Assessment of Uric Acid, Inorganic Phosphate, and Calcium on Diabetes Mellitus Patients

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ABSTRACT

Diabetes mellitus is one of the most common non-communicable diseases known to have a multi-systemic effect. This study was carried out to determine the Calcium, Uric acid and inorganic phosphate levels of Diabetes mellitus subjects in Ekpoma and environs. A total of 90 samples were used in this study comprising forty-five (45) Diabetes mellitus subjects and forty-five (45) non-diabetes mellitus subjects as control. Uric acid was determined using Uricase Method, Inorganic phosphate and Calcium was determined using Auto-analyzer. The results were presented using tables as mean ± standard deviation. Statistical analysis was done using one-way analysis of variance (ANOVA) and the student's t-test. Significant difference was accepted at $p<0.05$. The results obtained showed that the FBS (mg/dl) of the subjects and control was 239.77±36.64 and 87.53±11.29, Calcium (mmol/L) was 7.41±0.72 and 8.89±0.57, Uric acid (mg/dl) was 5.46±1.29 and 5.09±1.12, and Inorganic phosphate (mmol/L) was 4.73±1.05 and 3.19±0.57 respectively. FBS and Uric acid were higher in Diabetes mellitus subjects compared with control, however, only FBS was significant ($p<0.05$). Calcium and Inorganic phosphate were significantly lower ($p<0.05$) in Diabetes mellitus subjects compared with control group. There was significant difference ($p<0.05$) in the Uric acid of male subjects compared with female subjects, but there was no significant difference ($p>0.05$) in FBS, Calcium and Inorganic phosphate of male subjects compared with female subjects. There was significant difference ($p<0.05$) in FBS, Inorganic phosphate and Calcium of the subjects with respect to age, but Uric acid did not differ significantly ($p>0.05$). In conclusion, there was a positive correlation between plasma FBS and serum Inorganic phosphate (PO_4), and between FBS and Uric acid levels, but a negative correlation existed between plasma FBS and serum Calcium levels in Diabetes mellitus subjects.

Keywords: Diabetes mellitus, Uric acid, Calcium, Inorganic phosphate, Serum

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterized by chronic hyperglycemia from relative insulin deficiency, resistance, or both (Gale & Anderson, 2017). The estimated global prevalence of DM among adults aged 20–79 years in 2019 was reported by the International Diabetes Foundation to be 9.3%, affecting 463.0 million adults, and this figure is projected to increase to 578.4 million by 2030 and eventually, to 700.2 million adults, in 2045 (International Diabetes Federation, 2019). A recent systematic review of DM prevalence in Nigeria (2018), revealed a nation-wide prevalence of 5.7%, though with marked regional variations in prevalence (Uloko, Musa, Ramalan & Gezawa, 2018). Type 2 DM (T2DM) is the most common type of DM and results from a combination of insulin resistance and less severe insulin deficiency (Gale & Anderson, 2017). T2DM is also the most commonly seen diabetes presentation in older adults, though in recent times, it has been noted to be increasing in incidence among children, adolescents, and younger adults due to poor diet, obesity, and sedentary lifestyle. DM as a complex chronic disease requires multifactorial risk-reduction strategies beyond glycemic control (American Diabetes Association, 2018). The long-term metabolic derangement in DM leads to the affectation of different organs and systems in the body including the kidneys, nerves, eyes, and cardiovascular system. Insulin is the key hormone required for the storage and controlled release of chemical energy in form of glucose from food in the body (Gale & Anderson, 2017)

and hence, is the primary determinant of glycemic control. The landmark United Kingdom Prospective Diabetes Study showed that patients with tight control of glycaemia had fewer chronic complications; therefore, adequate glycemic control should be the primary aim of treatment. Short-term glycemic control of patients can be determined by self-monitoring of blood glucose using glucose meters (American Diabetes Association, 2018).

Uric acid (UA), the prime end product of purine catabolism and the precursor of gout, has been implicated in diabetes mellitus as well as in hyperlipidemias. There is a possible role of insulin in nucleotide metabolism (Kertes, 2013). High uric acid is considered as an independent risk factor for developing diabetes, hypertension, stroke and cardiovascular diseases. The clearance of UA is being reduced with increase in insulin resistance (Sluijs, Beulens, Spijkerman & Schulze, 2013). There is evidence suggesting hyperuricemia as an independent risk factor for impaired fasting glucose (IFG) and type 2 diabetes mellitus. Patients with hyperuricemia are at a significantly higher risk of progressing to type 2 diabetes mellitus (Xue, Tan, Ning, Zhang & Sun, 2015). A large number of researchers have begun to consider uric acid as a serum indicator of glycometabolic disorders, because of a correlation between uric acid and glucose metabolism by earlier authors (Adu, 2022).

Phosphate is essential for life, as it participates in the structure of cellular membranes as a material of nucleic acids, phospholipids and adenosine triphosphate. Additionally, inorganic phosphate plays a crucial role in cellular signaling through reactions of phosphorylation (Raikou, Kyriaki & Gavriil, 2020). Homeostasis of inorganic phosphate is affected by multiple interactions between the intestine, parathyroid glands, kidneys and bone. Serum inorganic phosphate levels are dependent on the absorption in the gut from dietary inorganic phosphate, the excretion and reabsorption of inorganic phosphate in the kidneys, and the movement of inorganic phosphate between the extracellular and skeletal pools. Parathyroid hormone and fibroblast growth factor 23 play an important role in the regulation of serum inorganic phosphate by mediating urinary inorganic phosphate removal (Sigrist, Tang & Beaulieu, 2013). Elevated serum inorganic phosphate is recognized as an independent predictor for advanced vascular disease in chronic kidney disease (CKD) (Toussaint, Pedagogos, Tan & Badve, 2012).

Calcium is a protean intracellular messenger involved in many biological processes. More than 99% of the calcium present in the human body is in the bone, the remaining being found mostly in the blood and extracellular fluid (Longo, Fauci, Kasper & Hauser, 2012). The biologically active form of calcium is the unbound (ionized) form and this ionized calcium needs to be maintained within a narrow range, because of the critical role it plays in a wide range of cellular functions (Longo *et al.*, 2012). Calcium is mainly regulated by parathyroid hormone (PTH) and Vitamin D and to a lesser extent, by calcitonin (Levy & Gleenson, 2017).

Over the past three decades, the number of people with diabetes mellitus has more than doubled globally, making it one of the most important public health challenges to all nations. The causes of the epidemic of diabetes mellitus are embedded in a very complex group of genetic and epigenetic systems interacting within an equally complex societal framework that determines behaviour and environmental influences. The chronic hyperglycemia of diabetes is associated with damage of several body organs which could be as a result of microvascular and macrovascular complications (Adu, 2022).

A metabolic imbalance in inorganic phosphate occurs from the early onset of diabetes mellitus and may lead to a reduction of high energy phosphates and tissue hypoxia. These changes take place in the cells and tissues in which the entry of glucose is not controlled by insulin. Changes in serum phosphate level are related with severity of diabetes mellitus. Uric acid being an end product of the purine metabolism is associated with an increased future risk of diabetes, it may reduce the future risk of gout through the uricosuric effect of glucose or the impaired inflammatory response. Also, hyperuricaemia has been presumed to be a consequence of the insulin resistance. Reduced serum calcium in patients with T2DM is attributed to excessive urinary calcium loss due to chronic hyperglycemia. PTH secretion is then stimulated in response to increased urinary calcium loss, to help maintain serum calcium levels (Levy & Gleenson, 2017). The importance of inorganic phosphate, calcium and uric acid in the pathogenesis of diabetes mellitus cannot be overemphasized, hence, the purpose of this study.

MATERIALS AND METHODS

This study is a community based cross-sectional analytical study designed to determine the Calcium, Inorganic phosphate and Uric acid levels in Diabetes mellitus subjects in Ekpoma and its environs.

Population of study: The population of this study comprised of ninety (90) individuals comprising of forty-five (45) Diabetes mellitus subjects and forty-five (45) non-diabetes mellitus subjects (control) in Ekpoma and environs, Edo State, Nigeria.

Diabetes mellitus subjects in Ekpoma and environs who gave their consent were included in this study. The patients who suffered from Type 2 diabetes mellitus with the acute complications of diabetes mellitus, those with a history of acute infections and other ailments like gross congestive heart failure, tuberculosis, gout, rheumatoid arthritis and skeletal muscle injury and renal failure and those who were on hypoglycaemic drugs and on insulin therapy were excluded from the study.

Sample Collection: Five mililitres (5.0mls) of blood sample was collected from fasting subjects via venipuncture and divided into two parts. One part (3ml) was dispensed into a plain container without any additive for the determination of Uric acid, Calcium and Inorganic phosphate. The sample was allowed to stand for one hour to clot. It was then centrifuged at 3000g for 10 min in order to separate blood cells and suspended particles from serum. The serum was aliquoted and stored at 40c until required for analysis. The remaining 2ml of blood was dispensed into fluoride oxalate anticoagulant bottle for estimation of fasting blood sugar.

Sample Analysis

Fasting Blood Sugar: The fasting blood sugar was determined using Glucose oxidase method (Megazyme, 2018).

Uric Acid: The uric acid estimation was done using uricase method.

Estimation of Calcium: Calcium was estimated using the method.

Estimation of Inorganic Phosphate: The method employed was based on the method.

Data management and Analysis: Information was extracted using a data collection sheet designed for the purpose. The data were coded and analysed using statistical package for social sciences (SPSS) version 21.0. This consisted of initial univariate and bivariates analyses, and then multivariate logistics regression analysis to identify the independent determinant of abnormal semen parameters in male infertility. Test of statistical significance was based on 95% confidence interval and $p<0.05$ using chi square test with fisher exact correction where applicable.

RESULT

Fasting blood sugar, Uric acid, Calcium and Inorganic phosphate of Diabetes mellitus subjects and control subjects

Table 1 showed the Fasting blood sugar (FBS), Uric acid (UA), Calcium (Ca) and Inorganic phosphate (PO4) of Diabetes mellitus subjects and control subjects. The results obtained in mean ± standard deviation showed that BMI (kg/m2) of the subjects and control was 27.20±2.79 and 21.20±2.60, FBS (mg/dl) was 239.77±36.64 and 87.53±11.29, Calcium (mmol/L) was 7.41±0.72 and 8.89±0.57, Uric acid (mg/dl) was 5.46±1.29 and 5.09±1.12, and Inorganic phosphate (mmol/L) was 4.73±1.05 and 3.19±0.57 respectively. Fasting blood sugar and Uric acid were higher in Diabetes mellitus subjects compared with control, however, only FBS was significant ($p<0.05$). Calcium and Inorganic phosphate were significantly lower ($p<0.05$) in Diabetes mellitus subjects compared with control group.

Table 1: Fasting blood sugar, Uric acid, Calcium and Inorganic phosphate of Diabetes mellitus subjects and control subjects

Parameters	Control n=45	Diabetes mellitus Subjects n=45	t-value	p-value
BMI (kg/m^2)	21.20±2.60	27.20±2.79	8.574	0.000
FBS (mg/dl)	87.53±11.29	239.77±36.64	22.642	0.000
UA (mg/dl)	5.09±1.12	5.46±1.29	1.204	0.238
PO_4 (mmol/L)	3.19±0.57	4.73±1.05	6.479	0.000
Ca (mmol/L)	8.89±0.57	7.41±0.72	5.958	0.000

***Values are significant at $p<0.05$**

Key: **FBS** = Fasting Blood Sugar; **PO_4** = Inorganic phosphate; **Ca** = Calcium; **UA** = Uric acid; N = Sample size

Fasting blood sugar, Uric acid, Calcium and Inorganic phosphate of Diabetes mellitus subjects with respect to gender

Table 2 showed the Fasting blood sugar (FBS), Uric acid, Calcium and Inorganic phosphate of Diabetes mellitus subjects with respect to gender. The results obtained in mean ± standard deviation showed that the FBS (mg/dl) of male and female subjects was 243.85±34.54 and 230.64±36.25, Uric acid (mg/dl) was 6.11±1.42 and 4.90±0.89, Inorganic phosphate (mmol/L) was 4.87±0.61 and 4.51±1.39, and Calcium (mmol/L) was 7.65±0.74 and 7.98±0.73 respectively. There was significant difference ($p<0.05$) in the Uric acid of male subjects compared with female subjects, but there was no significant difference ($p>0.05$) in FBS, Calcium and Inorganic phosphate of male subjects compared with female subjects.

Table 2: Fasting blood sugar, Uric acid, Calcium and Inorganic phosphate of Diabetes mellitus subjects with respect to gender

Parameters	Male n=23	Female n=22	t-value	p-value
FBS (mg/dl)	243.85±34.54	230.64±36.25	0.896	0.387
UA (mg/dl)	6.11±1.42	4.90±0.89	2.332	0.036

PO_4 (mmol/L)	4.87±0.61	4.51±1.39	0.817	0.428
Ca (mmol/L)	7.65±0.74	7.98±0.73	-1.249	0.234

Key: **FBS** = Fasting Blood Sugar; **PO_4** = Inorganic phosphate; **Ca** = Calcium; **UA** = Uric acid; N = Sample size

Fasting blood sugar, Uric acid, Calcium and Inorganic phosphate of Diabetes mellitus subjects with respect to age

Table 3 showed the fasting blood sugar (FBS), Uric acid, Calcium and Inorganic phosphate of Diabetes mellitus subjects with respect to age. The results obtained in mean ± standard deviation showed that the FBS (mg/dl) of the subjects in age group 40-50 years, 51-60 years and 61 – 70 years were 216.82±14.78, 244.45±41.43 and 284.60±20.30, Uric acid were 5.08±1.17, 5.58±1.57 and 5.86±0.82, Inorganic phosphate were 4.66±1.47, 4.65±0.83 and 5.24±0.62, and Calcium were 8.50±0.28, 7.44±0.63 and 7.26±0.47 respectively. There was significant difference ($p<0.05$) in FBS, Inorganic phosphate and Calcium of the subjects with respect to age, but Uric acid did not differ significantly ($p>0.05$).

Table 3: Fasting blood sugar, Uric acid, Calcium and Inorganic phosphate of Diabetes mellitus subjects with respect to age

Parameters	40–50 years n=18	51–60 years N=16	61–70 years n=11	F-value	p-value
FBS (mg/dl)	$216.82±14.78^a$	$244.45±41.43^b$	$284.60±20.30^c$	8.577	0.001
UA (mg/dl)	$5.08±1.17^b$	$5.58±1.57^b$	$5.86±0.82^b$	1.568	0.192
PO_4 (mmol/L)	$4.66±1.47^c$	$4.65±0.83^c$	$5.24±0.62^b$	3.469	0.026
Ca (mmol/L)	$8.50±0.28^d$	$7.44±0.63^d$	$7.26±0.47^c$	6.195	0.003

***Values in a row with different superscript is significant at $p<0.05$**

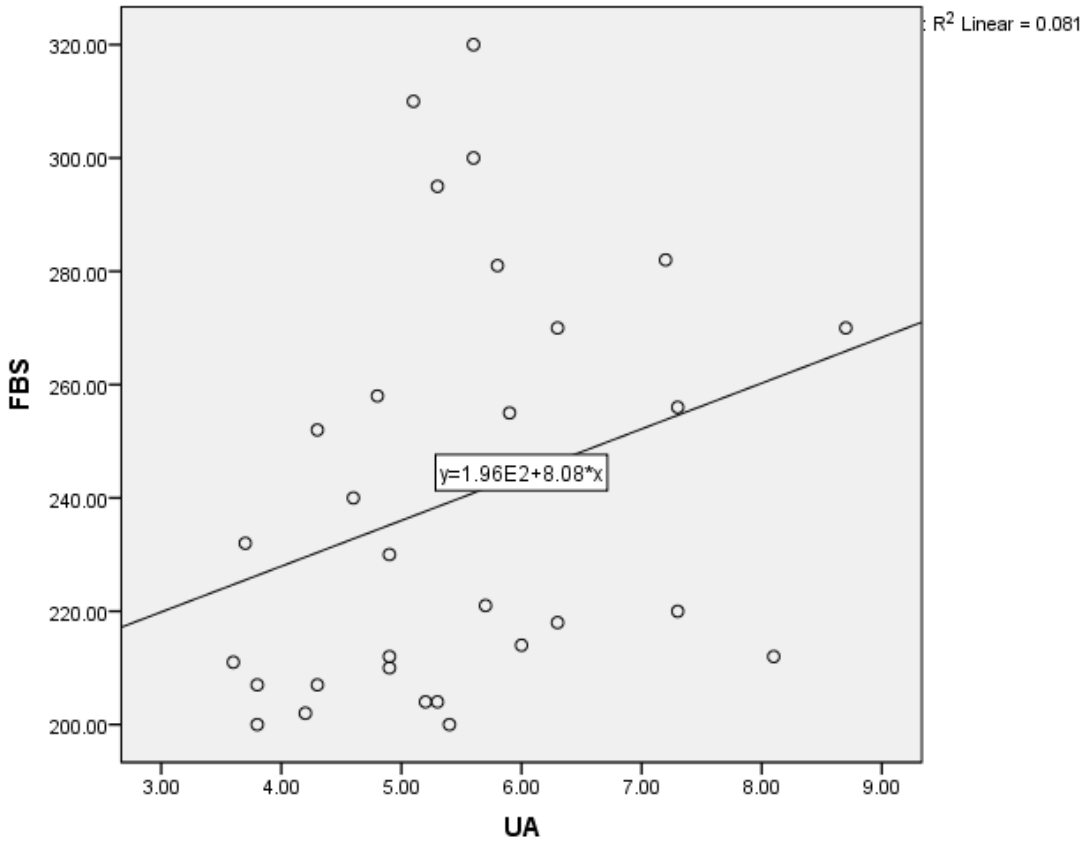

Figure 1: Scattered plot showing Pearson Correlation between plasma FBS levels and Uric acid (UA) levels in Diabetes mellitus subjects. There was a positive correlation between plasma Fasting blood sugar (FBS) and serum Uric acid (UA) levels in Diabetes mellitus subjects (Pearson correlation = 0.284) which was insignificant (p=0.128).

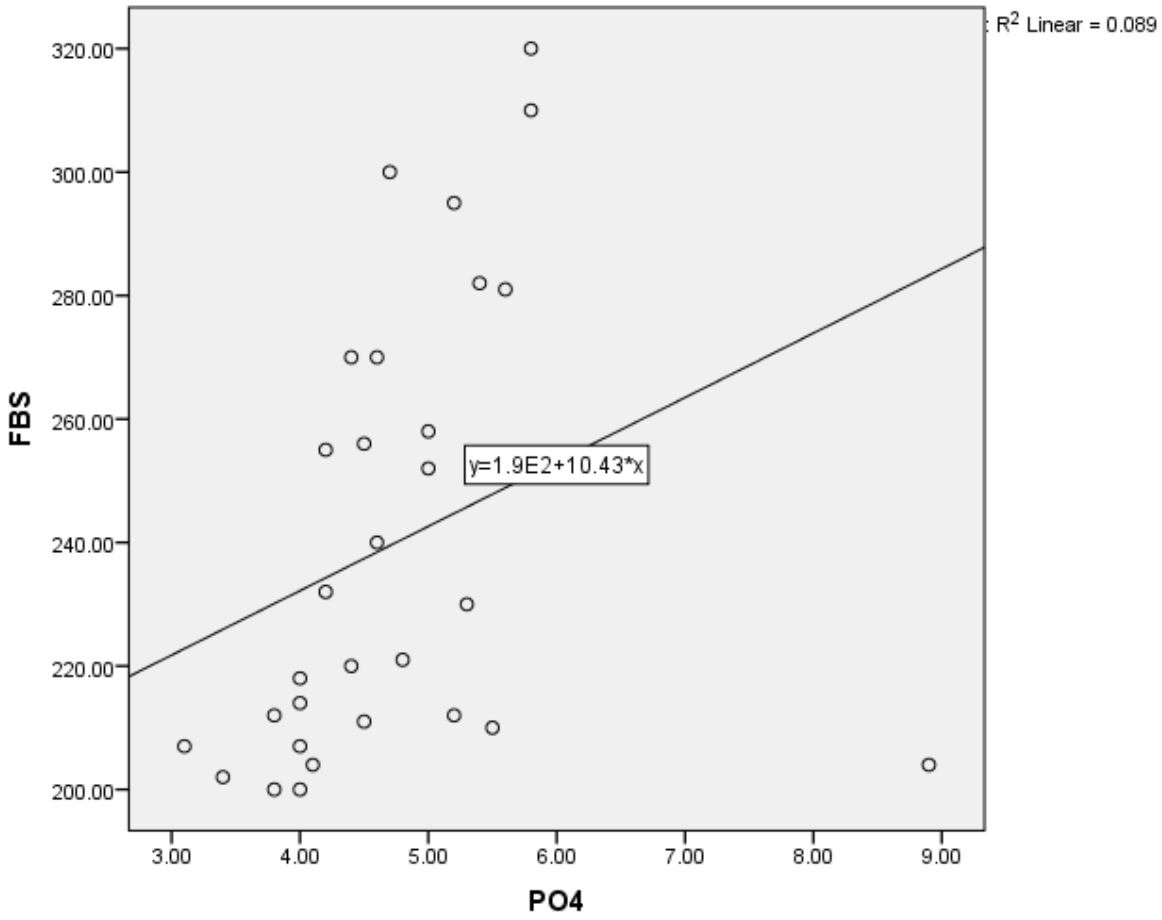

Figure 2: Scattered plot showing Pearson Correlation between plasma FBS levels and Inorganic phosphate (PO_4) levels in Diabetes mellitus subjects. There was a positive correlation between plasma Fasting blood sugar (FBS) and serum Inorganic phosphate (PO_4) levels in Diabetes mellitus subjects (Pearson correlation = 0.299) which was insignificant (p=0.108).

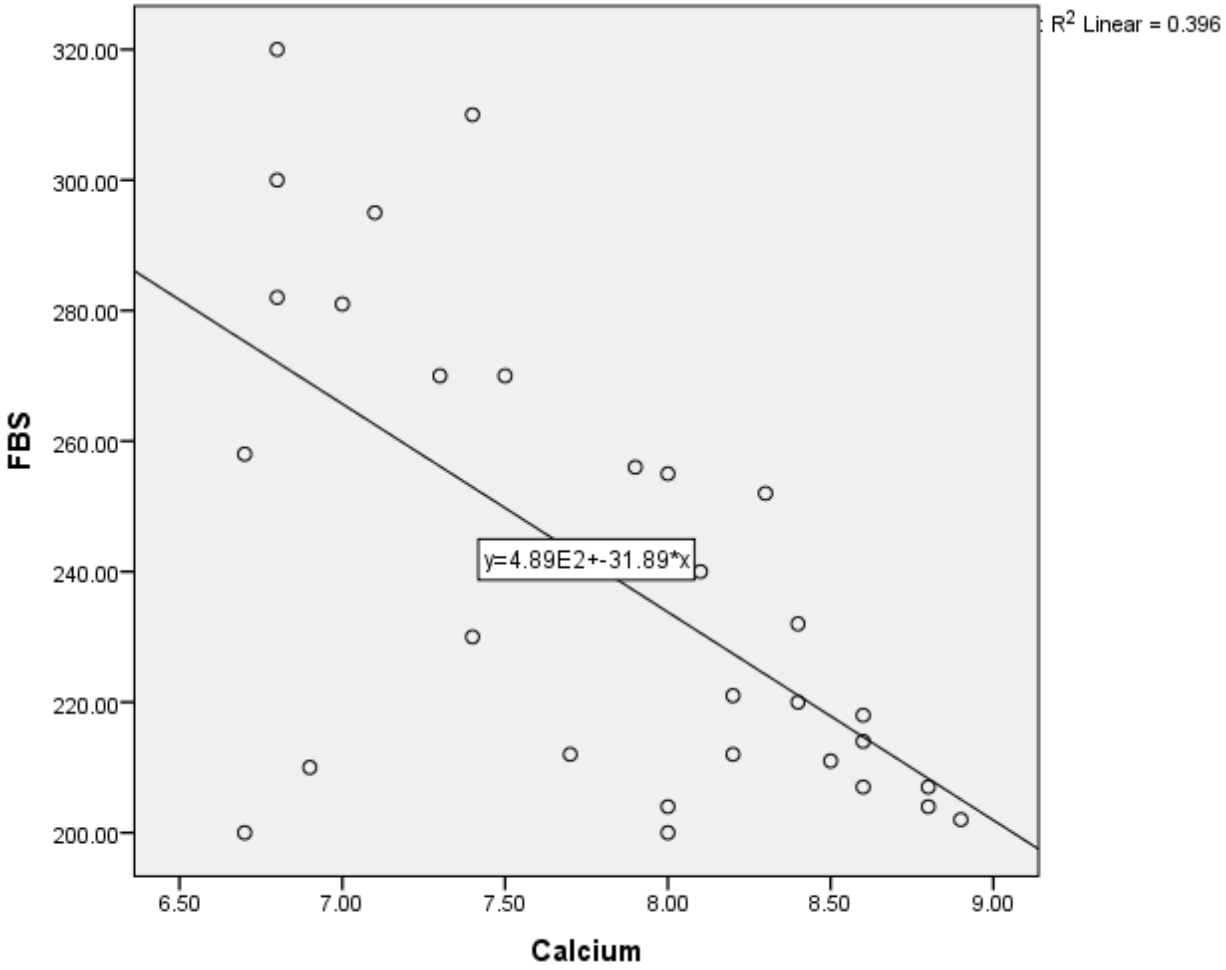

Figure 3: Scattered plot showing Pearson Correlation between plasma FBS levels and Calcium levels in Diabetes mellitus subjects. There was a negative correlation between plasma Fasting blood sugar (FBS) and serum Calcium levels in Diabetes mellitus subjects (Pearson correlation = -0.629) which was significant (p=0.000).

Relationship between Fasting blood sugar, Uric acid, Calcium and Inorganic phosphate of Diabetes mellitus subjects using Pearson correlation

The results obtained showed that FBS had non-significant positive correlation with Uric acid (p=0.128) and Inorganic phosphate (p=0.108), but have significant negative correlation with Calcium (p=0.000). Uric acid had non-significant positive correlation with Inorganic phosphate (p=0.457) and non-significant negative correlation with Calcium (p=0.141), while Inorganic phosphate had significant negative correlation with Calcium (p=0.022).

Table 4: Relationship between Fasting blood sugar, Uric acid, Calcium and Inorganic phosphate of Diabetes mellitus subjects using Pearson correlation

		FBS	Uric acid	Inorganic phosphate	Calcium
FBS	Pearson Correlation		0.284	0.299	-0.629**
	Sig. (2-tailed)		0.128	0.108	0.000
	N		45	45	45
Uric acid	Pearson Correlation	0.284		0.141	-0.275
	Sig. (2-tailed)	0.128		0.457	0.141
	N	45		45	45
Inorganic phosphate	Pearson Correlation	0.299	0.141		-0.416*
	Sig. (2-tailed)	0.108	0.457		0.022
	N	45	45		45
Calcium	Pearson Correlation	-0.629**	-0.275	-0.416*	
	Sig. (2-tailed)	0.000	0.141	0.022	
	N	45	45	45	

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

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

Discussion

In Nigeria, diabetes mellitus is one of the most common non-communicable diseases known to have a multi-systemic effect. Diabetes mellitus is said to affect the renin-angiotensin system which ultimately elevate the blood pressure of the individuals (Adu, 2022). This study was carried out to determine the Calcium, Uric acid and inorganic phosphate levels of Diabetes mellitus subjects in Ekpoma and environs. In this study, Diabetes mellitus subjects had significantly ($p<0.05$) higher fasting blood sugar when compared with apparently healthy subjects. There was no gender difference ($p>0.05$) in FBS of diabetes mellitus subjects but age difference existed ($p<0.05$). This is in tandem with the previous work by Momin *et al*. (2013), Raikou *et al.* (2020) and Adu (2022) which reported similar results in their study. Glucose has been accepted as a standard biomarker of diabetes mellitus.

This study observed that diabetes mellitus had non-significantly ($p>0.05$) higher uric acid when compared with apparently healthy subjects in this study. This is in line with earlier report by earlier authors (Dehghan *et al*., 2008; Adebisi *et al*., 2009; Adu, 2022) that did similar work on diabetes mellitus subjects. The higher uric acid concentration observed among diabetes mellitus may be due to the presence of hyperinsulinaemia as well as insulin resistance in diabetes mellitus subjects. Hyperinsulinemia has been observed to increase the activation of the hexose phosphate shunt, which promote the biosynthesis and transformation of purine, and ultimately increase the rate of uricogenesis (Adu, 2022).

There was no significant age difference ($p>0.05$) in the uric acid level of diabetes mellitus subjects, however, uric acid was significantly higher ($p<0.05$) in male subjects compared with female subjects. There was a positive correlation between uric acid and fasting blood sugar. This result is in agreement with the earlier work of Facchini *et al*. (1991), Dehghan *et al*. (2008), Alam *et al*. (2015) and Adu (2022) which did similar study on uric acid. This implies that fasting blood sugar increases with concomitant increase in uric acid. Glycosylated haemoglobin has been identified as glycemic biomarker by earlier authors (Alam *et al.*, 2015). Thus, uric acid can be accorded similar function as glycosylated haemoglobin because they are directly proportional as elucidated above (Adu, 2022).

The results from this study showed that serum calcium levels were significantly reduced ($p<0.05$) in subjects with Diabetes mellitus compared to normal subjects. This finding resonates with reports by several researchers elsewhere, who also found a significant reduction in the mean serum calcium levels of their DM subjects compared to non-DM subjects/controls (Najeeb, Aziz & Hamid, 2014; Safaa *et al.*, 2016; Marshnil & Mythili, 2018) but differs from that reported by Yousif and Ahmed (2014) who found no mean difference in the level of serum calcium between individuals with diabetes and normoglycemic participant. They attributed their finding to the relative availability of dietary calcium sources and partial control of hyperglycemia in their participants with DM, as studies have suggested that calcium optimization lessens the symptoms of DM and may even reduce the risk of developing T2DM in adults (Ahn *et al.*, 2017).

This decrease in serum calcium levels may be attributed to a number of factors. First, there is a heightened urinary loss of calcium as a result of hyperglycemia, which has been described by Sultan, Taha and Saber (2008) and this urinary calcium loss has been found to be proportional to the degree of glycosuria. In addition, volume depletion, which is common among T2DM subjects, may induce varying degrees of renal impairment, resulting in poor excretion of phosphorus and ultimately, high phosphate levels. The high level of phosphorous then accumulates and avidly binds ionized calcium in the blood, resulting in hypocalcemia (Ahn *et al.*, 2017). Furthermore, overtime, there is a gradual reduction in the secretion of PTH, (an effect mediated by hypomagnesemia – commonly seen in patients with diabetes), which may subsequently contribute to the disruption in calcium homeostasis, with resultant hypocalcemia (Ahn *et al.*, 2017).

There was no significant gender difference ($p>0.05$) in Calcium of diabetes mellitus subjects, but there was significant age difference ($p<0.05$). There was a negative correlation between plasma Fasting blood sugar (FBS) and serum Calcium levels in Diabetes mellitus subjects which was significant ($p=0.000$). This result is in agreement with some earlier reports elsewhere (Kanachana & Saikumar, 2014; Safaa *et al.*, 2016; Ahn *et al.*, 2017). In contrast, Yamaguchi *et al*. (2011) reported a positive correlation between serum calcium and fasting plasma glucose in men ($P\leq0.5$) but not in women. It is not clear why their finding was only positive for men. HbA1c is known to reflect the average glycemia over a 3-month period, and fasting plasma glucose only gives the current glycemic level at the time of measurement. The fact that Yamaguchi *et al*. (2011) used fasting plasma glucose in their study may also account for the difference found in their result because fasting plasma glucose does not represent effectively, long-term control of glycemia.

Inorganic phosphate were significantly lower ($p<0.05$) in Diabetes mellitus subjects compared with control group. This finding is in tandem with report from previous study reporting the same trend (Fang & Li, 2016). A previous study which included 162 patients with type 2 DM vs 82 hospitalized non-DM patients showed that serum P levels were lower in type 2 DM, due to the disturbance in metabolism (Fang & Li, 2016). Studies have shown that disturbances in the metabolism of inorganic phosphate in diabetes lead to early functional microvascular changes in the retina and kidneys (Ditzel & Lervang, 2010). Furthermore, the homeostatic function of the kidney is suboptimal in diabetics, because elevated blood glucose concentrations depolarize the brush border membrane for phosphate reabsorption, leading to a lack of intracellular phosphate and hyperphosphaturia with consequent hypophosphatemia (Girindra, Rashmi, Sanjeeb & Sushma, 2016).

Dietzel & Lervang (2010) found that maximal capacity of renal tubular reabsorption of phosphate/L of filtrate were significantly suppressed in diabetic patients and also reported that urinary phosphate excretion was three times higher in diabetic patients when compared to healthy controls this is in concordance with our study showing low phosphate levels in diabetic patients (Ditzel & Lervang, 2010). In contrast, Raikou *et al.* (2020) did not observe reduced serum inorganic phosphate in the diabetic group compared with the non-DM group. This discrepancy may be attributed to the fact that 69.1% of their subjects had low renal function defined by an eGFR less than 60 mL/min/1.73 m^2. The elimination of inorganic phosphate depends on renal function, thus a positive inorganic phosphate balance occurs in the early stage of renal dysfunction, although serum inorganic phosphate levels mainly increase in advanced stages of CKD and remain elevated in patients in the end stage of renal disease without dialysis treatment (Raikou *et al.*, 2020).

There was no significant gender difference ($p>0.05$) in inorganic phosphate of diabetes mellitus subjects, but there was significant age difference ($p<0.05$). There was a positive correlation between plasma Fasting blood sugar (FBS) serum Inorganic phosphate (PO_4) levels in Diabetes mellitus subjects (Pearson correlation = 0.299) which was insignificant ($p=0.108$). Our findings are in agreement with those of the previous study regarding the diabetic patients (Fang & Li, 2016; Raikou *et al.*, 2020). Fang and Li (2016) reported a positive correlation between serum glucose and serum inorganic phosphate in non-diabetics (n = 82), although in the type 2 diabetic group (n = 162) this correlation was found to be non-significant which is in line with our study. In contrast, Raikou *et al.* (2020) observed a positive correlation in all our subjects, but not separately in non-diabetics (n = 81) or diabetics (n = 29).

Conclusion

In conclusion, fasting blood sugar and Uric acid were higher in Diabetes mellitus subjects compared with control, however, only FBS was significant ($p<0.05$). Calcium and Inorganic phosphate were significantly lower ($p<0.05$) in Diabetes mellitus subjects compared with control group. There was significant difference ($p<0.05$) in the Uric acid of male subjects compared with female subjects, but there was no significant difference ($p>0.05$) in FBS, Calcium and Inorganic phosphate of male subjects compared with female subjects. There was significant difference ($p<0.05$) in FBS, Inorganic phosphate and Calcium of the subjects with respect to age, but Uric acid did not differ significantly ($p>0.05$). There was a positive correlation between plasma FBS and serum Inorganic phosphate (PO_4), and between FBS and Uric acid levels, but a negative correlation existed between plasma FBS and serum Calcium levels in Diabetes mellitus subjects.

Uric acid should be considered as additional biomarker in the evaluation of diabetes mellitus. Oral supplementation of all calcium and other minerals other than diet is recommended in Type-2 diabetes. Further studies focused on the relationship between bone mineralization and insulin therapy in patients with diabetes mellitus are necessary to detect osteopenia and prevent the development of osteoporosis later in life.

Ethical Approval and Informed Consent

Ethical approval for the collection of sample was obtained from the Ethics and Review Committee, Ambrose Alli University, Ekpoma, Edo State. Informed consent was also obtained from each subject who participated in the study before the collection of blood sample.

Conflict of Interest
The authors declare no conflicts of interest. The authors alone are responsible for the content and the writing of the paper.

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Authors' Contributions
The entire study procedure was conducted with the involvement of all authors.

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References

Adebisi, S.A., Oghagbon, E.K., Akande, T.M. & Olarinoye, J.K. (2009). Glycated haemoglobin and glycemic control of diabetics in Ilorin. *Nigerian Journal of Clinical Practice*, 12(1), 87-91.

Adu, M.E. (2022). Correlation of serum uric acid with glycemic indices of diabetes mellitus subjects. *Nigerian Journal of Biochemistry and Molecular Biology*, 37(1), 82-86

Ahn, C., Kang, J.H. & Jeung, E.B. (2017). Calcium homeostasis in diabetes mellitus. *Journal of Veterinary Science*, 18 (9), 261-266.

Alam, R., Verma, M.K. & Verma, P. (2015). Glycated hemoglobin as a dual biomarker in type 2 diabetes mellitus predicting glycemic control and dyslipidemia risk. *International Journal of Life-Sciences Scientific Research*, 1 (2), 62-65.

American Diabetes Association (2018). Standards or medical care in diabetes-2018. *Diabetes Care*, 41 (1), 1-2.

Dehghan, A., Hoek, M., Sijbrands, E.J., Hofman, A. & Witteman, J.C. (2008). High serum uric acid as a novel risk factor for type 2 diabetes. *Diabetes Care*, 31(2), 361–362.

Ditzel, J. & Lervang, H.H. (2010). Disturbance of inorganic phosphate metabolism in diabetes mellitus: Clinical manifestations of phosphorus-depletion syndrome during recovery from diabetic ketoacidosis. *Diabetes Metabolic Syndrome & Obesity*, 3 (1), 319-24.

Facchini, F., Chen, Y.D., Hollenbeck, C.B. & Reaven, G.M. (1991). Relationship between resistance to insulin-mediated glucose uptake, urinary uric acid clearance, and plasma uric acid concentration. *The Journal of the American Medical Association*, 266(21), 3008–3011.

Fang, L. &, Li X. (2016). Level of serum phosphorus and adult type 2 diabetes mellitus. *World Journal of Diabetes*, 5 (1), 132-135.

Gale, E.A. & Anderson, J.V. (2017). Diabetes mellitus. In: Kumar P, Clark M, editors. Kumar and Clark's Clinical Medicine, 9th ed. Edinburg: Saunders Elsevier, Pp. 1241-1279.

Girindra, K.B., Rashmi, R., Sanjeeb, K. & Sushma, Y. (2016). Serum inorganic phosphate concentration and glycated hemoglobin percent in type 2 diabetes mellitus – A hospital based study. *International Journal of Health Science & Research*, 6 (1), 96-104.

Kanachana, N. & Saikumar, P. (2014). Serum calcium levels in type 2 diabetes mellitus. *Journal of Dental & Medical Science*, 13 (1), 1-3.

Kertes, P.J. (2013). Evidence based eye care. Philadelphia. Lippincott Williams and Wilkins, Pp. 448

Levy, M.J. & Gleenson, H. (2017). Endocrine diseases. In: Kumar P, Clark M, editors. Kumar and Clark's Clinical Medicine. 9th ed. Edinburg: Saunders Elsevier; Pp. 1175-240.

Longo, D.L., Fauci, A.S., Kasper, D.L., Hauser, S.L., Jameson, J. & Loscalzo, J. (2012). Bone and mineral metabolism in health and diseases. In: Harrison's Principles of Internal Medicine. 18th ed. United States of America: New York, NY: McGraw-Hill, Pp. 204-206.

Marshnil, R.W. & Mythili, C. (2018). Correlation of serum calcium levels with glycated haemoglobin in type 2 diabetes mellitus patients – A comparative study. *International Journal of Science Research*, 7 (1), 1-6.

Megazyme, A.P. (2018). Glucose Oxidase Assay Procedure. In: Bray Business Park, Bray, Ireland, Pp. 1-8.

Momin, A.A., Bankar, M.P. & Bhoite, G.M. (2013). Glycosylated hemoglobin (HbA1C): association with dyslipidemia and predictor of cardiovascular diseases in type 2 diabetes mellitus patients. *International Journal of Health Science Research*, 3(8), 40-46.

Najeeb, Q., Aziz, R. & Hamid, S. (2014). To evaluate the levels of glycated haemoglobin, serum calcium, magnesium, phosphorus, uric acid and microalbuminaemia in patients with newly diagnosed type 2 DM. *International Journal of Research in Medical Science*, 2 (1), 1462-1465.

Raikou, V.D., Kyriaki, D. & Gavriil, S. (2020). Importance of serum phosphate in elderly patients with diabetes mellitus. *World Journal of Diabetes,* 11 (10), 416-424.

Safaa, A.E., Wigan, A.R., Nazik, I.A. & Nabiela, M.E. (2016). Serum calcium levels in correlation with glycated haemoglobin in type 2 diabetic Sudanese patients. *Advances in Diabetes Metabolism*, 4 (1), 59-61.

Sigrist, M., Tang, M., Beaulieu, M., Espino-Hernandez, G., Er, L., Djurdjev, O. & Levin, A. (2013). Responsiveness of FGF-23 and mineral metabolism to altered dietary phosphate intake in chronic kidney disease (CKD): results of a randomized trial. *Nephrology*, 18 (3), 161-169.

Sluijs, I., Beulens, J.W.J, van der, D.L., Spijkerman A.M.W., Schulze, M.B. & Van Der, S.Y.T. (2013). Plasma uric acid is associated with increased risk of type 2 diabetes independent of diet and metabolic risk factors. *The Journal of Nutrition*, 143(1), 80–85.

Sultan, E., Taha, I. & Saber, L.M. (2008). Altered bone metabolic markers in type 2 diabetes mellitus: Impact of glycaemic control. *Journal of Taibah University of Medical Science*, 2 (2), 104-106.

Toussaint, N.D., Pedagogos, E., Tan, S.J., Badve, S.V., Hawley, C.M., Perkovic, V. & Elder, G.J. (2012). Phosphate in early chronic kidney disease: associations with clinical outcomes and a target to reduce cardiovascular risk. *Nephrology*, 17 (5), 433-444.

Uloko, A.E, Musa, B.M, Ramalan, M.A, Gezawa, I.D, Puepet, F.H, Uloko, A.T, Borodo, M.M. & Sada, K.B. (2018). Prevalence and risk factors for diabetes mellitus in Nigeria: a systematic review and meta-analysis. *Diabetes Therapy*, 9 (3), 1307–1316

Xue, B., Tan, J.B., Ning, F., Sun, J.P., Zhang, K.Y., Liu, L., Wang, S.J., Zhang, D.F., Qiao, Q. & Pang, Z.C. (2015). Association between serum uric acid and prevalence of type 2 diabetes diagnosed using HbA1c criteria among Chinese adults in Qingdao, China. *Biomedical and Environmental Sciences*, 28 (12), 884– 893.

Yamaguchi, T., Kanazawa, I., Takaoka, S. & Sugimoto, T. (2011). Serum calcium is positively correlated with fasting plasma glucose and insulin resistance, independent of parathyroid hormone, in male patients with type 2 diabetes mellitus. *Metabolism*, 60 (5), 1334-1339.

Yousif, A.A. & Ahmed, S.O. (2014). Estimation of Serum Calcium and Phosphorus Levels in Sudanese Patients with Type 2 Diabetes Mellitus. Sudanese University of Science and Technology (BSc Dissertation); Pp. 51-68.