
| Albumin g/dL | Patient | 5.297±0.261 | 5.325±0.314 | 5.244±0.245 | 5.381±0.312 |
| | Control | 3.962±0.330 | 3.987±0.348 | 3.823±0.318 | 4.126±0.283 |
| | P-Value | 0.05 | 0.05 | 0.05 | 0.05 |

The average albumin level in children was greater than that of adults [30], which explains why the albumin levels in the children were higher than those in the control group. Zinc excretion in urine may also rise as a result of hypoalbuminemia brought on by a reduction in binding protein availability [31].

**The Levels of ALT, AST, ALP, and TSB**

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Table (11) displays the serum levels of ALT, AST, ALP, and bilirubin in patients and controls, expressed as mean± SD. When comparing the serum levels of the patient group to the control group, there was a substantial increase ($P < 0.05$) in all of the ALT, AST, ALP, and TSB levels.

As indicated by table (12), there was a significant difference between males and females in the case of ALP at the probability level of ($P < 0.05$), with the value of (112.436±15.250) U/L in males and (101.385±11.890) U/L in females. However, there were no significant differences observed between groups based on gender or age. Additionally, the serum levels of ALP in the patients were substantially higher ($P < 0.05$) than in the control group. One enzyme that is found in the liver's bile duct lining cells is called ALP. Despite the lack of clarity surrounding its exact physiological function, serum ALP activity has long been employed as a marker of bone and hepatocellular diseases [32].

**Table (11): Level of ALT, AST, ALP and bilirubin in the blood of patients with hemolytic anemia and compared it with control group**

| Parameters | Mean ± SD | | P - Value |
|---|---|---|---|
| | Patient | Control | |
| (ALT) U/L | 51.222±8.229 | 36.503±2.874 | 0.05 |
| (AST) U/L | 50.028±8.093 | 35.686±10.502 | 0.05 |
| (ALP) U/L | 106.928±14.320 | 65.169±6.758 | 0.05 |
| TSB con. mg/dL | 1.253±0.246 | 0.850±0.111 | 0.05 |

**Table (12): Level of concentration of ALT, AST, ALP and TSB in the blood of patients with hemolytic anemia in different genders and age groups**

| Groups / Parameters | | Mean ± SD | | | |
|---|---|---|---|---|---|
| | | Gender Group | | Age Group | |
| | | Males | Females | Less than 10 years | More than 10 years |
| (ALT) U/L | Patient | 52.858±7.287 | 49.473±8.926 | 52.635±0.080 | 49.712±8.257 |
| | P-Value | 0.05 | | 0.05 | |
| | Control | 36.501±3.593 | 36.504±2.048 | 36.518±3.245 | 36.487±2.553 |
| | P-Value | ns | | ns | |
| (AST) U/L | Patient | 53.496±4.849 | 53.218±3.990 | 52.760±4.386 | 54.004±4.440 |
| | P-Value | ns | | 0.05 | |
| | Control | 38.607±5.136 | 38.566±4.579 | 34.629±10.576 | 36.744±10.687 |
| | P-Value | ns | | 0.05 | |
| (ALP) U/L | Patient | 112.436±15.250 | 101.385±11.890 | 116.423±46.886 | 104.365±24.241 |
| | P-Value | 0.05 | | 0.05 | |
| | Control | 77.883±15.615 | 75.988±15.734 | 75.391±14.601 | 78.480±16.584 |
| | P-Value | 0.05 | | 0.05 | |
| TSB mg/ dL | Patient | 1.287±0.207 | 1.216±0.280 | 1.290±0.244 | 1.213±0.245 |
| | P-Value | ns | | ns | |
| | Control | 0.863±0.129 | 0.837±0.093 | 0.870±0.123 | 0.829±0.098 |
| | P-Value | ns | | ns | |

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Blood ALP levels are a sensitive marker for the presence of liver infiltrative disorders as well as intrahepatic and extrahepatic biliary blockage [33]. Additionally, as indicated by table (12), there were no statistically significant variations ($P < 0.05$) in the bilirubin levels in the serum of patients according to their age or gender, although there was a statistically significant rise ($P < 0.05$) in the patients' serum in comparison to the control group.

The results contradict research conducted by *Kamal and Hassan. (2021)* have revealed that gender influences the occurrence of jaundice in neonates, with male infants having a lower risk than female infants [34]. Various degrees of liver disease exist. Because ALT is restricted to the liver, unlike AST, which is abundant in other organs such as the kidneys, brain, and heart, it is considered the most reliable indicator of hepatocellular damage [35]. The AST, ALP, and ALT ratios of male G6PD defective patients were considerably greater than those of female G6PD deficient patients. This is in line with a recent study by [36], which found that the impact of sickle cell disease on biochemical indicators was more favorable for females.

According to *Airaodion et al*, an elevated AST/ALT (De Ritis) ratio indicates hepatotoxicity [37]. Consequently, A number of factors could be responsible for the abnormalities found in liver function tests rather than just one. In this investigation, G6PD-deficient participants had considerably greater quantities of total protein and albumin than the control groups. This is consistent with other research that looked at the age-biochemical liver function test correlation in sickle cell anemia patients in a stable state [38]. Because the G6PD deficit disrupts the equilibrium between the rates of protein synthesis and breakdown, as well as the removal or clearance of total protein and albumin, it is possible that the liver's functional activity has risen [39].

However, a higher overall protein intake could encourage dehydration, which is bad for the equilibrium of cells [40]. This will have a detrimental impact on the patient's health as well as the liver's metabolic activities. The concentration of albumin, which binds and transports metal ions, bilirubin, and medicines, is used to assess the liver's metabolic activity. Significant increases in these indicators could mean that the liver is producing more of it. Serum protein levels are regulated by liver synthesis, which also shows the liver's capacity for synthesis; G6PD deficient patients showed a significant increase ($p < 0.05$) in serum protein levels when compared to controls [41].

The plasma load of AST and bilirubin are generally elevated in individuals with G6PD deficiency due to persistent hemolysis; however, the relatively elevated levels of ALT and AST may be explained by various forms of hepatocyte injury [42]. (American Association of Clinical Chemistry, 2021) New research shows that men have slightly higher levels of bilirubin than women [42].

Heme, myoglobin, the iron-containing tetrapyrrole component of hemoglobin, and many enzymes break down to produce bilirubin. Microsomal heme oxygenases carry out heme cleavage to produce biliverdin, which biliverdin reductase then reduces to bilirubin. Bilirubin

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is an antioxidant that is healthy in small concentrations, but in large doses, it can damage the nervous system (BIND). Because bilirubin binds to plasma albumin, hepatocytes absorb it quickly, UGT1A1 conjugates bilirubin with glucuronide, and ATP-dependent pumping into bile canaliculi prevents bilirubin from being harmful to tissue [43].

A fraction of the bilirubin glucuronides generated by hepatocytes positioned downstream of sinusoidal blood flow are reabsorbed by hepatocytes that are released into sinusoidal circulation. Anomalous reuptake, reduced glucuronidation of bilirubin, decreased bilirubin excretion from the body via the canaliculi, or increased bilirubin synthesis can all contribute to hyperbilirubinemia [44].

**Correlation of biochemical variables**

The correlation coefficient (r) has been computed to describe the relationship and degree of correlation between the numerous researched measures based on the association between two variables from the same sample. Table (13) demonstrated the relationship between biochemical tests. Where "$r^2$" ($r^2 \leq 0.962$) revealed the highest correlation between parameters.

**Table (13): The highest values of ($r^2$) between biochemical parameters in patients with G6PD deficiency**

| G6PD deficiency | MIOX | Hepcidin | Haptoglobin | Total Protein | Albumin | (AST) | (ALT) | (ALP) | TSB |
|---|---|---|---|---|---|---|---|---|---|
| MIOX | 1 | .599** | -.090 | .430** | -.342* | -.003 | .546** | .097 | .554** |
| Hepcidin | .599** | 1 | -.168 | .287* | -.424** | -.085 | .448** | -.001 | .468** |
| Haptoglobin | -.090 | -.168 | 1 | -.178 | -.006 | -.299* | -.203 | .826** | -.261 |
| T. Protein | .430** | .287* | -.178 | 1 | .173 | .330** | .864** | -.082 | .962** |
| Albumin | -.342* | -.424** | -.006 | .173 | 1 | .284* | .039 | -.098 | .048 |
| (AST) | -.003 | -.085 | -.299* | .330** | .284* | 1 | .409** | -.329* | .292* |
| (ALT) | .546** | .448** | -.203 | .864** | .039 | .409** | 1 | -.048 | .908** |
| (ALP) | .097 | -.001 | .826** | -.082 | -.098 | -.329* | -.048 | 1 | -.070 |
| TSB | .554** | .468** | -.261 | .962** | .048 | .292* | .908** | -.070 | 1 |

Gray Color indicated to highest values of $r^2$.
**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).

Actually, in G6PD-deficient patients, there is a higher risk of thrombosis and hemolysis as well as a lower metabolism of oxidative stress [45], [46]. As such, those who are deficient in G6PD are more prone to liver dysfunction. Hemolytic anemia may be more common in those with G6PD deficiency. In this study, we investigate novel biochemical markers to identify individuals with G6PD deficiency. Both the patient and control groups had their serum biochemical markers—Myo-inositol Oxidase, Hepcidin, Haptoglobin, total protein, albumin, total bilirubin, ALP, ALT, and AST—examined. Patients with G6PD deficiency had elevated levels of several biochemical markers.

A person with hemolytic illness has problems with the metabolic processes in their liver. ALP, ALT, and AST are the biomarker enzymes that measure liver health, and rose in G6PD-deficient patients [47]. The results in table (13) shows there are correlations between liver enzymes with new biomarkers Myo-inositol Oxidase, Hepcidin, Haptoglobin, and all of them associated with hemolytic disorders. According to clinical evidence, Also through the results from table (13), figure (1) shows that there is a strong positive correlation between total protein and TSB, where had big value of $r^2$ which means that when Total proteine levels rise, the level of TSB rises, also the same thing hapen with correlation between TSB and ALT figuer

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(2), as well as AST and ALT, as shown in figure (3), and total protein with ALT as shown in figure (4).

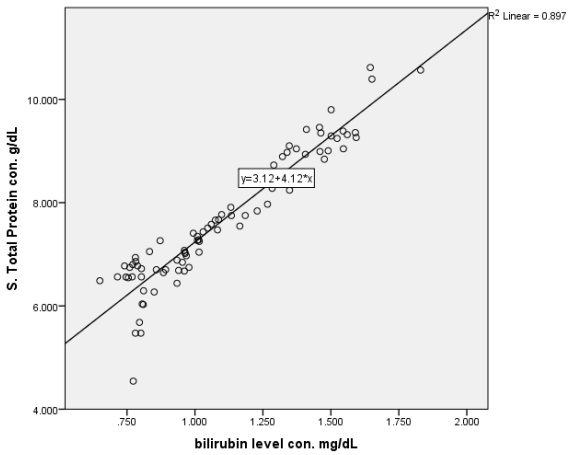


**Figure (1): Correlation between total protein and TSB**

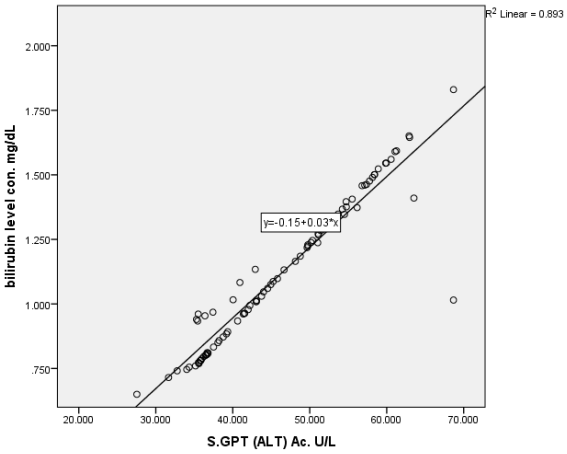


**Figure (2): Correlation between TSB and ALT**

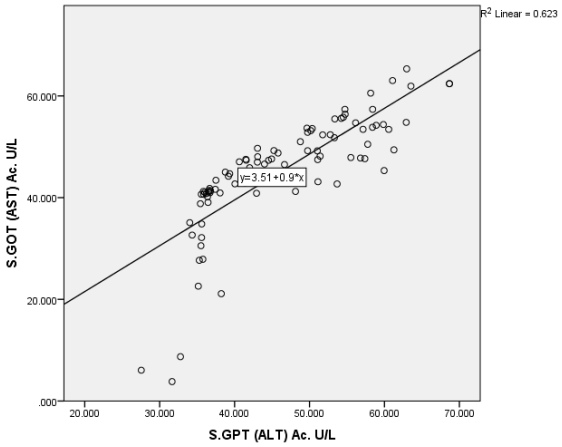


**Figure (3): Correlation between AST and ALT**

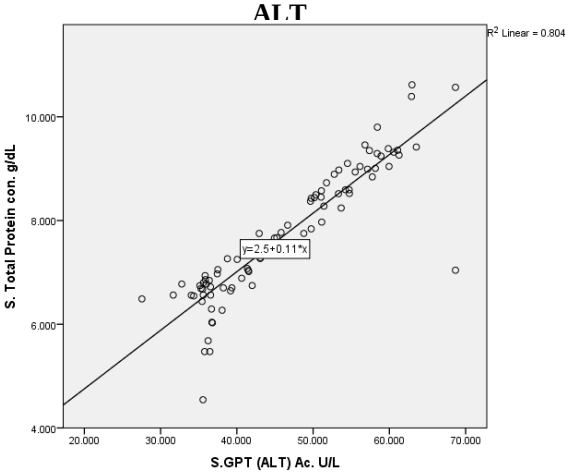


**Figure (4): Correlation between total protein and ALT**

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Through the above results that there was a strong positive correlation between Haptoglobin and (ALP), which means that when Haptoglobin level rise, the level of (ALP) rises. And through P value, the study shows that this a correlation is mathematically significant, as showed in figure (5). The same thing is true for the myo- inositol oxidase with Hepcidin, TSB and ALT as showed in the figures (6), (7) and (8) respectively.

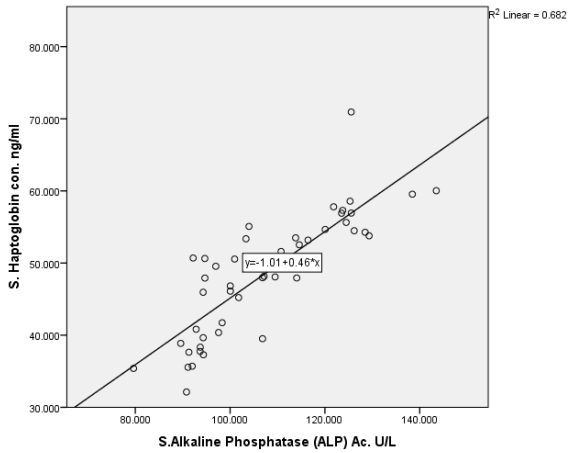


**Figure (5): Correlation between Haptoglobin and (ALP)**

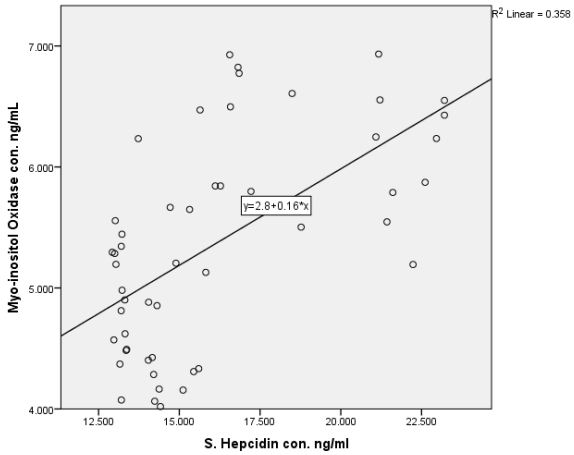


**Figure (6): Correlation between Myo- inositol oxidase and Hepcidin**

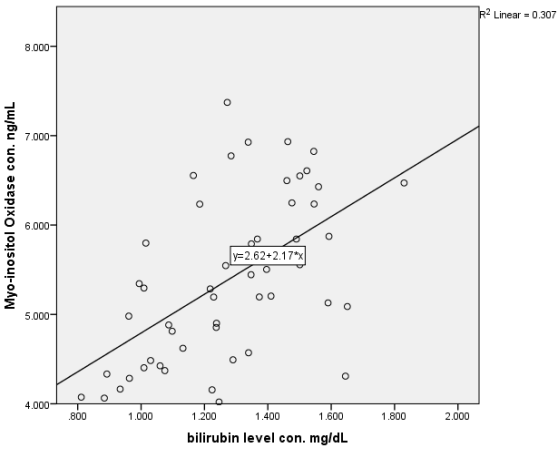


**Figure (7): Correlation between Myo- inositol oxidase and (TSB)**

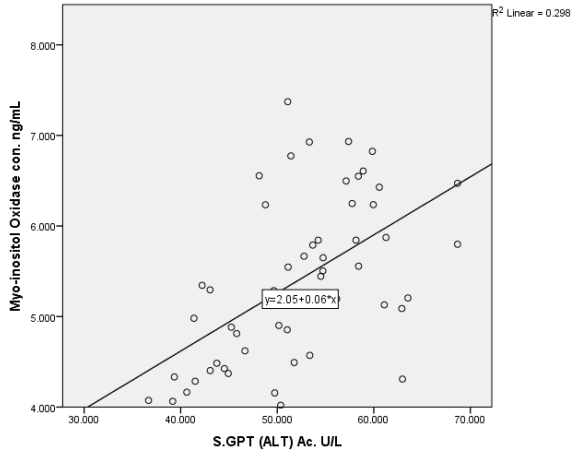


**Figure (8): Correlation between Myo- inositol oxidase and (ALT)**

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## Conclusions

Patients' serum glucose-6-phosphite dehydrogenase activity was lower than that of the control group, which had an impact on most other biochemical indicators and impaired their functionality. Patients lacking G6PD have seen an increase in the liver's functional activity, which is harmful to cellular balance because it disrupts the equilibrium between the rates of protein synthesis and breakdown and removal. This will have a detrimental effect on the liver's metabolic processes and, in turn, the health of the patients. There may be more than one factor contributing to the abnormalities in the liver function tests rather than just one. In this research, the Myo-inositol Oxidase, Hepcidin, Haptoglobin, AST, ALP, ALT, Bilirubin level, total protein and albumin concentrations of G6PD-deficient individuals were significantly higher than those of control groups. We noticed through the values of $r^2$ that there is a strong positive correlation between some biochemical parameters, especially Myo-inositol Oxidase, Hepcidin, Haptoglobin, enables us to rely on these parameters in diagnosing patients with G6PD deficiency.

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