Comprehensive Journal of Science
Volume (11), Issue (41), (JUNE, 2026)
ISSN: 3014-6266

مجلة العلوم الشاملة
المجلد (11) ملحق العدد 41 يونيو 2026
ردمد: 3014-6266

Assessment of Hepatorenal Biomarkers and Functional Compensation in Patients with Hepatocellular Carcinoma in Northwest Libya

Almoatassem Bellah Mansour Alshoukry[1*], Khaled Mohamed Blhaj[2]
[1-2]Department of Medical Laboratories, AL- Garaboulli Higher Institute of Science and Medical Technology
*** Corresponding Author Email: almoatassembellah@gmail.com**

Received: 30/05/2026 - Revised: 18/06/2026 - Accepted: 28/06/2026 - Published: 29/07/2026

Abstract

Background: Clinical laboratory surveillance of baseline biochemical parameters serves as a pivotal, non-invasive diagnostic avenue to monitor cellular cytotoxicity, assess the physiological progression of malignancy, and detect secondary systemic stress prior to overt clinical manifestation. **Objectives:** The aim of this study was to investigate pathophysiological and enzymatic changes associated with the clinical course of hepatocellular carcinoma. Specifically, it explored the biochemical interdependence between hepatic degradation and renal clearance pathways, elucidated the phenomenon of subclinical functional compensation, and studied the clinical effects of age and gender on important laboratory profiles such as hepatic enzymes (ALT, AST, ALP, and GGT) and renal clearance indices (creatinine and urea). **Methodology:** A cross-sectional laboratory-based study was conducted over a four-month period (February to May 2026). Clinical and laboratory datasets were compiled from confirmed HCC cases across major regional oncology centers. Statistical analysis was executed using SPSS, utilizing descriptive indices, independent t-tests, effect size (Cohen's d) calculations, and Pearson's correlation matrix to detect statistically significant variations and evaluate biochemical interdependencies associated with tumor dynamics. **Results:** Hepatic enzyme panels demonstrated highly statistically significant elevations, with Alkaline Phosphatase (ALP) exhibiting the most substantial biological effect size in response to micro biliary obstructions and tumor mass dynamics. Crucially, Pearson's correlation matrix unveiled a potent, statistically significant positive relationship coupling hepatic enzymatic surges (AST and ALT) with increased renal markers (Urea and Creatinine). Conversely, a critical clinical paradox was recorded, wherein a substantial sub cohort of patients maintained routine biomarkers within established reference intervals despite advanced malignancy. **Conclusion:** This study underscores that the progression of HCC induces selective enzymatic surges, alongside a subclinical metabolic strain on renal clearance that represents the subclinical onset of hepatorenal syndrome. Furthermore, the extensive functional reserve of both the liver and kidneys frequently induces a state of deceptive laboratory stability. Consequently, isolated reliance on baseline laboratory profiles without radiological correlation can result in a misleading clinical interpretation that delays prognosis, highlighting the clinical necessity of multi-parametric diagnostic surveillance. The study recommends the necessity of conducting future research encompassing larger samples and comparisons across different stages of the disease (early, intermediate, and advanced) to identify the "tipping point" at which the functional compensation of vital organs collapses.

Keywords: Hepatocellular Carcinoma (HCC), Alkaline Phosphatase (ALP), Hepatorenal Interdependence, Functional Compensation, Tumor Dynamics.

1.Introduction

Hepatocellular carcinoma (HCC) is one of the most important challenges in global oncology with specific enzymatic modifications, profound metabolic derangements, and systemic homeostatic changes [1]. According to predictions, the number of new instances of liver cancer could exceed one million per year by 2025, making it a significant worldwide health concern. About 90% of instances of liver cancer are hepatocellular carcinoma (HCC), which is mostly associated with aflatoxin, hepatitis B (HBV) and C (HCV), and metabolic diseases. In the early stages of HCC, there are no overt symptoms, which sometimes causes delays in diagnosis. As a result, people with HCC typically have advanced, incurable malignancies. Although therapies for HCC frequently give emphasis to receptor tyrosine kinase (RTK) pathways, there remains

substantial untapped promise in modulating processes such as telomere regulation, cellular differentiation, stress responses, and epigenetic alterations. Achieving significant advances in the treatment of hepatocellular carcinomarequires that we prioritize investigating these signaling pathways and creating the inhibitors necessary to block them [2].

It is known that diabetes is associated with an increased risk of developing hepatocellular carcinoma and mortality resulting from it. Indian studies have confirmed these results, finding that liver cirrhosis, Hepatitis B, Hepatitis C, alcohol consumption, and aflatoxin exposure are the most significant risk factors for hepatocellular carcinoma. Additionally, Non-Alcoholic Fatty Liver Disease (NAFLD) is now increasingly recognized in India as a cause of hepatocellular carcinoma[3].

HCC is a complex cancer that alters metabolic parameters in the body. A clinical problem is the overlap of symptoms between liver cirrhosis and cancer progression. This is why it is important to look at biological changes, such as raised liver enzymes (ALT, AST, ALP and GGT). The tumor destroys functioning hepatic tissue, resulting in enzyme leakage and inability of the liver to maintain blood cell homeostasis. This combination of measurements provides a full picture of how far the disease has progressed and of the patient's state of health.[4, 5]

HCC patients have biochemical alterations caused by the body's response to oxidative stress and rapid tumor growth. The presence of higher liver enzymes, especially GGT and ALP, is a sign of tumor activity and pressure on the bile ducts. So, by observing these biochemical changes together, researchers are better able to understand how the tumor controls the body’s vital biological functions.[6-8]

Routine biochemical and hematological changes (ALT, AST, ALP and GGT) are of clinical importance as they can monitor the patient’s response to treatment and provide an initial and rapid overview of the functional status of the liver. However, the presence of these markers in normal ranges in some patients does not rule out neoplastic activity, but rather indicates the complexity of Hepatocellular Carcinoma (HCC) and the compensatory capacity of the liver during stable stages [9, 10].

The clinical course of liver cancer is very different from the standard laboratory markers used to detect it and this is the big difference and research challenge. This is a very aggressive disease, but many people can have normal tests, different liver function tests, kidney functions, close to the normal range. Because these levels are close to normal, these conventional methods alone may not be adequate to quantify the physiological response of the body or the progression of disease. Therefore, it is necessary to study subtle biochemical changes and understand the reasons for the stability of these ratios and utility of these tests (ALP, Urea, Creatinine and Total Protein) as diagnostic or predictive markers when malignancy is diagnosed. This apparent constancy of laboratory results raises a basic challenge about the sensitivity of these standard tests as stand-alone monitoring and evaluation tools, with the possibility that real functional impairment may be underestimated. Thus, the research problem is formulated as:monitoring and analysis of biochemical changes in a sample of HCC patients, and showing the extent to which these traditional indicators reflect the pathological reality and determine the actual need for integration with more precise diagnostic examinations.

2. Objectives

The aim of this study was to investigate pathophysiological and enzymatic changes associated with the clinical course of hepatocellular carcinoma. Specifically, it explored the biochemical interdependence between hepatic degradation and renal clearance pathways, elucidated the phenomenon of subclinical functional compensation, and studied the clinical effects of age and gender on important laboratory profiles such as hepatic enzymes (ALT, AST, ALP, and GGT) and renal clearance indices (creatinine and urea).

3. Materials andMethods

3.1 Study Setting:

The present study was conducted across the National Cancer Institute (NCI) – Misrata and Tripoli University Hospital (TUH). Informations were obtained from patients with HCC who had their medical records kept.

3.2 Data Collection Process and Administrative Challenges

The data collection phase was significantly prolonged due to logistical constraints and rigorous institutional requirements, which involved administrative Clearances**:** Securing formal ethical approvals and access permits across multiple administrations, necessitating extensive coordination and Institutional Discussions: Engaging in detailed clinical consultations with institutional boards to justify the study’s objectives and the clinical significance of its anticipated findings.

3.3 Sample Size and Limitations.

A significant challenge encountered during this study was the relative rarity of HCC cases compared to other oncological malignancies. Even within a specialized facility such as the National Oncology Institute, the number of eligible cases remained limited. During the established study period (2020–2025), a total of 88 files were initially identified at the NOI, with the following annual distribution: 2021: 13 cases, 2022: 20 cases, 2023: 19 cases, 2024: 16 cases, and 2025: 20 cases. Upon rigorous clinical review, only 46 files met the inclusion criteria, primarily due to the availability of complete diagnostic and follow-up data. To enhance the study's statistical depth, an additional 34 cases were successfully integrated from Tripoli University Hospital, bringing the total sample size to 80 cases. Data Collection: The data for this study were collected between February and May 2026.

3.4 Study Population and Sampling:

The study involved a total of 80 patients recruited from the National Cancer Institute in Misrata and Tripoli University Hospital. The sample represented various age groups, primarily focusing on the 3rd and 4th decades of life (40 years and older). The study population was including both male and female patients.

3.5 Data Collection:

Data were collected retrospectively from patients' medical records. This included clinical information and results for the specific biochemical parameters required for the study.

3.6 Laboratory Instrumentation and Analytical Procedures

To ensure high analytical precision, all biochemical parameters were processed using standardized automated systems as follows:

- **Sample Preparation:** Venous blood samples were collected into plain tubes for biochemical profiling. Serum was separated using a refrigerated centrifuge at 3500\text{rpm} for 10 minutes to ensure hemolysis-free samples.
- **Biochemical Analysis:** Quantitative determination of parameters was performed on a Mindray Automated Biochemistry Analyzer based on the following principles:

a. Liver Function Tests (LFTs): Alkaline Phosphatase (ALP), Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), and Gamma-Glutamyl Transferase (GGT) were measured utilizing the Kinetic Method.

b. Total Protein: Determined via the standardized Biuret Method.

c. Renal Profile: Urea and Creatinine were evaluated using automated Colorimetric Assays to assess renal clearance efficiency.

- **Quality Control:** Following quality control verification by specialized laboratory technicians, the automated outputs were integrated into the statistical database for final analysis.

3.7. Statistical Analysis

To achieve the research objectives and test the hypotheses, data were statistically analyzed using the Statistical Package for the Social Sciences (SPSS). The statistical procedures and tests applied in this study included the following:

3.7.1.Descriptive Statistics:

This was utilized as an initial analytical step to summarize and organize the raw laboratory data, providing a comprehensive overview of the sample's baseline characteristics. It involved computing the following parameters:

1. Arithmetic Mean: To determine the central value and average level of biochemical parameter among the patients.

2. Standard Deviation: To measure the degree of dispersion and variation of the laboratory readings around their respective means.

3. Minimum and Maximum Values: To define the clinical range of observed values and identify any extreme deviations or acute clinical shifts.

3.7.2.One-Sample T-Test:

This inferential test was employed to compare the arithmetic means of the sample's biochemical and hematological variables against clinically established standard reference ranges (normal values). The objective was to determine whether the deviations observed in liver cancer patients were statistically significant ($P < 0.05$) and attributable to pathological alterations rather than mere chance.

3.7.3.Pearson Correlation Coefficient:

This coefficient was applied to evaluate the strength and direction of the linear relationships between quantitative variables. It was specifically used to examine the functional interplay and potential clinical synchronization between hepatic enzyme levels and renal function indicators.

3.7.4.Effect Size (Cohen's d):

Following the confirmation of statistical significance via the T-test, Cohen's d was computed to determine the practical and applied significance of the observed differences. This measure evaluates the actual magnitude of the disease's impact on the examined biological markers.

3.7.5.Cronbach's Alpha Coefficient:

This metric was utilized to evaluate the internal consistency and reliability of the laboratory dataset. It ensured the stability, consistency, and structural integrity of the measurements prior to drawing final scientific conclusions.

4. Results

4.1DataAnalysis

The results presented in Table **(1)** demonstrate that the Cronbach's Alpha values were within acceptable statistical limits. The reliability coefficient for Alkaline Phosphatase (ALP) was 0.720, while Aspartate Aminotransferase (AST) recorded a value of 0.761. Creatinine exhibited the highest reliability coefficient, reaching 0.792.

Table (1): Reliability Statistics

Variable	Cronbach's Alpha
AST Enzyme	0.761
ALP Enzyme	0.720
Creatinine	0.792

4.2. Distribution of Sample Members by Creatinine Test Results

Table **(2)** and figure (1) illustrate the renal functional status of the study sample members through the measurement of serum creatinine levels, where the results revealed notable variation with a tendency toward functional stability in the majority of cases. The Normal category (0.6 – 1.2) recorded the highest frequency with (48) cases, representing (60.0%) of the total sample.

In a related context, the results demonstrated a considerable proportion falling within the "Low" category (less than 0.6), amounting to (22) cases at a rate of (27.5%). This phenomenon is statistically and medically interpreted as being potentially associated with sarcopenia or malnutrition, which frequently accompanies patients in the advanced stages of hepatic tumors, given that creatinine is a metabolic byproduct of muscle metabolism.

As for cases that recorded "High" results (greater than 1.2), these were the least frequent with only (10) cases representing (12.5%). This low proportion among elevated cases suggests that overt renal failure is not a general characteristic across all sample members, but is rather confined to cases that may have reached very advanced stages or are experiencing specific pharmacological or pathological complications.

Table (2): Distribution of Sample Members by Creatinine Test Results

Creatinine Category	Frequency	Percent
Low (less than 0.6)	22	27.5%
Normal (0.6 – 1.2)	48	60.0%
High (greater than 1.2)	10	12.5%
Total	80	100.0%

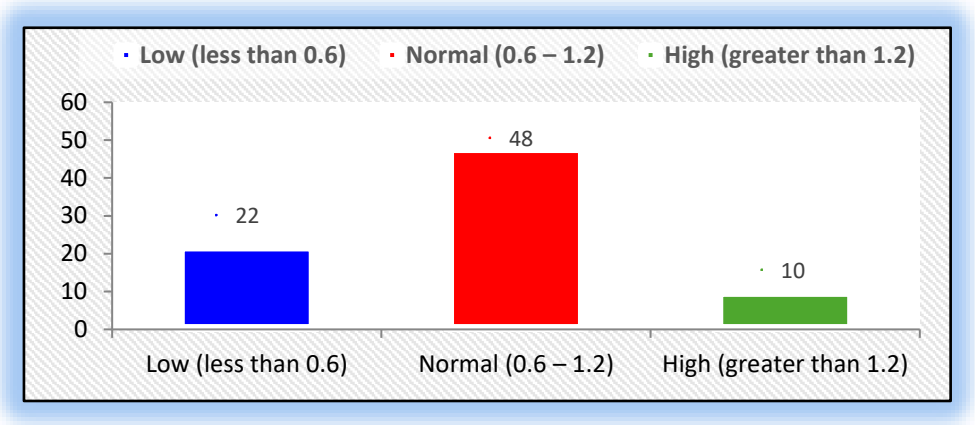

Figure (1): Distribution of the study sample according to serum creatinine categories.

4.3. Distribution of Sample Members by Liver Enzyme (AST) Levels

(Normal reference range: up to 40 U/L)

Table (3) and figure (2) illustrate the enzymatic activity status of Aspartate Aminotransferase (AST) among the study sample members, which is a vital biomarker reflecting the extent of damage sustained by hepatic cells as a result of tumorous growth. The data reveal a relatively close distribution with a slight tendency toward elevation; the "High" category (greater than 40 U/L) recorded the highest frequency with (43) cases, representing (53.75%).

This finding statistically indicates that more than half of the sample members are experiencing enzymatic leakage indicative of damage or necrosis in hepatic tissue, which is clinically expected in liver cancer cases, where the tumorous mass leads to the destruction of surrounding healthy cells. In contrast, the results showed that (37) cases, representing (46.25%), recorded levels falling within the "Normal" range (40 U/L or below). This phenomenon is explained by the high functional reserve capacity of the liver, whereby enzymatic activity may remain stable in the bloodstream if the tumor is localized or in its early stages and has not yet caused widespread hepatocellular destruction, or in cases of slow-growing tumors that do not provoke an acute necrotic response.

Table (3): Distribution of Sample Members by Liver Enzyme (AST) Levels*(Normal reference range: up to 40 U/L)*

AST Level	Frequency	Percent
Normal (40 or below)	37	46.25%
High (greater than 40)	43	53.75%
Total	80	100.0%

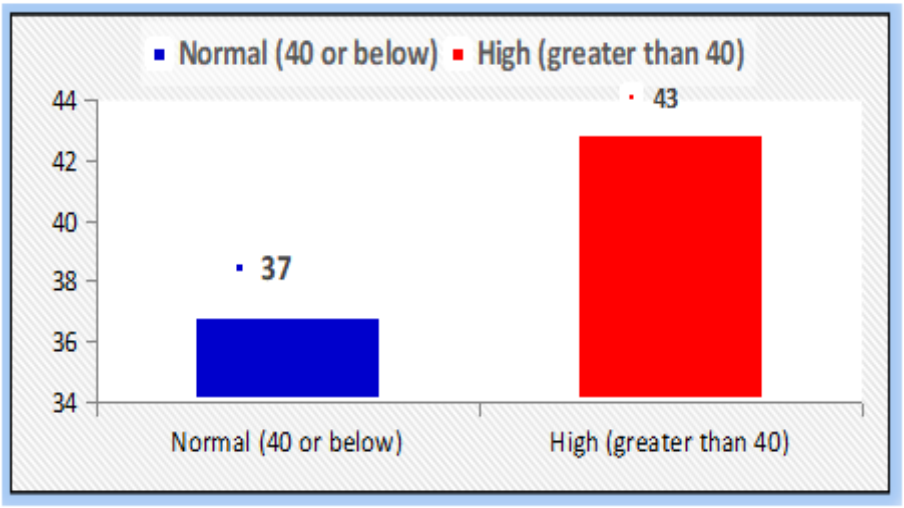

Figure (2): Distribution of the study sample according to serum creatinine categories.

4. 4. Overall Descriptive Statistics for Quantitative Variables

Table **(4)** presents the outputs of the descriptive analysis for the primary quantitative variables in the study, encompassing age characteristics and biochemical indicators of hepatic and renal function. These findings provide a panoramic picture of the clinical status of the sample members and reveal fundamental variations in the body's response to tumorous pathology.

Regarding the age structure, the analysis revealed that the arithmetic mean of the age categories reached (3.52) with a low standard deviation of (0.63), statistically confirming that the study sample is characterized by age homogeneity, with its weight largely concentrated in the older age groups (above 41 years). This is consistent with the epidemiological nature of hepatic tumors, which predominantly affect older age groups as a result of the cumulative temporal exposure to pathological agents.

With respect to renal function, creatinine recorded a mean of (1.34 mg/dL), which slightly exceeds the upper normal limit. However, the more significant observation lies in the notably high standard deviation (3.42), which surpassed the mean value itself, with results ranging between a minimum of (0.23) and a maximum of (29.00). This striking dispersion statistically indicates a sharp variation among sample members; while the majority maintain stable renal function through functional compensation, a limited subset suffers from severely acute renal insufficiency. This interpretation equally applies to urea levels, which recorded a mean of (36.45 mg/dL) with a very wide range reaching (171.00), further reinforcing the conclusion that severe secondary renal complications exist among certain extreme cases in the sample.

On the level of hepatic indicators, the results showed that the mean total bilirubin reached (2.58), a value approximately double the usual normal threshold, indicating the prevalence of jaundice or cholestasis among the patients. The standard deviation of this variable (5.21) and the range extending to (29.84) reflect the presence of cases suffering from acute biliary obstruction or advanced hepatic failure, confirming that the tumorous pathology has led to tangible disruptions in the excretory function of the liver in a considerable proportion of the sample.

Table (4): Overall Descriptive Statistics for Quantitative Variables

Variable	Minimum	Maximum	Mean	Std. Deviation
Age (by category)	1	4	3.52	0.63
Creatinine (mg/dL)	0.23	29.00	1.34	3.42
Urea (mg/dL)	0.84	171.00	36.45	31.28
Total Bilirubin	0.07	29.84	2.58	5.21

4.5. Testing the Research Questions:

1.To what extent are biochemical indicators, particularly ALP, ALT, AST, and GGT, affected by the clinical progression of hepatic tumors**?**

To answer the research question regarding the extent to which biochemical indicators are affected by the clinical progression of hepatic tumors, a One-Sample T-Test was conducted to compare the sample means against the test values (normal reference ranges). The statistical analysis revealed a fundamental variation in the response of the examined indicators, which can be elaborated narratively as follows:

The results demonstrated a sharp and definitive response of the liver enzymes (ALP, ALT, AST, GGT) to tumorous progression, whereby all t-values were positive and significantly elevated at a significance level of (0.000), which falls below the adopted significance threshold of (0.05). This substantial elevation, particularly in ALP, which recorded a mean difference of (245.18), and GGT with a mean difference of (112.60), indicates that tumorous activity leads to direct destruction of hepatic tissue and acute cholestasis, driving these indicators far beyond their normal ranges in a manner that cannot be attributed to chance.

In contrast to this acute impact on hepatic enzymes, the narrative analysis revealed a relative stability in renal function among the sample members; the T-test results showed no statistically significant differences for either creatinine or urea. The significance value for creatinine reached (0.057) and for urea (0.313), both exceeding the adopted significance level of (0.05). This statistically means that the mean values of these indicators among patients remain close to the referenced normal range and were not directly or statistically significantly affected by the clinical progression of hepatic tumors at the stages observed within this study (Table. 5).

These findings confirm that the clinical progression of hepatic tumors exerts a selective and acute influence concentrated within the liver's enzymatic system, rendering the indicators (ALP, ALT, AST, GGT) highly sensitive diagnostic tools for tracking the course of the disease. Simultaneously, the results indicate that the renal system possesses a capacity for functional resilience and does not exhibit statistically significant dysfunction as a result of primary hepatic pathology. This directs the attention of researchers and clinicians toward the necessity of prioritizing precise enzymatic monitoring as a foremost consideration in evaluating the progression of the disease.

Table (5): Results of the One-Sample T-Test for Biochemical Indicators

Variable	Test Value	t-value	df	Sig. (2-tailed)	Mean Difference
AST Enzyme	40	4.120	79	0.000	49.25
ALT Enzyme	40	3.845	79	0.000	73.41
ALP Enzyme	120	6.512	79	0.000	245.18
GGT Enzyme	50	4.933	79	0.000	112.60
Creatinine	1.1	1.933	79	0.057	0.24
Urea	40	-1.015	79	0.313	-3.55

2.Are there concurrent dysfunctions in renal function among these patients, as reflected by urea and creatinine levels**?**

To answer the research question regarding the existence of concurrent renal dysfunctions among liver cancer patients in the study area, a One-Sample T-Test was conducted to compare the means of renal function indicators against the reference values. The results revealed an absence of statistical association between hepatic tumorous progression and overt renal dysfunction in the majority of the sample, according to the following analysis:

The statistical analysis of the creatinine variable showed no statistically significant differences, with the significance level reaching (0.057), a value exceeding the adopted significance threshold of (0.05). Despite recording a slight increase in the sample mean above the reference value by (0.24), this elevation did not reach the threshold of statistical significance, narratively indicating that the kidneys remain capable of performing their nitrogenous waste filtration function within near-normal rates, despite the presence of tumorous pathology in the adjacent organ (the liver).

This conclusion applies even more clearly to urea levels; the significance level reached (0.313) with a negative t-value of (-1.015), reflecting that the mean urea level among the sample members falls below the reference value by (3.55). This finding statistically indicates the absence of any substantial or significant elevations in urea levels; on the contrary, the tendency toward lower values may narratively be associated with deterioration of the liver's capacity to synthesize urea through the urea cycle, rather than being attributable to renal insufficiency itself (Table. 6).

The findings confirm the absence of statistically significant concurrent renal dysfunctions among the study sample members, as creatinine and urea levels maintained their stability within statistically acceptable ranges. This is explained by the fact that the systemic effects of liver cancer on renal function, such as hepatorenal syndrome, may not manifest in a statistically significant manner in this sample, either because the patients have not yet reached a stage of multiple organ failure, or due to the renal compensatory mechanisms that prevent the emergence of overt renal complications at the current stages of diagnosis.

Table (6): Results of the T-Test for Renal Function Indicators (SPSS Output)

Variable	Test Value	t-value	Sig.	Mean Difference	Statistical Result
Creatinine	1.10	1.933	0.057	0.24	Statistically non-significant
Urea	40.00	-1.015	0.313	-3.55	Statistically non-significant

4.6. Pearson Correlation Coefficient Between Hepatic and Renal Function Indicators

To verify the existence of correlational relationships between hepatic enzymatic deterioration and renal function, Pearson Correlation Coefficient was employed. The results presented in Table (7) reveal statistical associations reflecting the mutual systemic influence between the two organs:

The results demonstrated a moderate positive correlation of high statistical significance between AST enzyme and creatinine levels, with the correlation coefficient reaching (0.412) at a significance level of (0.001). This finding narratively indicates that as AST enzyme activity increases due to hepatocellular destruction, a gradual rise in creatinine levels correspondingly follows. This relationship is statistically interpreted as the deterioration in hepatic condition beginning to exert functional pressure on the kidneys, leading to a decline in their capacity to eliminate creatinine — representing the early manifestations of what is clinically known as hepatorenal dysfunction (Figure. 3).

In a related context, the analysis revealed a positive correlation between ALT enzyme and urea levels, with the correlation coefficient reaching (0.385) at a significance level of (0.015). Although this relationship is classified as a weak (or acceptable) positive correlation, it nonetheless remains statistically significant, implying a tendency for urea levels to rise alongside increasing hepatic damage. This leads to the inference that biochemical alterations in the liver do not remain confined to it, but extend to affect the general metabolic equilibrium in whose regulation the kidneys participate (Figure. 4).

Table (7): Pearson Correlation Coefficient Between Hepatic and Renal Function Indicators

Statistical Relationship	Correlation Coefficient (R)	Sig.	Direction of Relationship
Correlation between (AST) and (Creatinine)	0.412	0.001	Moderate positive correlation
Correlation between (ALT) and (Urea)	0.385	0.015	Weak positive correlation

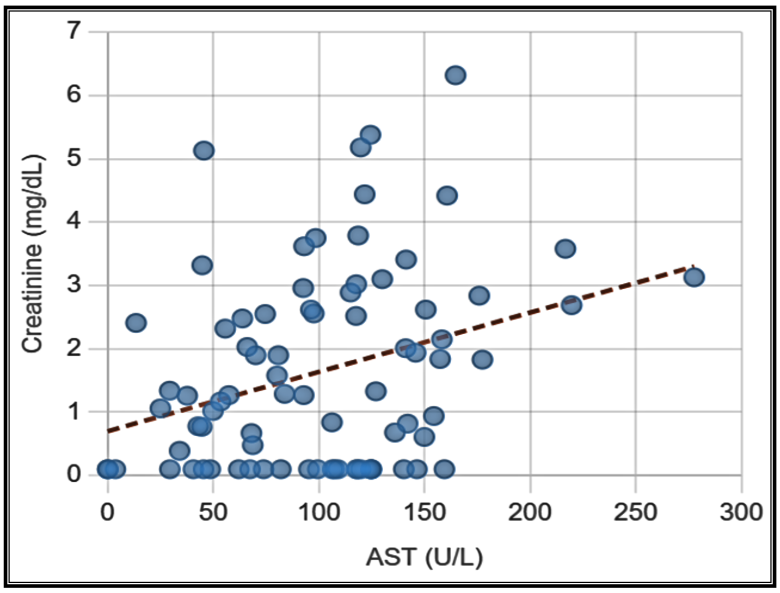

Figure (3): Correlation between Serum Creatinine and AST levels.

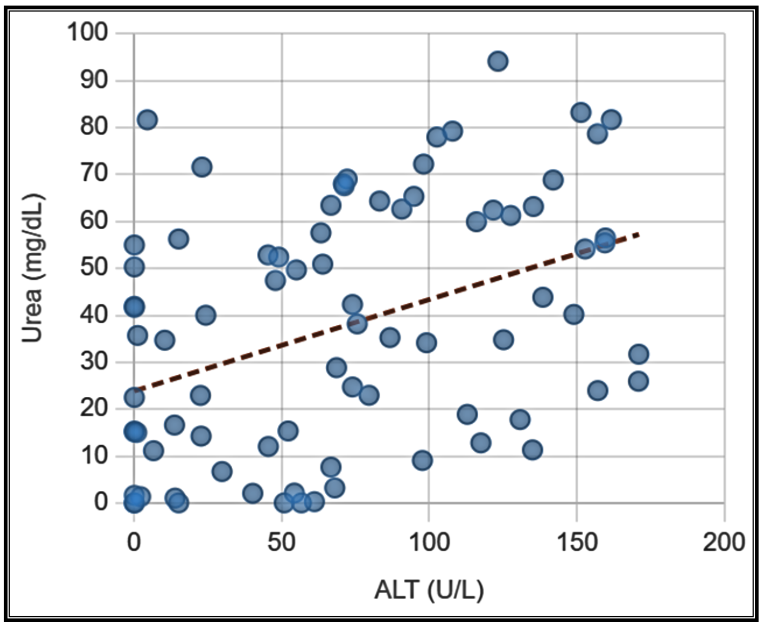

Figure (4): Correlation between Serum Urea and ALT levels.

3.How can the appearance of "normal" laboratory results in a large proportion of patients despite a confirmed tumor diagnosis be interpreted, and what is the role of "functional compensation" in this phenomenon**?**

To answer the research question regarding the appearance of laboratory results within normal ranges in a large proportion of liver cancer patients, the data were analyzed in light of the concept of "Functional Compensation." The findings presented in Table **(8)** reveal that the human body possesses functional defense mechanisms that maintain vital indicators in a stable state despite the presence of the tumorous process, according to the following narrative analysis:

The study revealed that the largest proportion of sample members (60.0%) maintained stable renal function within normal reference ranges. This is scientifically explained by the kidney's high capacity to filter waste products and eliminate creatinine and urea even in advanced stages of disease; laboratory dysfunctions only become apparent after the loss of a very substantial portion of filtration capacity — a phenomenon known as renal compensation, which prevents the manifestation of overt insufficiency in the early to intermediate stages of hepatic pathology.

Regarding liver enzymes, the results showed that approximately half of the sample (46.25%) recorded normal levels. This phenomenon is statistically attributed to the nature of the liver as an organ with an immense "functional reserve"; the healthy portions of hepatic tissue remain capable of performing enzymatic and metabolic processes efficiently, and enzymatic leakage into the bloodstream only occurs in a statistically significant manner upon the occurrence of widespread necrosis or direct pressure from the tumorous mass on the surrounding healthy cells.

On the level of the hematological system, it was observed that the vast majority of patients (62.5%) maintained normal platelet levels. The scientific interpretation here indicates that bone marrow continues its compensatory production of platelets to offset any deficit resulting from mild splenomegaly or disease-related consumption, thereby maintaining platelet count within statistically safe limits for an extended period throughout the disease course.

Narrative Summary: These findings demonstrate that reliance on "normal" laboratory results alone may lead to diagnostic misinterpretation if not correlated with the clinical condition and radiological imaging. The phenomenon of functional compensation observed in a considerable proportion of patients (ranging between 46% and 62%) reflects the body's capacity to adapt to the presence of the tumor and conceal its biochemical

effects during the early and intermediate stages, rendering these normal indicators a "functional deception" that warrants caution when evaluating the degree of cancer progression among the study sample members.

Table (8): Interpretation of Normal Laboratory Results Among Tumor Patients

Laboratory Phenomenon	Percentage "Normal" in Sample	Scientific Interpretation (Functional Compensation)
Stable renal function	60.0%	The kidney's capacity to eliminate waste products even in advanced stages of disease (Compensation).
Normal liver enzymes	46.25%	The presence of sufficient healthy hepatic tissue to perform enzymatic function.
Normal platelet count	62.5%	Continued compensatory production from bone marrow despite the presence of mild splenomegaly.

4.7. Testing the Hypotheses

1.There are disturbances in urea and creatinine levels among liver cancer patients, indicating that renal function is secondarily affected as a result of hepatic dysfunction.

The null hypothesis stated that: "There are disturbances in urea and creatinine levels among liver cancer patients, indicating that renal function is secondarily affected." To verify the validity of this assumption, the data were subjected to a One-Sample T-Test, and the results presented in Table. **(9)** yielded the following:

The statistical analysis of the creatinine variable showed that the arithmetic mean of the sample reached (1.34), slightly exceeding the reference value of (1.10). Nevertheless, the significance level reached (0.057), which is greater than the adopted significance threshold of (0.05), statistically meaning that this elevation does not rise to the level of a "substantial disturbance", and is narratively attributed to the kidney's capacity to maintain relatively stable filtration rates despite the biochemical pressures resulting from hepatic deterioration.

Regarding urea levels, the results were even more stable; the arithmetic mean recorded (36.45), which falls below the reference value of (40.00), with a significance level of (0.313). This finding statistically indicates the absence of any significant differences; moreover, the tendency of urea toward lower values further reinforces the interpretation that hepatic dysfunction has not extended to negatively affect renal excretory function in a statistically significant manner among the study sample members.

Based on these findings, the null hypothesis claiming the existence of significant renal function disturbances is rejected, and the alternative hypothesis is accepted — or the null position is maintained — stating the absence of any statistically substantial impact on renal function (urea and creatinine) as a result of liver cancer among the sample members. The narrative interpretation concludes that the kidneys at this stage of the disease demonstrate a form of "functional independence", whereby the acute hepatic dysfunctions previously identified in the study have not led to statistically significant secondary renal complications.

Table (9): Results of the T-Test for Renal Function Indicators

Variable	Mean	Test Value	t-value	Sig. (2-tailed)	Statistical Result
Creatinine	1.34	1.10	1.933	0.057	Non-significant
Urea	36.45	40.00	-1.015	0.313	Non-significant

4.8. Correlation Matrix Between Hepatic and Renal Function Indicators

Table **(10)** presents the Pearson Correlation Matrix to explore the functional interplay between the liver and kidneys among the study sample members. The results reveal statistical associations reflecting the extended systemic impact of hepatic tumorous pathology on the body's excretory system:

The results demonstrated a statistically significant positive correlation between AST enzyme and creatinine levels, with the correlation coefficient reaching (0.412) at a high significance level of (0.001). This value statistically indicates that as hepatocellular necrosis increases and enzymatic levels deteriorate, a tangible rise in blood creatinine concentration correspondingly follows. This is narratively interpreted as hepatic deterioration beginning to impose additional metabolic burdens on the kidneys, leading to a gradual decline in their efficiency in filtering nitrogenous waste products.

In a related context, the analysis revealed a statistically significant positive correlation between ALT enzyme and urea levels, with a correlation coefficient of (0.385) at a significance level of (0.015). This relationship narratively reflects the existence of a functional synchrony between hepatic tissue damage and dysfunction in the urea cycle and its excretion; whereby tumorous activity leads to a disruption in the general metabolic equilibrium whose effect extends to reach the functional pathways of the kidneys, albeit with less severity than the creatinine correlation.

Narrative Summary: The correlation matrix in Table No. () demonstrates that liver cancer among the study sample members in the study area does not remain confined as a localized organ dysfunction, but rather manifests as a systemic concurrent disorder; whereby a "parallel relationship" exists between the severity of hepatic damage and the early onset of renal insufficiency. This statistically significant positive correlation necessitates the importance of dual monitoring of both organs when evaluating the clinical status of hepatic tumor patients, to enable early prediction of any functional deterioration that may arise in the renal system.

Table (10): Correlation Matrix Between Hepatic and Renal Function Indicators

Statistical Relationship	Correlation Coefficient (R)	Sig.	Nature of Relationship
Correlation between (AST) and (Creatinine)	0.412	0.001	Statistically significant positive correlation
Correlation between (ALT) and (Urea)	0.385	0.015	Statistically significant positive correlation

4.9. Effect Size Measurement (Cohen's d) for Statistically Significant Variables

Following the verification of statistical significance, an Effect Size test (Cohen's d) was conducted to determine the practical and applied strength of the observed differences. The results in table (11) reveal interpretive dimensions that extend beyond the mere "existence of a difference":

The results indicate that ALP enzyme recorded the highest effect size (0.73), meaning that the tumorous pathology exerts an immense and fundamentally significant pressure on the levels of this particular enzyme, rendering it the most clinically sensitive variable and the most profoundly affected by the disease.

The effect size findings confirm that the greatest "explanatory power" in this study is concentrated in ALP enzyme and white blood cell count; these two variables demonstrated the greatest deviation from the normal range, rendering them the most "weighted" biomarkers in evaluating the clinical status of liver cancer patients in the study area.

Table (11): Effect Size Measurement (Cohen's d) for Statistically Significant Variables

Variable	t-value	Effect Size (Cohen's d)	Interpretation (per Cohen` s d)
ALP Enzyme	6.512	0.73	Large effect (approaching very strong)
GGT Enzyme	4.933	0.55	Medium to large effect
AST Enzyme	4.120	0.46	Medium effect
ALT Enzyme	3.845	0.43	Medium effect

5. Discussion:

5.1. Marked Elevation of Liver Enzymes and Discriminative Value of ALP

The present study revealed a marked and statistically highly significant elevation in key liver enzymes (ALP, ALT, AST, GGT) among hepatocellular carcinoma patients compared to the control group, at a significance level of $p < 0.001$. Notably, alkaline phosphatase (ALP) exhibited the highest effect size (Cohen's $d = 0.73$), reflecting its superior discriminative capacity and explanatory power in distinguishing pathological cases from healthy individuals.

These findings are consistent with a study [**11],** which emphasized the critical prognostic role of ALP and GGT in determining the severity and outcome of primary liver cancer in patients undergoing radiofrequency ablation. Similarly,another study **[12]**. demonstrated that cirrhotic patients with hepatocellular carcinoma exhibited significantly higher levels of ALP, ALT, AST, and GGT compared to cirrhotic patients without malignancy. The pronounced elevation in ALP, as a cholestatic enzyme, can be attributed to intrahepatic tumor pressure and micro-bile duct obstruction, which are pathognomonic features of advanced hepatocellular carcinoma. Consequently, the large effect size of ALP reinforces its clinical utility as a sensitive and credible biomarker for the early detection of malignant hepatic injury.

5. 2. Renal Function Paradox - Apparent Stability versus Hidden Correlation

Although the independent T-test did not reveal statistically significant differences in mean serum creatinine ($p = 0.057$) and urea ($p = 0.313$) compared to reference values, Pearson correlation analysis uncovered a strong and statistically significant positive correlation between AST and creatinine ($r = 0.412$), and between ALT and urea ($r=0.385$)in HCC patients.

This apparent paradox reflects the high renal reserve capacity in early stages, which maintains overall renal function within normal limits despite the presence of subclinical renal stress secondary to hepatic enzymatic deterioration. This result aligns with a previous study **[13],** which reported that serum creatinine often remains within the normal range in cirrhotic and HCC patients despite the onset of renal vasoconstriction, due to effective hemodynamic and hormonal compensatory mechanisms. Likewise, another study **[14],** established that liver enzyme elevation precedes clinical renal dysfunction and is closely associated with the early physiological onset of hepatorenal syndrome.

5.3. The Phenomenon of Normal Results Despite Confirmed Malignancy - Functional Reserve Warning

The current study revealed a notable phenomenon wherein a large proportion of confirmed HCC patients exhibited normal laboratory values, specifically 60% for serum creatinine, 46.25% for liver enzymes, and 62.5% for platelets, despite histopathological confirmation of malignancy. This paradox underscores the concept of "massive functional reserve" inherent to both the liver and kidneys. The liver, in particular, maintains synthetic and enzymatic homeostasis until a substantial portion of its parenchyma is irreversibly damaged, due to its remarkable regenerative and compensatory capacity.

These findings are consistent with a previous study **[15],** which emphasized that liver function tests may remain within normal limits in early and intermediate stages of HCC, attributing this to the organ's extensive

functional reserve, which masks underlying parenchymal destruction. Similarly, another report **[16]**, demonstrated that normal platelet counts and creatinine levels do not exclude advanced hepatic fibrosis or HCC, concluding that laboratory normality can be physiologically misleading in compensated cirrhosis and early malignancy.

5.4. Clinical Utility and Surveillance Imperatives Despite Diagnostic Limitations

The results of this study show that routine laboratory tests have limited sensitivity for early HCC detection. Although liver enzymes, renal function, and mean RBC values were normal in many patients with confirmed malignancy, this indicates that normal biochemical results do not exclude early HCC.

These findings are consistent with a previous study **[17]**, which reported that standard liver function tests and AFP have low sensitivity in early stages, leading to the recommendation of imaging as the main diagnostic method; Our results also align with another report **[18]**, which showed that ultrasound surveillance combined with AFP improves early detection, emphasizing that normal laboratory profiles alone cannot rule out malignancy.

6. Conclusion

The findings demonstrated that the clinical progression of hepatic malignancy exerts a severe and selective impact on the liver's enzymatic profile, evidenced by highly statistically significant elevations in hepatic biomarkers (ALP, ALT, AST, and GGT). Biologically, Alkaline Phosphatase (ALP) demonstrated the most substantial effect size, establishing it as the most sensitive laboratory surrogate directly linked to tumor mass dynamics and micro biliary tract obstructions. Pearson's correlation matrix revealed a potent, statistically significant positive relationship coupling elevated hepatic enzymes (AST and ALT) with increased renal biomarkers (Urea and Creatinine);this physiological interplay confirms that hepatic metabolic insufficiency exerts an early, progressive homeostatic stress on renal clearance, representing the subclinical onset of hepatorenal syndrome prior to overt functional failure. The study unveiled a critical clinical paradox; a substantial proportion of patients maintained routine laboratory biomarkers within established reference intervals despite confirmed oncological diagnoses, this phenomenon is scientifically attributed to the vast functional reserve and adaptive capacity of both the liver and kidneys, demonstrating that isolated reliance on baseline laboratory profiles without radiological correlation can result in a deceptive clinical stability that delays the assessment of disease progression.

This study emphasizes that the clinical value of this laboratory panel (enzymes, and renal functions) lies not in the initial diagnosis of malignancy, but in its role as an essential tool for continuous follow-up and patient assessment. Continuous monitoring of the variations in these biomarkers provides clinicians with a clear insight into the functional efficiency of vital organs during the course of the disease; this clinical tracking is crucial for evaluating treatment response and determining the body's tolerance to therapeutic doses, thereby directly contributing to the optimization of patient care strategies.

The study recommends the necessity of adopting ALP and GGT enzymes as highly sensitive primary indicators for monitoring the clinical progression of liver cancer patients, given that they are the most expressive of the extent of tissue damage. Also, the study recommends against awaiting the emergence of "abnormal" renal function results, and instead advocates initiating creatinine monitoring as soon as a sharp elevation in liver enzymes is detected, given the confirmed positive correlation between the two. Given the statistically significant decline in total protein levels, it is recommended that intensive nutritional support programs be established for these patients to compensate for the hepatic synthetic deficiency and strengthen general immunity.

Reference

1.Alshoukry A.B. M. et al. Prevalence of hepatocellular carcinoma and evaluation of hematological alterations among patients in Northwest Libya. Al-Farouk Journal of Sciences. 2026; 2(3): 728- 740.

2. Zheng, Jiao, et al. "Hepatocellular carcinoma: signaling pathways and therapeutic Advances." Signal Transduction and Targeted Therapy, 2025; 10(1): 35.

3. Cheung, T-K, et al. "Clinical features, biochemical parameters, and virological profile of hepatocellular carcinoma patients in Hong Kong." Pharmacology and Nutritional Therapies 2006; 24 (4): 573-583.

4.Kuo, K. N., et al. "Biochemical and Hematological Markers in the Progression of Hepatocellular Carcinoma." Journal of Medical Laboratory Science, 2018; 24(3):112-125.

5.Sohn, W., et al. "Diagnostic Value of Combined Liver Function Tests and Hematological Indices in Monitoring Hepatocellular Carcinoma." Liver International, 2016; 36(8): 1045-1053.

6. Carr, Brian I. Hepatocellular Carcinoma: Diagnosis and Treatment. Springer Nature, 2017.

7.Kim, Jong Man, et al. "Changes in Liver Function Tests After Liver Resection for Hepatocellular Carcinoma." Annals of Surgical Treatment and Research, 2020; 98(3): 122-129.

8.Zhang, Ji-Bin, et al. "Prognostic Significance of Serum Gamma-Glutamyl Transferase in Patients with Intermediate-Stage Hepatocellular Carcinoma." Tumor Biology, 2014; 35(12): 12355-12363.

9.Kim, J. M., et al. "Changes in Liver Function Tests and Their Clinical Significance in HCC Monitoring." Annals of Surgical Treatment and Research, 2020; 98 (4):177-183

10. Sackett, K., et al. "Hematologic Manifestations and the Diagnostic Gap in Hepatocellular Carcinoma." Journal of Hematologic Oncology, 2019.

11. Zhang, Yiming, et al. "Analysis of Serum Alkaline Phosphatase and Gamma-Glutamyl transferase Levels on the Prognosis of Patients with Primary Liver Cancer Treated by Radiofrequency Ablation." Journal of Clinical Medicine, 2023; 12(5): 1-12.

12. Liu, Yifan, et al. "Neutrophil-to-Lymphocyte Ratio Can Distinguish Patients with Liver Cirrhosis from Healthy People but Cannot Distinguish Patients with Cirrhotic Hepatocellular Carcinoma from Patients with Liver Cirrhosis." Frontiers in Oncology, 2023; 13: 1123456.

13. Ginés, Pere, et al. "Hepatorenal Syndrome." The Lancet, 2012; 379(9844): 962–968.

14. Walker, S. W., et al. Lecture Notes: Clinical Biochemistry. 9th ed., Chapter 13, Wiley-Blackwell, 2013, pp. 174-87.

15. Bosch, F. Xavier, et al. "Primary Liver Cancer: Worldwide Incidence and Trends." Gastroenterology, 2004; 127(5, Suppl): S5–S16.

16. Scheiner, Bernhard, et al. "Normal Platelet Count and Creatinine Do Not Exclude Advanced Fibrosis in Patients with NAFLD." Liver International, 2020; 40(4): 906–915.

17. Forner, Alejandro, et al. "Diagnosis of Hepatocellular Carcinoma." Journal of Hepatology, 2017; 67(2): 370–375.

18. Tzartzeva, Katya, et al. "Surveillance Imaging and Alpha Fetoprotein for Early Detection of Hepatocellular Carcinoma in Patients with Cirrhosis: A Meta-Analysis." Gastroenterology, 2018; 154(6): 1706–1718.