Factors favoring the toxic effects of metformin in subjects with type 2 diabetes in two referral hospital in Douala, Cameroon

ABSTRACT

Introduction: The Metformin is a first line agent for the treatment of type 2 diabetes that can be used alone or in combination with sulfonylureas thiazolidinediones, incretin-based drugs, sodium/glucose cotransporter-2 inhibitors, or other hypoglycemic agents. Metformin is the most used anti-hyperglycemic agent for the treatment of Type 2 Diabetes Mellitus. It is considered as a very good drug, with low risk and high benefit. The Metformin liver and pancreatic intoxication can be due to massive ingestion or to a progressive accumulation due to renal failure, hence an elevated blood amylase and transaminases levels. Fatal cases due to metformin intoxication have been described.

Method: The study was an analytical cross sectional study which was carried out in the Douala General Hospital and the Douala Laquintinie Hospital from the 1st of March 2021 to the 30th of May 2021. Our study population included type 2 diabetic patients above 40years of age who are strictly on oral antidiabetic drugs who came to consult in the Douala General Hospital and the Douala Laquintinie Hospital, the exclusion criteria were; Patients infected with hepatitis A, B or hepatitis C, diabetic patients suffering from other pathologies like fatty liver disease and cirrhosis, liver cancer and others, patients suffering from terminal renal failure, patients who have been on NSAI drugs for long period and also taking alcohol or those with hemolyzed blood. For ethical consideration, after presenting and filling of the consent form, 5ml of blood was collected from each participant for the analyses, serum was conserved at a temperature of -15 to -20°C and the samples were finally analyzed in 2 series on the Biotecnica 1500 chemistry analyzer. Statistical analysis was done on Microsoft Excel 2013 version.

Results: A total of 102 participants were enrolled, female gender was dominant, and the mean age was 69 years. Most of participants felt under neurological clinical effects (tiredness, dizziness, and tingling sensation). We had an average GOT of 28.3, with a minimum of 7.0 and a maximum of 207, an average GPT of 19.8 with a minimum of 5.9 and a maximum of 90.7 and an average amylase was 45.7 with a minimum value of 11.5 and a maximum value of 470. On the other hand, our average GFR was 74.3 with a minimum of 12.8 and a maximum of 153.2. From the study population, 90 where on metformin among which 79 were on stages 2-5 of kidney failure.

Conclusion: This study highlights the risk of liver toxicity for diabetic patient under metformin surfing from renal failure.

Key words: Metformin**,** Type 2 diabetes, Hepatotoxicity, Biochemical parameters.

INTRODUCTION

Type 2 diabetes is a major health problem associated with excess mortality and morbidity. Vascular complications are one of the most serious consequences of this disorder. Moreover, type 2 diabetes is also a risk factor for cerebral complications, including cognitive impairment and dementia. However, it has been shown that tight glycemic control contributes to reduce the incidence of diabetes-associated complications. Metformin is a potent antihyperglycemic agent widely used in the management of type 2 diabetes whose main actions are the suppression of gluconeogenesis and the improvement of glucose uptake and insulin sensitivity. [1]

This study is mainly devoted to describe the variation of biochemical parameters, correlation metformin toxicity and renal failure.

METHODS

An analytical cross-sectional study was carried out at the internal medicine department of the diabetology unit of the two referral hospitals; Douala General Hospital and Douala Laquitinie Hospital (DGH DL) for the collection of information, the investigation and the blood sample.

We included Type 2 diabetic patients > 40 years old on strictly oral antidiabetics who consulted in the diabetology department of the DGH and the DLH.

Will not share our samples with patients

- Patients infected with hepatitis A, B or hepatitis C.
- Diabetic patients suffering from other pathologies like fatty liver disease and cirrhosis, liver cancer and others.
- Patients suffering from terminal renal failure.
- Patients who have been on non-steroidal anti-inflammatory drugs for long and also taking alcohol.

This study is a simple random sampling (probability sampling) through a systematic recruitment process of all persons fulfilling all the inclusion criteria and available to participate in the study. The number of participants in the hospital was calculated from COCHRAN'S formula

$$n^o = \frac{z^2\, p\,(1-p)}{e^2}$$

n^o= sample size

z= z-score z=1.96

e= margin of error e= 0.05

p= standard deviation p= 0.06

$$\text{Sample size: } \frac{(1.96)^2 \times 0.06(1-0.06)}{(0.05)^2} = 86$$

From the Cochran's formula, at least 86 patients were to participate in the study. We finally worked with 102 participants.

PROCEDURE

Sample recruitment was done at the DGH and DLH at the endocrino-diabetology units. The patients recruited were those who fulfilled all the inclusion criteria and are available to participate in the study. The patients were received and the information about the study was well explained to them with the help of the inform consent.

DATA ANALYSIS

Data was collected using Microsoft excel and Kobo Collect. Statistical analysis will be done using the Microsoft excel 2013 software. After a general description of the population, the quantitative variables was represented using mean value and standard deviation meanwhile those of the qualitative variables was represented as percentages. Quantitative comparison of variables was done using the spearman rho test, while qualitative comparison of variables was done using the Pearson chi-squared test (χ^2).

RESULTS

GLOBAL DISTRIBUTION OF STUDY POPULATION ACCORDING TO OUR INCLUSION CRITERIA

A total of 955 diabetic patients consulted from March 2021 to mid-May 2021.

467 patients from the DGH and 447 from the DLH. Out of these 955 patients, 41 were suffering from DT1 and 914 from DT2. We approached 441patients in both hospitals.

291 of these patients were on insulin or insulin and oral antidiabetics.

39 of these patients refused to participate in the study (too weak, had to consult a close family member, already ran the tests, in a haste to go home, doesn't want the blood to be collected)

111 patients give their consent

7 patients filled the questionnaire but we didn't collect the sample

2 samples were hemolyzed.

102 samples were collected and analyzed and the end. Representing 10.7% of the population

Distribution according age

The most occurring age range being between 56 and 60 with a minimum of 35 and a maximum of 81 (fig 1)

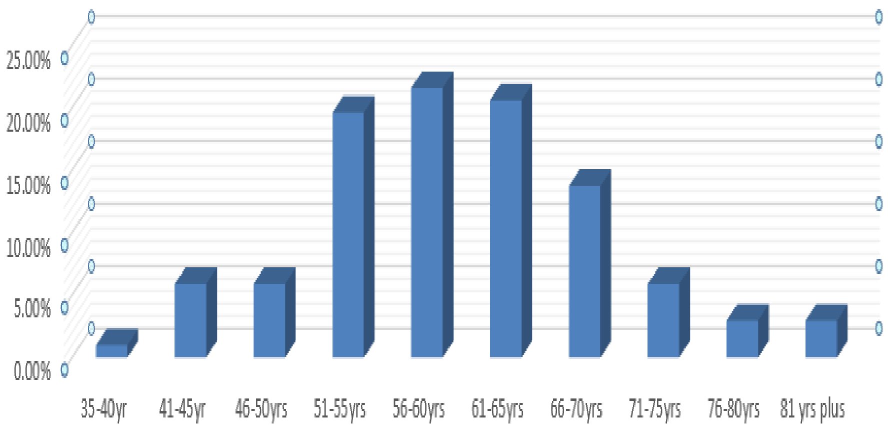

Figure 1: distribution according to age

DISTRIBUTION OF CLINICAL AND BIOLOGICAL PARAMETERS

- ***Distribution of blood sugar level***

From our study population, 59 patients had their blood sugar levels above the normal range (> 1.26g/l) which represents 58% of our study population while 43 patients had normal blood sugar levels with a representation of 42%. (Fig 2)

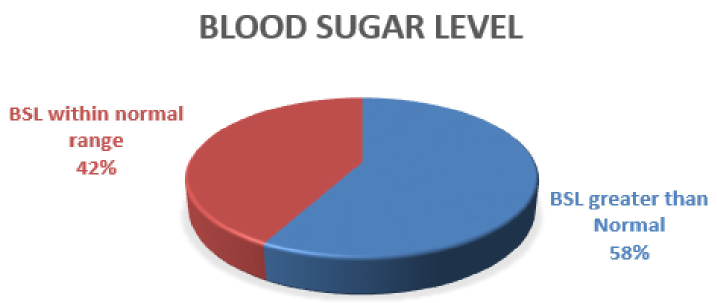

Figure 2: Distribution of blood sugar level

- ***Distribution of comorbidity***

Patients who feel tired represent 89.2% of the total population which is the most occurring case followed by patients who feel dizzy represented by 50.0% of the total population, followed by itches 37.3% and hypertension, 18.6%. (Fig 3)

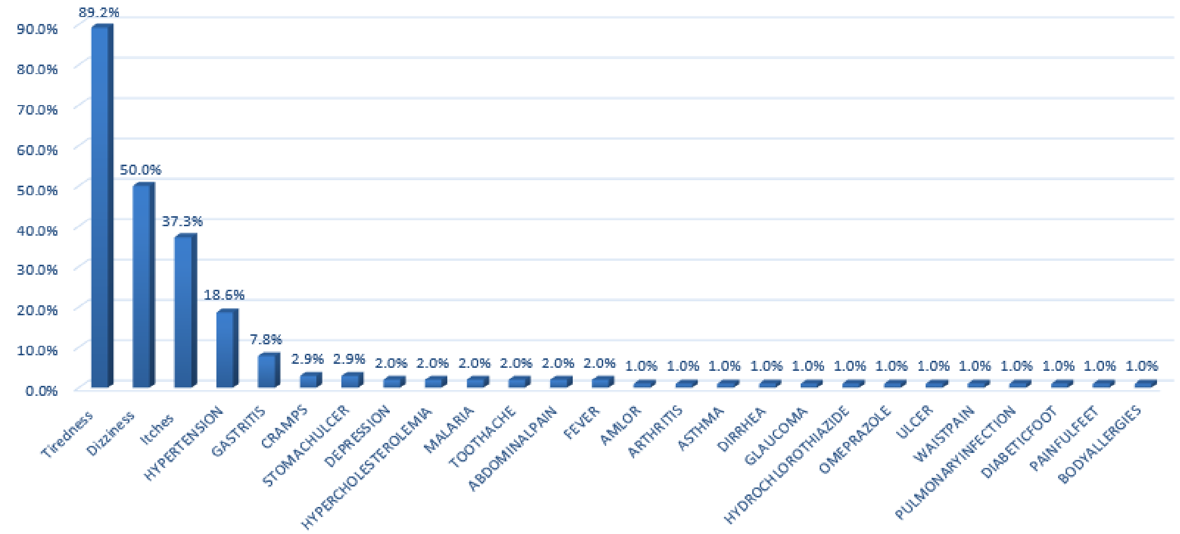

Figure 3: Distribution of comorbidity

- ***Distribution of creatinine***

Half of our study population, 51 patients had their creatinine levels within the normal range (9-13mg/dl in men and 6-11mg.dl in women) which is 50% of the total population.40 patients were above the normal range,>13mg/dl in men and > 11 mg/dl in women, which represent 39% of the total population. (Fig 4)

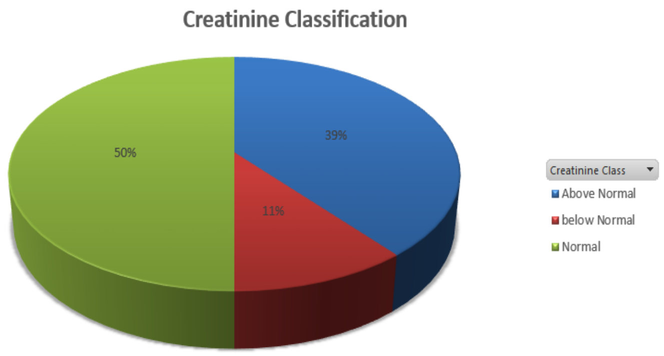

Figure 4: Distribution of creatinine

- ***Distribution of GOT***

From our study population of 102 patients, 14 patients had GOT values that are greater than the normal range (> 40UI/L) which represents 14% of our total population. 88 patients had values within the normal range (5-40UI/L), which represent 86% of our study population. (Fig 5)

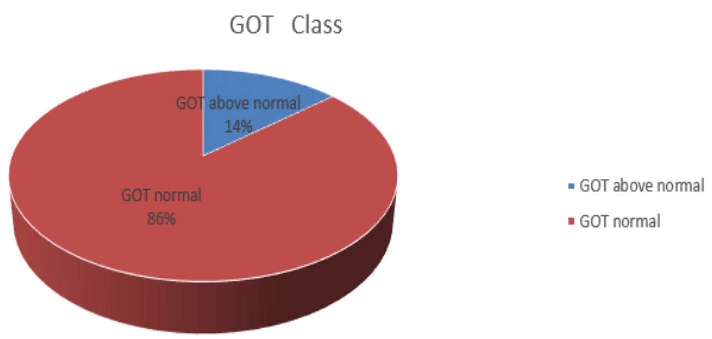

Figure 5: Distribution of GOT

- ***Distribution of GPT***

5 patients of 102 had GPT greater than the normal range (> 45UI/L), which represent 5% of the total population and 97 patients within the normal range (5-45UI/L) which represent 95% of our study population. (Fig 6)

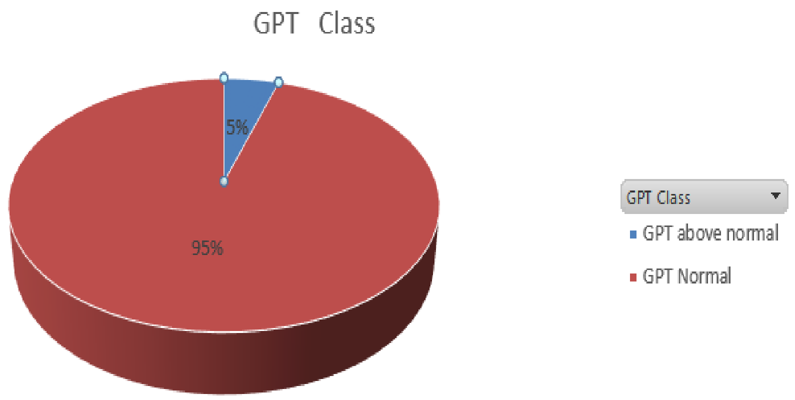

Figure 6: Distribution of GPT

- ***Distribution of amylase***

From 102 patients, 17 patients which represents 17% of our population had amylase values greater than normal range (> 53UI/L) while 85 patients, 83% had amylase values within the normal range. (Fig 7)

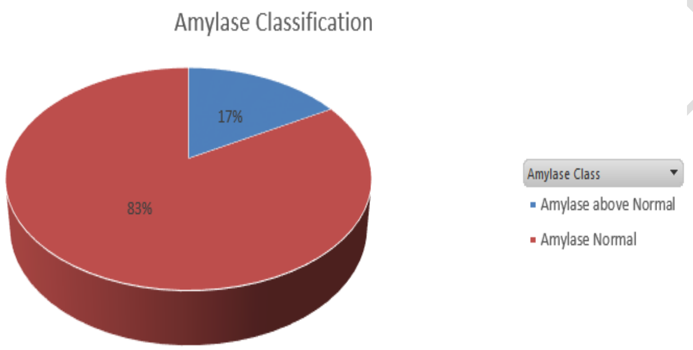

Figure 7: Distribution of amylase

- ***Distribution of GFR***

From our study population, 43 patients of 102 which represent 42.16% of the total population had their GFR within 60-89ml/min/1.73m^2 which is stage 2 of GFR classification and defined as a stage of chronic renal failure. 30 patients in stage 3, representing 29.41% of the total population and 5 patients in stage 4 which represents 4.90% of the population. 1 patient was at the level of end stage renal disease. (Fig 8)

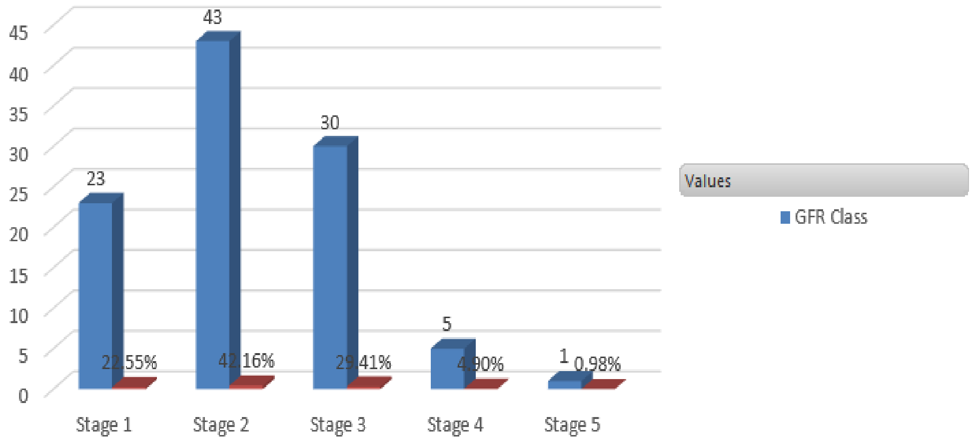

Figure 8: Distribution of GFR

- ***Average of GFR with respect to metformin consumption***

This is the distribution of GFR in relation to those who take metformin and those who are not taking metformin. Here we discovered that those who are in stage 5 which is terminal renal failure are only on monotherapy. (Fig 9)

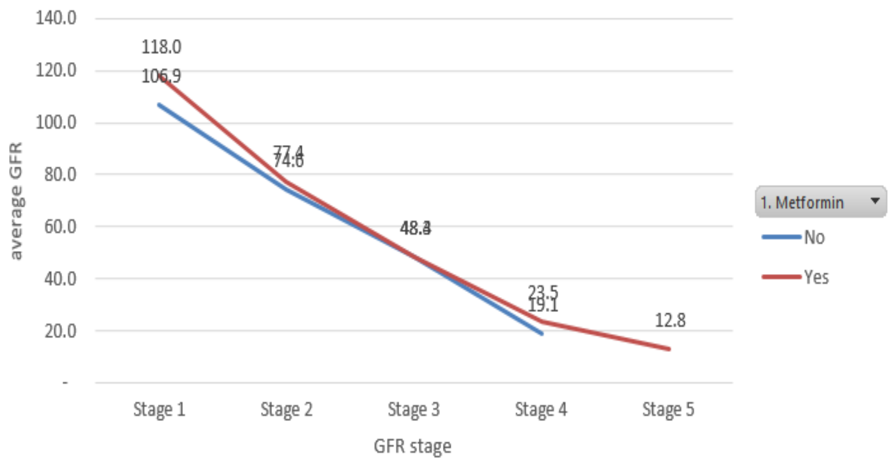

Figure 9: Average of GFR with respect to metformin consumption.

CORRELATION BETWEEN GOT, GPT, AMYLASE IN RELATION TO GFR.

There is a significant correlation between GOT, GPT and amylase in relation to GFR. The correlation significance is at the 0.01 level.

Table 1: Correlation between GOT, GPT and amylase in relation to GFR

			GOT	GPT	AMYLASE	GFR
Spearman's rho	GOT	Correlation Coefficient	1.000	.587**	.113	-.345**
		Sig. (2-tailed)		.000	.257	.000
		N	102	102	102	102
	GPT	Correlation Coefficient	.587**	1.000	.039	-.249*
		Sig. (2-tailed)	.000		.694	.012
		N	102	102	102	102
	AMYLASE	Correlation Coefficient	.113	.039	1.000	-.287**
		Sig. (2-tailed)	.257	.694		.003
		N	102	102	102	102
	GFR	Correlation Coefficient	-.345**	-.249*	-.287**	1.000
		Sig. (2-tailed)	.000	.012	.003	
		N	102	102	102	102

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

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

Using the spearman's rho correlation test, we noticed that for patients who are not on metformin, there is no significant correlation between GOT, GPT and amylase in relation to GFR, while for patient who are on metformin, we have a correlation significance of 0.01 level in relation to GOT, GPT and amylase in relation to GFR.

Table 2: Correlation between GPT, GOT and amylase in relation to GFR and metformin

1. Metformin				GOT	GPT	AMYLASE	GFR
0	Spearman's rho	GOT	Correlation Coefficient	1.000	.658*	.294	-.119
			Sig. (2-tailed)		.020	.354	.713
			N	12	12	12	12
		GPT	Correlation Coefficient	.658*	1.000	.095	-.368
			Sig. (2-tailed)	.020		.770	.240
			N	12	12	12	12
		AMYLASE	Correlation Coefficient	.294	.095	1.000	.399
			Sig. (2-tailed)	.354	.770		.199
			N	12	12	12	12
		GFR	Correlation Coefficient	-.119	-.368	.399	1.000
			Sig. (2-tailed)	.713	.240	.199	
			N	12	12	12	12
1	Spearman's rho	GOT	Correlation Coefficient	1.000	.576**	.097	-.369**
			Sig. (2-tailed)		.000	.365	.000
			N	90	90	90	90
		GPT	Correlation Coefficient	.576**	1.000	.040	-.228*
			Sig. (2-tailed)	.000		.707	.030
			N	90	90	90	90

			GOT	GPT	AMYLASE	GFR
	AMYLASE	Correlation Coefficient	.097	.040	1.000	-.361**
		Sig. (2-tailed)	.365	.707		.000
		N	90	90	90	90
	GFR	Correlation Coefficient	-.369**	-.228*	-.361**	1.000
		Sig. (2-tailed)	.000	.030	.000	
		N	90	90	90	90

****. Correlation is significant at the 0.01 level (2-tailed). *. Correlation is significant at the 0.05 level (2-tailed**

Correlation between GOT, GPT, amylase in relation to GFR and Glimepide

Patients who are not on glimepiride present a significant correlation between GOT and amylase with respect to GFR meanwhile there is no significant correlation with patients who are taking glimepiride.

Table 3: correlation of Glimepiride

2. Glimepiride				**GOT**	**GPT**	**AMYLASE**	**GFR**
0	Spearman's rho	GOT	Correlation Coefficient	1.000	.571**	.118	-.404**
			Sig. (2-tailed)		.000	.330	.001
			N	70	70	70	70
		GPT	Correlation Coefficient	.571**	1.000	.045	-.227
			Sig. (2-tailed)	.000		.709	.059
			N	70	70	70	70
		AMYLASE	Correlation Coefficient	.118	.045	1.000	-.427**
			Sig. (2-tailed)	.330	.709		.000
			N	70	70	70	70
		GFR	Correlation Coefficient	-.404**	-.227	-.427**	1.000
			Sig. (2-tailed)	.001	.059	.000	
			N	70	70	70	70
1	Spearman's rho	GOT	Correlation Coefficient	1.000	.626**	.090	-.210
			Sig. (2-tailed)		.000	.625	.249
			N	32	32	32	32
		GPT	Correlation Coefficient	.626**	1.000	-.038	-.369*
			Sig. (2-tailed)	.000		.835	.037
			N	32	32	32	32
		AMYLASE	Correlation Coefficient	.090	-.038	1.000	.010
			Sig. (2-tailed)	.625	.835		.956
			N	32	32	32	32
		GFR	Correlation Coefficient	-.210	-.369*	.010	1.000
			Sig. (2-tailed)	.249	.037	.956	
			N	32	32	32	32

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

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

Correlation between GOT, GPT, amylase in relation to GFR and Gliclazide

Patients who are not on gliclazide present a significant correlation between GOT, GPT and amylase with respect to GFR meanwhile there is no significant correlation with patients who are taking gliclazide.

Table 4: correlation of Gliclazide

3. Gliclazide				**GOT**	**GPT**	**AMYLASE**	**GFR**
0	Spearman's rho	GOT	Correlation Coefficient	1.000	.708**	.164	-.332**
			Sig. (2-tailed)		.000	.148	.003
			N	79	79	79	79
		GPT	Correlation Coefficient	.708**	1.000	.099	-.353**
			Sig. (2-tailed)	.000		.387	.001
			N	79	79	79	79
		AMYLASE	Correlation Coefficient	.164	.099	1.000	-.230*
			Sig. (2-tailed)	.148	.387		.042
			N	79	79	79	79
		GFR	Correlation Coefficient	-.332**	-.353**	-.230*	1.000
			Sig. (2-tailed)	.003	.001	.042	
			N	79	79	79	79

Table 5: Correlation between GOT, GPT, amylase in relation to GFR and Vidagliptin

Patients who are not on vidagliptin present a significant correlation between GOT, GPT and amylase with respect to GFR meanwhile there is no significant correlation with patients who are taking vidagliptin.

What is your therapy				**GOT**	**GPT**	**AMYLASE**	**GFR**
Bitherapy	Spearman's rho	GOT	Correlation Coefficient	1.000	.586**	.291	-.414**
			Sig. (2-tailed)		.000	.076	.010
			N	38	38	38	38
		GPT	Correlation Coefficient	.586**	1.000	.102	-.319
			Sig. (2-tailed)	.000		.541	.051
			N	38	38	38	38
		AMYLASE	Correlation Coefficient	.291	.102	1.000	-.242
			Sig. (2-tailed)	.076	.541		.143
			N	38	38	38	38

				GOT	GPT	AMYLASE	GFR
		GFR	Correlation Coefficient	-.414**	-.319	-.242	1.000
			Sig. (2-tailed)	.010	.051	.143	
			N	38	38	38	38
Monotherapy	Spearman's rho	GOT	Correlation Coefficient	1.000	.645**	.149	-.324*
			Sig. (2-tailed)		.000	.335	.032
			N	44	44	44	44
		GPT	Correlation Coefficient	.645**	1.000	.039	-.314*

Stage 2-5

Group 1

Correlations

			GOT	GPT	AMYLASE	GFR
Spearman's rho	GOT	Correlation Coefficient	1.000	.567**	.044	-.100
		Sig. (2-tailed)		.000	.698	.380
		N	79	79	79	79
	GPT	Correlation Coefficient	.567**	1.000	.032	-.091
		Sig. (2-tailed)	.000		.780	.425
		N	79	79	79	79
	AMYLASE	Correlation Coefficient	.044	.032	1.000	-.325**
		Sig. (2-tailed)	.698	.780		.004
		N	79	79	79	79
	GFR	Correlation Coefficient	-.100	-.091	-.325**	1.000
		Sig. (2-tailed)	.380	.425	.004	
		N	79	79	79	79

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

				GOT	GPT	AMYLASE	GFR
Tritherapy	Spearman's rho	GOT	Correlation Coefficient	1.000	.484*	-.138	-.297
			Sig. (2-tailed)		.030	.561	.203
			N	20	20	20	20
		GPT	Correlation Coefficient	.484*	1.000	-.209	-.066
			Sig. (2-tailed)	.030		.376	.782
			N	20	20	20	20
		AMYLASE	Correlation Coefficient	-.138	-.209	1.000	-.325
			Sig. (2-tailed)	.561	.376		.162
			N	20	20	20	20
		GFR	Correlation Coefficient	-.297	-.066	-.325	1.000
			Sig. (2-tailed)	.203	.782	.162	
			N	20	20	20	20

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

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

				GOT	GPT	AMYLASE	GFR
			Sig. (2-tailed)	.000		.800	.038
			N	44	44	44	44
		AMYLASE	Correlation Coefficient	.149	.039	1.000	-.384*
			Sig. (2-tailed)	.335	.800		.010
			N	44	44	44	44
		GFR	Correlation Coefficient	-.324*	-.314*	-.384*	1.000
			Sig. (2-tailed)	.032	.038	.010	
			N	44	44	44	44

Table 6: correlation of patients suffering from renal failure

Group 1	**stage2-5**					
		Correlations[a]				
			GOT	GPT	AMYLASE	GFR
Spearman's rho	GOT	Correlation Coefficient	1.000	.567**	.044	-.100
		Sig. (2-tailed)		.000	.698	.380
		N	79	79	79	79
	GPT	Correlation Coefficient	.567**	1.000	.032	-.091
		Sig. (2-tailed)	.000		.780	.425
		N	79	79	79	79
	AMYLASE	Correlation Coefficient	.044	.032	1.000	-.325**
		Sig. (2-tailed)	.698	.780		.004
		N	79	79	79	79
	GFR	Correlation Coefficient	-.100	-.091	-.325**	1.000
		Sig. (2-tailed)	.380	.425	.004	
		N	79	79	79	79

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

Table 7: correlation of patients not suffering from renal failure

			GOT	**GPT**	**AMYLASE**	**GFR**
Spearman's rho	GOT	Correlation Coefficient	1.000	.484*	.276	-.143
		Sig. (2-tailed)		.019	.203	.516
		N	23	23	23	23
	GPT	Correlation Coefficient	.484*	1.000	-.091	.074
		Sig. (2-tailed)	.019		.678	.738
		N	23	23	23	23
	AMYLASE	Correlation Coefficient	.276	-.091	1.000	-.369
		Sig. (2-tailed)	.203	.678		.083
		N	23	23	23	23
	GFR	Correlation Coefficient	-.143	.074	-.369	1.000
		Sig. (2-tailed)	.516	.738	.083	

	N	23	23	23	23
***. Correlation is significant at the 0.05 level (2-tailed).**					
a. GFRclN = Group 0					

During our research period, we were interested to confirm the fact that the most used oral antidiabetic drugs are the biguanides as mentioned earlier. So we went to pharmacies and with the help of well-structured forms containing all the oral antidiabetics, we were able to get the following information:

We went to 14 pharmacies and from there we notice that the most dispensed oral antidiabetics were biguanides with a percentage of 51% followed by sulfonylureas with a percentage of 31.6%.

NB: This work is out of our scope of study but we thought it wise to do a research in pharmacies for justific,ation purposes.

DISCUSSIONS

Since numerous medications and disease states can cause abnormalities in liver and pancreatic enzymes, [2] it is important for us to be able to distinguish the cause(s) and take the appropriate actions. In this effect, our results can be linked with some possible bias due to the fact that some patients could be taking other drugs that are unknown which could probably increase the toxic effects on the liver and pancreas, and also considering the fact that we did not measure the previous creatinine level of the patients. [1-2]

For our analytical study, we collected 104 samples all together but 2 were rejected for being haemolyzed and 102 proceed for the Study.

In the distribution of population according to age, the mean age value was 59years, and the most occurring age rang being from 56 to 60 years (21.49%), 61 to 65 years (20.67%). This can be compared with a study done by Spiller and Quadrani in 2004 where the age range was between 48-80 years but with a mean value of 62years. Spiller and Quadrani[precised that in the adult population, the adverse outcomes of the drug are evenly distributed across the age span. This age range is predominated by elderly adults due to the fact that our study is based on adult population suffering from T2D. [3]

Evaluating our population according to their pathology shows most of our participants feld under neurological clinical effects (tiredness, dizziness and tingling sensations representing 89.2%, 50.0%, 37.3% respectively), followed by hypertension with 18.6%. This is different from a study done by Spiller and Quadrani and Mbaya JCN [3-4] where they analyzed the clinical features in both acute and acute on chronic metformin exposures reported to the Toxic Exposure Surveillance System and observed the presence of hypotension, tarchycardia, nausea/vomiting, drowsiness/dizziness, acidosis, hyperglycemia occurrences and coma may be prognostic of a severe or fatal outcome.

For our biological parameters, we had an average GOT of 28.3 UI/L, with a minimum of 7.0 UI/L and a maximum of 207 UI/L and an average GPT of 19.8 UI/L with a minimum of 5.9 UI/L and a maximum of 90.7 UI/L. From our study population, a representation of 14% had GOT levels above the normal while 5% had GPT levels above normal, which can be compared with case studies done by Cone JC al [6] on the Hepatotoxicity associated with metformin therapy in treatment of Type 2 Diabetes Mellitus with nonalcoholic fatty liver disease, where a type 2 diabetic patient was rushed to the hospital and had a GOT 623U/L and GPT level of 571U/L. Another case study done by Miralles-Linares F et al [8] and Lheureux PE [10] on metformin induced hepatotoxicity demonstrated that the patients who were on metformin had GOT of 290 U/L and GPT 861 U/L levels above normal. Therefore if there is a modification of the pharmacokinetics of the drugs, due to renal failure, it will lead to metformin accumulation and hence hepatotoxicity. [8-10]

Average amylase level was 45.7 UI/L with a minimum value of 11.5 UI/L and a maximum value of 470 UI/L. A representative population of 17% had amylase levels above the normal range. This is similar to a case study done by Lee E Goltokh S[7] on Metformin induced acute pancreatitis precipitated by renal failure, where a diabetic patient on metformin had an amylase level of 250 U/L, another case study by Alsubaie S and Almalki MH [5] on Metformin induced acute pancreatitis with amylase levels of 462U/L, and another case study by Gioia et al[6] on Pancreatitis and metformin with amylase levels of 2050U/L. These case studies demonstrated that patients who were taking metformin presented elevated levels of amylase greater than the normal values. The reason for this could be due renal failure which reduced metformin excretion, causing toxicity leading to pancreatitis. Since after analyzing our result, we noted a significant correlation between GFR and amylase. [5-6]

With respect to the GFR, we had a mean value of 74.3 ml/min/1.73m^2 with a minimum of 12.8 ml/min/1.73m^2 and a maximum of 153.2 ml/min/1.73m^2. From our study population, of 102 participants, 90 where on metformin and 79 of these 90 where in the stages 2-5 of kidney failure. This can be compared to case studies done by Miralles Lina and and Gioia et al [8-9], with serum creatinine levels above the normal range,(516 umol/l, 58 μmol/L and 3.2 mg/dl respectively), we calculated their corresponding GFRs, (8.1ml/min/1.73m^2, 189.3ml/min/1.73m^2, 24.5ml/min/1.73m^2 respectively) and noticed that 2 of these 3 patients who were on metformin were at terminal renal failure. This can be justified by the fact that, nephropathy is a known complication of diabetes due to high blood glucose levels and hence destruction of blood vessels in the kidney. Hence decrease in the rate of glomerular filtration.

From our results using the Spearman's rho test, we were able to bring out a correlation between the increased levels of biochemical markers and the therapeutic protocols of our study population. We noticed there is a significant correlation of 0.01 between GOT, GPT and amylase in relation to GFR, and patients on metformin with low GFR showed a significant correlation of 0.01 between GOT, GPT and amylase. This implies that renal failure (could also be caused by diabetic complication) induces an accumulation of metformin in circulation, hence an increases in GOT, GPT and amylase in patients who are on metformin hence hepatotoxicity and pancreatitis.

On the contraury, patient who was on other oral antidiabetic drugs (glimepiride, gliclazide, vidagliptin) didn't show any significant correlation between GOT, GPT and amylase in relation to GFR. This proves that hepatotoxicity and pancreatitis of these classes of oral antidiabetic drugs are uncommon.

We also did the correlation of GPT, GPT and amylase in relation to GFR and therapy, and patients who were on biotherapy and tritherapy didn't show any significant correlation meanwhile patients who were on monotherapy (metformin) showed a significant correlation of 0.01 between GOT, GPT and amylase in relation to GFR. Summarily,

CONCLUSION

- A majority of participants were females, with most represented age range between 56-60years,with an increased BMI in most of the population
- A percentage of patients in our study population are having increased amylase levels than transaminases levels, which shows that patients on metformin are susceptible to pancreatitis than hepatitis.
- Diabetic patients who are on metformin and suffering from renal failure have a higher possibility of suffering from liver and pancreatic toxicity.

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

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