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Original Investigation

Correlations of hepatorenal functions among Diabetes patients attending tertiary care centers at Janakpurdham

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ABSTRACT

INTRODUCTION: Diabetes mellitus (DM) has multiple long-term consequences linked to hepatorenal pathophysiology. The long-term DM is associated with evidences of abnormal liver and renal function. However, this yet to be clearly established, especially in rural low to mid-income countries like Nepal. Thus, we aimed to assess correlations of hepatorenal functions among diabetes patients attending tertiary care centers at Janakpurdham, Nepal.**MATERIALS AND METHODS:** A total of 227 diabetes patients attending medicine OPD of Janaki Medical College teaching hospital, Ramdiaya and Ram Janaki Hospital, Janakpur were enrolled. Under aseptic conditions, blood samples were collected. Semi-automatic analyzers were used for all biochemical investigations. Pearson correlation test was used to observe correlation between the various hepatorenal functions in diabetic patients. A p-value less than 0.005 was considered to be significant.**RESULTS:**Out of total 227 diabetes patients, 132 (58.1%) were male and 95 (41.9%) were female. Significant results were obtained regarding the correlation between the hepatic and renal profile with SGOT [SGPT (p=0.000); Urea (p=0.049)]. Significant correlations were found between the liver and renal profile with SGPT [Albumin (p=0.050); Creatinine (p=0.020)] and with urea [Creatinine (p=0.000)]. Similarly, there was a significant correlation between the renal profile and liver with urea [Creatinine (p=0.000)] and for creatinine [Sodium (p=0.000)].**CONCLUSIONS:**Among diabetic patients, there was a substantial correlation between the liver and renal profiles.The etiology of various forms of diabetes mellitus is significantly influenced by hepatorenal factors among diabetics.

Keywords: Aspartate aminotransferase, alanine aminotransferase, creatinine, diabetes, hepatorenal, urea, fasting blood sugar.

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INTRODUCTION

Even though diabetes mellitus is more prevalent in developed nations, it occurs worldwide. Elevated blood sugar levels and disturbances in insulin production and function characterize diabetes as group of metabolic disorders. The term 'type 1 diabetes" (T1DM), "type 2 diabetes" (T2DM), gestational diabetes (GDM), and additional subtypes such as maturity-onset diabetes in young people and latent autoimmune diabetes in adults are included in diabetes category. Genetic predisposition, obesity, a sedentary lifestyle, poor dietary habits, stress, urban lifestyle, impaired glucose tolerance, and hypertension are risk factors for developing diabetes [1]. Diabetes and persistent hyperglycemia raise the likelihood of long-term complications that compromise the efficiency of several organ systems. Retinopathy, nephropathy, neuropathy, cardiovascular disorders, and vasculopathy are the most frequent consequences. These complications of diabetes can lead to significant damage to associated organs and promote a variety of other metabolic health problems [2].

Diabetes, also referred to as hepatogenous diabetes, can arise as an unforeseen consequence of cirrhosis, a liver disease [3]. It has been noted that insulin resistance, obesity, and fatty liver are causes of liver damage that lead to hepatic disease. The metabolic homeostasis of glucose is impaired in the presence of hepatic disease due to insulin resistance, glucose intolerance, and diabetes [4]. Hepatogenous diabetes might be seen as a sign of severe liver disease because the diabetes causes liver function to decline [5]. Various liver conditions, including nonalcoholic fatty liver disease (NAFLD), hepatocellular carcinoma, and cirrhosis have been associated with diabetes [6]. The liver plays a crucial role in maintaining glucose homeostasis, insulin clearance, and the production

of inflammatory cytokines. Common liver enzymes such as alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) are involved in these processes [7].

In addition to their physiological functions, abnormal serum levels of these enzymes can indicate liver or bile duct injury [8]. Increased liver enzyme activity may also indicate inflammation, which can disrupt insulin signaling. NAFLD, which is associated with insulin resistance and the risk of diabetes, can be assessed through measures of liver enzymes [6]. Clinical and experimental studies have shown that an elevated influx of free fatty acids from visceral adipose tissue can lead to hepatic steatosis and insulin resistance [9]. Furthermore, research has demonstrated that elevated levels of GGT and ALT enzymes are associated with an increased risk of developing T2DM in the future. These findings highlight the potential role of liver enzymes as markers for diabetes and its associated complications [8].

Renal complication of diabetes is also a significant public health issue and possibly related to the chronic liver disease in hepatorenal syndrome [10]. Patients with diabetes mellitus can also develop renal disease, particularly after years of disease progression, and renal disease can also occur in the context of liver cirrhosis, either as glomerular injury or as hepatorenal syndrome [11,12]. Few research, nevertheless, have examined the relationships between lipid profiles, dyslipidemia, and liver enzymes in T2D patients; however, information regarding the correlations between hepatorenal functions and diabetes is scarce in Nepal. Hence, we aimed towards the assessment of correlations of hepatorenal functions in diabetes patients attending tertiary care centers of Janakpurdham, Nepal.

MATERIALS AND METHODS

Study design and setting:

The hospital based cross-sectional study was carried out from April to August of 2022 at the Janaki Medical College Teaching Hospital (JMCTH), Ramdaiya, along with Ram Janaki Hospital, which is situated in Janakpurdham, Dhanusha, Nepal.

Participants, sample size and sampling technique:

A total of 227 consecutive patients attending medicine OPD on every fifth day of week at JMCTH, Ramdaiya and 2nd day of week at Ram Janaki Hospital, Janakpur diagnosed as T2DM or already taking treatment for T2DM during the study period were enrolled. The patient was confirmed by laboratory investigations report prescribed by physician in Medicine OPD. Patients with alcohol consumption, known liver disease, viral hepatitis, and steatogenic medication were excluded.

Data collection procedure and study variables

Fasting and post-prandial venous blood sample was collected using serum separator test tube following aseptic procedure. Standard operating procedures were followed for estimating different blood parameters. Erba Chem-5 semi-automated analyzer was used to test renal function, and Erba Chem-7 semi-automated analyzer was used to test liver function and blood sugar using kinetic method. Na+ and K+ was measured using electrolyte analyzer (Core-LYTE) through ion selective electrode method.

Statistical analysis and data management:

The data was entered to SPSS version 21 statistical package for analysis. Descriptive statistics were used to summarize the frequency distributions. Pearson correlation test was applied to observe correlation between different hepatorenal functions among diabetes patients. P-value less than 0.005 was considered to be significant.

Ethical consideration:

Institutional review committee of Janaki Medical College Teaching Hospital, Ramdaiya provided ethical approval towards this study (Ref: IRC/29/2079-080).

RESULTS

Table-1|General characteristics of Type II diabetic patients

Characteristics	Mean	SD	Minimum	Maximum
Age	48.99	14.69	24	80
Gender	**n**	**%**		
Male	132	58.1	-	-
Female	95	41.9	-	-

Table 1 depicts general characteristics of Type II diabetic patients. Out of total 227 diabetes patients, 132 (58.1%) were male and 95 (41.9%) were female. The mean and SD for age among patients was found to be 48.99 and 14.69 with range from 24 to 80.

Table-2|Blood Sugar level among type II diabetic patients

Characteristics	Mean	SD	Minimum	Maximum
FBS	111.36	29.67	63	234
PPBS	192.02	83.35	110	452

(FBS-Fasting blood sugar; PPBS-Post prandial blood sugar)

Table 2 presents the blood sugar level among diabetes. The patient's fasting blood sugar mean and standard deviation were found to be 111.36 and 29.67, respectively, with a range of 63 to 234. The postprandial blood sugar ranged from 110 to 452, with a mean and SD of 192.02 and 83.35, respectively.

In liver profile, the mean and SD for Serum Bilirubin Total among patients was found to be 0.60 and 0.55 with range from 0.2 to 3.9. The mean and SD for SGOT among patients was found to be 53.08 and 24.61 with range from 4.2 to 194 while for SGPT it was 48.63 and 46.42 with range from 10.7 to 676. The mean and SD for ALP among patients was found to be 70.5 and 31.66 with range from 32 to 174. Among the renal profile, the mean and SD for urea among patients was found to be 41.69 and 16.83 with range from 5.6 to 97.6. Similarly, the mean and SD for creatinine among patients was found to be 1 and 0.65 with range from 0.1 to 6.2. All other biochemical hepatorenal variables with mean and standard deviation are as shown in Table 3.

Table 4 depicts the correlations of liver profile and renal profile among type II diabetes patients. Correlation of renal and liver profile were found to be significant with age [FBS

(p=0.000); PPBS (p=0.000); SBC (p=0.028); SGOT (p=0.000);

Table-3| Liver profile and renal profile among Type II diabetic patients

Parameters	Mean	SD	Mini-mum	Maxi-mum
Liver Profile				
Total Bilirubin	0.60	0.55	0.2	3.9
Conjugated bilirubin	0.21	0.28	0.1	2.3
SGOT	53.08	24.61	4.2	194.0
SGPT	48.63	46.42	10.7	676.0
ALP	70.5	31.66	32	174
Total Protein	7.7	10.80	3	140
Albumin	4.41	1.06	2.1	8.6
Renal Profile				
Urea	41.69	16.83	5.6	97.6
Creatinine	1.00	0.65	0.1	6.2
Sodium	135.81	9.70	5.4	154.0
Potassium	3.81	2.74	2.30	44.20

(SGOT- Serum glutamate oxaloacetic transaminase, SGPT- Serum glutamate pyruvic transaminase; ALP-Alkaline Phosphatase)

Urea (p=0.003)]. Similarly, correlation of liver and renal profile were found to be significant with FBS [PPBS (p=0.000); SGOT (p=0.014); Sodium (p=0.015)]. With PPBS, a significant correlation was observed between the liver and renal profile [SGOT (p=0.000); Urea (p=0.002)]. Serum total bilirubin appeared to be significantly correlated with the liver and renal profile [SBC (p=0.000); SGPT (p=0.041); ALP (p=0.000); Albumin (p=0.000); Urea (p=0.013); Creatinine (p=0.013); Sodium (p=0.002)]. Conjugated bilirubin and the liver and renal profiles were found to be significantly correlated [ALP (p=0.000); albumin (p=0.015); creatinine (p=0.016)].

Significant results were obtained regarding the correlation between the hepatic and renal profile and SGOT [SGPT (p=0.000); Urea (p=0.049)]. Significant correlations were seen between the renal profile and liver and SGPT [Albumin (p=0.050); Creatinine (p=0.020)]. ALP analysis revealed a substantial connection between the liver and renal profile [Albumin (p=0.001); Creatinine (p=0.000)]. Albumin and the hepatic and renal profiles were shown to be significantly correlated [Creatinine (p=0.000)].

Likewise, there was a significant correlation between the renal profile and liver with urea [Creatinine (p=0.000)]. Similarly, there was a substantial correlation between creatinine and the liver and renal profile [Sodium (p=0.000)]. Our findings revealed that there was a significant correlation between the renal profile and the liver with sodium [FBS (p=0.015); conjugated bilirubin (p=0.013); creatinine (p=0.000). Nevertheless, there was no apparent correlation between the renal and liver profiles and total protein, sodium, or potassium.

DISCUSSION

Hepatorenal patho-physiology are implicated in diabetes and its cardiovascular complications [13,14]. Out of the 227 diabetic patients in our study, 132 (58.1%) were male and 95 (41.9%) were female. In a study carried out in Nepal, similar results were observed regarding the gender distribution of diabetic cases: 131 (52.6%) and 118 (47.4%) for males and females, respectively in the line with our findings [15]. Our results are consistent with a similar study done at Bir Hospital Nepal, wherein of the 210 diabetes patients, 119 (56.6%) were male and 91 (43.3%) were female [16].

In a different study, which was carried out in Ethiopia, 232 diabetes cases (60.4%) were male and 152 cases (39.5%) were female [17]. However, out of 139 elderly diabetic patients in Kanungu District, Uganda, 38 (27.3%) were male and 101 (72.7%) were females almost comparable to our results [18]. It has been shown by recent studies that male are more likely than female [19-21] to have T2DM, but the reason for this difference is unclear. Male sex has been considered a risk factor for type 2 diabetes in recent years [19].

The results of our study depicts the patient's age ranged from 24 to 80, with a mean and standard deviation of 48.99 and 14.69, respectively. Comparable results to our findings were found in a study of T2DM patients at the B.P. Koirala Institute of Health Sciences in Dharan, Nepal [22]. Salih et al. [23] and Shrestha et al. [24] also depicted approximately similar outcomes.

In our study, age was significantly correlated with the renal and hepatic profiles [FBS (p=0.000); PPBS (p=0.000); SBC (p=0.028); SGOT (p=0.000); Urea (p=0.003)]. Aging is known to be a significant risk factor for the majority of chronic diseases, including diabetes and cardiovascular problems. In an epidemiological investigation involving 10,800 middle-aged adults, insulin resistance was found to be closely associated with elevated liver enzyme levels [25]. Therefore, aging plays a widely role in cardiovascular risk assessment approaches in diabetes [26,27]. Another risk factor for acute liver damage is aging [28]. Moreover, the growing incidence of renal diabetes and the correlation between kidney disease and other comorbidities in the elderly are frequent [29].

Likewise, a significant relationship was noted between the liver and renal profile and FBS [PPBS (p=0.000); SGOT (p=0.014); Sodium (p=0.015). Earlier studies showed that elevated FPG levels were associated with elevated liver enzyme levels [30]. The main pathophysiological mechanism explaining the positive correlation between liver enzyme levels and FPG levels may be due to insulin resistance and decreased insulin sensitivity [31,32].

Our results showed that there was a significant correlation between the liver and renal profile with PPBS (SGOT (p=0.000); Urea (p=0.002)]. It is commonly accepted that type 2 diabetes is an independent risk factor for liver fibrosis [33,34]. Non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes (T2DM) are closely associated, and T2DM is a significant risk factor for the development of liver fibrosis, but the role of 2-h postprandial blood glucose (PPG) as a biomarker in this process remains unclear [35]. While there are no comparable studies that show a direct correlation between PPG and liver fibrosis, some studies [36-38] showed that liver fibrosis was improved by lowering postprandial glucose, which suggests an indirect correlation between both of them. Moreover,

Table -4| Correlations of liver profile and renal profile among type II diabetes patients

		Age	FBS	PPBS	SBT	SBC	SGOT	SGPT	ALP	Total protein	Albumin	Urea	Creatinine	Sodium	Potassium
Age	Pearson Correlation	1	0.465**	0.536**	0.096	0.146*	0.256**	-0.010	0.023	0.082	0.046	0.194**	0.118	0.048	-0.096
	Sig. (2- tailed)		0.000	0.000	0.147	0.028	0.000	0.877	0.735	0.220	0.489	0.003	0.076	0.474	0.148
FBS	Pearson Correlation	0.465**	1	0.705**	0.119	0.094	0.163*	0.124	0.156*	0.004	0.028	0.098	0.035	0.161*	0.023
	Sig. (2- tailed)	0.000		0.000	0.074	0.160	0.014	0.063	0.019	0.953	0.671	0.141	0.600	0.015	0.729
PPBS	Pearson Correlation	0.536**	0.705**	1	-0.057	-0.001	0.255**	0.036	-0.024	-0.039	0.109	0.203**	0.036	-0.011	-0.030
	Sig. (2- tailed)	0.000	0.000		0.396	0.986	0.000	0.587	0.721	0.560	0.103	0.002	0.593	0.869	0.651
Total Bilirubin	Pearson Correlation	0.096	0.119	-0.057	1	0.763**	-0.069	-0.136*	0.439**	-0.020	-0.260**	-0.164*	0.165*	0.205**	0.013
	Sig. (2-tailed)	0.147	0.074	0.396		0.000	0.304	0.041	0.000	0.759	0.000	0.013	0.013	0.002	0.844
Conjugated bilirubin	Pearson Correlation	0.146*	0.094	-0.001	0.763**	1	-0.027	-0.079	0.378**	-0.038	-0.161*	-0.052	0.159*	0.007	0.016
	Sig. (2- tailed)	0.028	0.160	0.986	0.000		0.684	0.233	0.000	0.570	0.015	0.436	0.016	0.914	0.809
SGOT	Pearson Correlation	0.256**	0.163*	0.255**	-0.069	-0.027	1	0.256**	-0.094	0.048	0.049	0.131*	-0.068	-0.047	-0.017
	Sig. (2- tailed)	0.000	0.014	0.000	0.304	0.684		0.000	0.157	0.475	0.463	0.049	0.305	0.484	0.799
SGPT	Pearson Correlation	-0.010	0.124	0.036	-0.136*	-0.079	0.256**	1	-0.043	-0.005	0.131*	-0.087	-0.154*	-0.061	-0.069
	Sig. (2- tailed)	0.877	0.063	0.587	0.041	0.233	0.000		0.518	0.936	0.050	0.192	0.020	0.359	0.301
ALP	Pearson Correlation	0.023	0.156*	-0.024	0.439**	0.378**	-0.094	-0.043	1	0.046	-0.221**	-0.031	0.329**	0.095	-0.036
	Sig. (2- tailed)	0.735	0.019	0.721	0.000	0.000	0.157	0.518		0.495	0.001	0.644	0.000	0.154	0.590
Total protein	Pearson Correlation	0.082	0.004	-0.039	-0.020	-0.038	0.048	-0.005	0.046	1	-0.010	0.069	0.088	0.018	-0.008
	Sig. (2- tailed)	0.220	0.953	0.560	0.759	0.570	0.475	0.936	0.495		0.885	0.302	0.185	0.786	0.907
Albumin	Pearson Correlation	0.046	0.028	0.109	-0.260**	-0.161*	0.049	0.131*	-0.221**	-0.010	1	0.006	-0.265**	0.037	0.021
	Sig. (2- tailed)	0.489	0.671	0.103	0.000	0.015	0.463	0.050	0.001	0.885		0.931	0.000	0.581	0.754
Urea	Pearson Correlation	0.194**	0.098	0.203**	-0.164*	-0.052	0.131*	-0.087	-0.031	0.069	0.006	1	0.230**	-0.062	0.027
	Sig. (2- tailed)	0.003	0.141	0.002	0.013	0.436	0.049	0.192	0.644	0.302	0.931		0.000	0.349	0.691
Creatinine	Pearson Correlation	0.118	0.035	0.036	0.165*	0.159*	-0.068	-0.154*	0.329**	0.088	-0.265**	0.230**	1	-0.388**	0.022
	Sig. (2- tailed)	0.076	0.600	0.593	0.013	0.016	0.305	0.020	0.000	0.185	0.000	0.000		0.000	0.745
Sodium	Pearson Correlation	0.048	0.161*	-0.011	0.205**	0.007	-0.047	-0.061	0.095	0.018	0.037	-0.062	-0.388**	1	0.036
	Sig. (2- tailed)	0.474	0.015	0.869	0.002	0.914	0.484	0.359	0.154	0.786	0.581	0.349	0.000		0.586
Potassium	Pearson Correlation	-0.096	0.023	-0.030	0.013	0.016	-0.017	-0.069	-0.036	-0.008	0.021	0.027	0.022	0.036	1
	Sig. (2- tailed)	0.148	0.729	0.651	0.844	0.809	0.799	0.301	0.590	0.907	0.754	0.691	0.745	0.586	

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

hyperglycemia is linked to microvascular problems such as neuropathy, retinopathy, and nephropathy as well as macrovascular problems such as coronary artery disease, peripheral artery disease, and stroke [39]. A significant microvascular consequence of type 2 diabetes that affects 40% of individuals is diabetic nephropathy [40]. The main cause of the emergence and advancement of various complications is uncontrolled hyperglycemia for a number of years [39].

Our results depicts significant correlation between liver and renal profile with serum total bilirubin was [SBC (p=0.000); SGPT (p=0.041) ALP (p=0.000); Albumin (p=0.000); Urea (p=0.013); Creatinine (p=0.013); Sodium (p=0.002)]; with conjugated bilirubin [ALP (p=0.000); albumin (p=0.015); creatinine (p=0.016)]; with SGOT [SGPT (p=0.000); Urea (p=0.049)]; with SGPT [Albumin (p=0.050); Creatinine (p=0.020)]; with ALP [Albumin (p=0.001); Creatinine (0.000]; and with albumin was found to be significant [Creatinine (p=0.000] respectively. In a study of North Ethiopia population, Shibabaw et al. also noted that patients with diabetes had higher SGPT and SGOT levels [7]. Additionally, multiple studies revealed differences in liver enzyme levels across genders. Elevation in SGPT, SGOT, and GGTP has been associated to gender and age, as reported by Noroozi et al. [6]. In the research of Bora et al., SGPT is the most often increased enzyme in females and ALP in males [41]. Increased ALT and GGTP were found to be strongly associated to an increased risk of type 2 diabetes in a study conducted by Wang et al. [42]. Among those with diabetes, Balogun et al. found a significant prevalence of abnormal LFTs, ranging from 70 and 72.1 % [43].

Liver dysfunction in diabetics worsens with advancing diabetes, hence assessment of liver function should also be part of diabetes complication management as reported by Dundi et al. [44]. The established fact is that the glycation and subsequent oxidative stress in tissues that arise as a consequence of long-term diabetes is a contributing factor to these changes in liver enzymes. Because of hepatocellular dysfunction, oxidative stress and cytokine production lead to changes in liver enzymes [45]. Prior scientific published literatures depicts that elevated liver enzyme levels was indicative of decreased insulin sensitivity, insulin resistance, and the onset of type 2 diabetes [31,32,46]. Fasting plasma glucose (FPG) is the most commonly used index to monitor the occurrence of early type 2 diabetes, which is of great significance in the prevention of diabetes. Even though earlier research revealed a substantial correlation between liver enzyme levels and FPG levels [46,47].

The correlation between liver and renal profile with urea [Creatinine (p=0.000)]; with creatinine [Sodium (p=0.000]; with sodium [conjugated bilirubin (p=0.013); Creatinine (p=0.000)] was found to be significant. However, no correlation between liver and renal profile with total protein, sodium, potassium was found. In a different study, the HbA1c level was substantially associated with blood urea and serum creatinine levels [48]. In diabetic individuals, creatinine and urea are helpful prognostic markers and indicators of renal impairment. In accordance with Amartey et al. [49], these findings are consistent with those of the diabetic population followed up at the clinical laboratory in Ghana regarding creatinemia and uremia. Other measures used to investigate renal function include albuminuria and glycosuria, which show whether or not measurable levels of albumin and glucose are present in the urine [50,51]. The limited sample size and hospital setting of the study, as well as being unable to follow up with the patients are a few limitations of this study. Hence, it cannot be related to all the diabetic population of Janakpurdham, Madhesh province, Nepal.

CONCLUSIONS

The liver and renal profile were significantly correlated with each other among diabetic patients. The hepatorenal parameters play significant role in the pathogenesis of different types of DM. Regular monitoring of liver and renal parameters is vital for management of diabetes effectively and preventing potential complications. In addition, it is recommended that therapeutic approaches are essential to accomplish these liver and renal parameters in DM so that, the prevalence of DM could be reduced.

ADDITIONAL INFORMATION AND DECLARATIONS

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Conflict of interest: None declared

Author's Contribution: Study design, data collection, reviewing the literature, analyzing and interpreting the results, and writing the first draft - SP, MKS,BY,OPY; editing of the manuscript's first version-OPY, RN ; modification of the manuscript's second draft, management of references, and final approval with academic critics-SP,OPY,VKS. Following each author's evaluation, the final manuscript was approved for publication.

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