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Analysis of Fasting Urine pH as a Predictor of Insulin Resistance in Type 2 Diabetes Mellitus

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ABSTRACT

Background and aim: Recent research articles suggest that a low urine pH related to more complications in type 2 diabetes mellitus. Our aim was to study of insulin resistance in type 2 diabetes patients using homeostasis model assessment and analysis of fasting urine pH as a predictor of insulin resistance in type 2 diabetes.

Materials and methods: This prospective study was conducted in our hospital with type 2 diabetes mellitus patients during the period 2019 to 2020. A total of 102 patients have been taken for the study. Participants were isolated into two groups with urine pH <5.5 and the group with urine pH ≥ 5.5. We then further investigated the association between low urine pH levels and insulin resistance. Descriptive data were shown as the mean value of (Standard error) or number (%). The unpaired two sample t-test was used for analysis of continuous variables and the Chi-square test used for estimation of categorical variables.

Results: Participants with urine pH <5.5 have high fasting blood glucose , HOMA IR index ,high triglycerides (P values <0.0001,P values <0.04, and P values <0.001 respectively) whereas patients with urine pH >5.5 have strong positive association with lower triglycerides levels and better glycemic control indicated by low HbA1C(P values <0.001,P values <0.0001 respectively). A significant inverse relationship was observed between urine pH levels and the extent of insulin resistance

Conclusion: These observational findings concluded that fasting low urine pH can be used as simple, noninvasive, and easily available tool to estimate insulin resistance.

Key words: Diabetes, Urine pH, HOMA IR, HbA1C

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INTRODUCTION

Among the existing endocrine disorders, diabetes is the most prevalent. Statistics show that over 160 million people worldwide suffer this chronic disease, and projections state that by 2030, over 364 million patients will be victims of this disease [1]. Apart from β cell malfunctioning, there are other physiological connections to the progression of type II diabetes mellitus disease, an aversion to insulin molecule by the target tissues, resulting from the abnormal secretion of insulin. Glucose homeostasis is majorly regulated by insulin in the body. To establish insulin resistance, environmental and genetic factors should be taken into consideration [2,3]. Insulin resistance contributes to imbalanced glucose tolerance and plays a vital role in the progression of diabetes mellitus. Therefore, insulin resistance is a condition provided by a large amount of insulin needed to acquire a normal quantitative response [4]. In the pathogenesis, measuring insulin has advanced the process of playing a fundamental task. Maalouf et al. proved that a remarkable characteristic of a renal behavior of insulin resistance is the decrease in urinary pH [5].

The metabolic conditions such as obesity, hypertension, dyslipidemia, insulin resistance combined express the characteristics of metabolic syndrome that advances the chances of developing cardiovascular disease, renal diseases, and type II diabetes mellitus [6,7,8]. Statistics show that 20-30% of adults in most countries manifest metabolic syndrome [9]. Due

to various biological experiments, the Gamma-Glutamyl Transferase (GGT) and Homeostatic Model Assessment Insulin Resistance Index (HOMA-IR) are majorly associated with metabolic syndrome. Moreover, some researchers have established a connection between insulin resistance with diabetes mellitus and obesity with unduly acidic urine with a pH of less than 5.5, which are the renowned components of metabolic syndrome [10-12]. Recently, a group of researchers published a report which states that a decrease in the pH of urine falls under predictive and causative factors for the enhancement of metabolic syndrome [13]. Other studies also reported an indirect correlation between the number of metabolic syndromes and urine pH [14]. Therefore, the primary objective of this study will find the relationship between insulin resistance and low urine pH in type II diabetes mellitus patients.

METHODS AND MATERIALS

The subjects used in this study were type II diabetes mellitus patients picked at random in our facility in 2019. The total number of patients who responded to the survey was 102. A written consent translated to every patient's local dialect was administered to them, where they all signed to authenticate the study. The subjects were mostly diabetic adults aged between 30-60 years who had live with the condition for less than 20 years. The subjects had the following diseases were not taken, dehydration, bladder dysfunction, nephrolithiasis, intrinsic renal disease, hyperuricemia, respiratory and metabolic acidosis. The subjects who had lived with the condition for more than 20 years were exempted from the study—the subjects issued with a fixed meal plan provided by the hospital in 24 timing duration. From the cubital vein, three milliliters of blood were drawn after fasting for 12 hours. After that, the urine pH was tested using pH Electrodes. The standard procedures were carried out to determine biological parameters for this study. The study involved using glucose oxides to determine the glucose level in the commercial kit test. Fasting insulin levels and glucose levels were employed to measure the homeostasis model assessment for insulin resistance using the formula provided.

HOMA-IR=Fasting glucose (mmol/l) 22.5*Fasting insulin (μIU/ml).

Statistical analysis

In expressing the mean value (standard error), descriptive statistics were used to represent the average in percentage form. The unpaired t-test test statistic was utilized to analyze the continuous variables and chi-square test for categorical variables. In determining the sociodemographic parameters, general characteristics, and anthropometric parameters of the patients who tested below 5.5 pH values, and those with above were taken and classified into two categories. Then, the biochemical results were analyzed compared to the variables using the chi-square test and t-test statistic. After that, several logistic regressions were used to examine the patients' relative risk factors of the patients whose urine tested below 5.5 pH. Values and those whose pH urine values tested above 5.5 Adjustments were made on parameters like age and sex for primary data analysis while smoking and drinking status of the individuals were categorized under the secondary category for further analysis. The significance level of this test was set at $P<0.05$.

RESULTS

Out of the 102 diabetic patients, 46 women and 56 men were examined in the study. Using the two ages represented in this study, the mean value was 51 years and 25.3kg/m^2 for the body mass index. From the results obtained, the level of fasting insulin levels, serum creatinine and HDL-C statistically insignificant for both genders ($P>0.05$). Features of the subject's variables using the urine pH ≥ 5.5 were related using parameters such as metabolic parameters, anthropometric, sociodemographic, and renal functions (Table 1).

When these variables were compared, the results showed no statistical relationship between the sex, age, smokers, and alcoholic groups as the P value obtained from the test statistics was >0.05. Study group with urine pH <5.5 showed high BMI which was statistically significant ($p<0.006$). It is important to note that there was no observable difference in the diastolic BP, ure, serum creatinine clearance and levels for the two groups ($p>0.05$). The HOMA-IR, and fasting glucose level of the participants with the urine pH ≥ 5.5 was less than for the patients who recorded urine pH< 5.5 ($P<0.04$ and $<P\leq0.0001$) respectively.

Table 1: Baseline characteristics by gender.

Variables	Males (n=56)	Females (n=46)	Total (n=102)	P Value Two tailed	Unpaired t test t value
Mean age (years)	54 ± 0.6	48 ± 0.8	51 ± 0.8	0.0001	6.11
BMI	24.2 ± 0.2	26.4 ±0.2	25.3 ±0.2	0.0001	7.7
Systolic BP	124 ±2	116 ± 2	120 ± 2	0.006	2.8
Diastolic BP	86 ± 2	80 ±2	83 ±2	0.0382	2.1
Fasting blood sugar	118 ± 2	102 ± 2	110 ± 2	0.0001	5.6
Fasting Insulin	10 ± 0.3	10.2 ± 0.2	10.1 ± 0.1	0.5975	0.52
Total cholesterol	198 ± 4	174 ± 4	186 ± 4	0.0001	4.2
LDL-C	146 ± 4	130 ± 2	138 ± 2	0.0011	3.3
HDL -C	42 ± 2	46 ±2	44 ± 2	0.164	1.4
Triglycerides	186 ± 4	142 ± 4	164 ± 4	0.0001	7.7
Urea	24 ± 0.2	22 ± 0.2	23 ± 0.2	0.001	7
Creatinine	0.9 ± 0.1	0.8 ± 0.1	0.85 ± 0.1	0.48	0.7

Table 2: Characteristics of study variables by urine pH and demographic parameters.

Variables	Urine pH <5.5 (n=58)	Urine PH >5.5 (n=44)	P Value	Chi-square and t value
Age years	48 ± 2	46 ± 2	0.48	t= 0.06
Males	32	22	0.92	Chi- square Values=0.009
Females	28	20		
Smokers	32	30	0.3	Chi- square Values=1.07
Non smokers	20	30		
Alcoholics	32	22	0.89	Chi- square Values= 0.017
Non alcoholics	30	18		
BMI	24.8 ± 0.2	24 ± 0.2	0.006	t=2.77
Systolic BP	126 ± 2	118 ± 2	0.006	t=2.77
Diastolic BP	84 ± 2	80 ± 2	0.16	t=1.3
Urea	22 ± 2	18 ± 1	0.1	t=2.6
Sr creatinine	0.9 ± 0.2	0.8 ± 0.1	0.489	t=0.69
Fasting blood glucose	116 ± 2	98 ± 2	0.0001	t=6.24
Fasting insulin	10.4 ± 0.2	10 ± 0.1	0.1	t=1.6
HOMA IR	2.7 ± 0.1	2.4 ± 0.1	0.04	t=2.08
Total cholesterol	194 ± 4	186 ± 4	0.16	t=1.3
LDL -C	130 ± 4	128 ± 4	0.72	t=0.34
HDL-C	38 ± 2	44 ± 2	0.04	t=2.08
Triglycerides	186 ± 4	140 ± 2	0.001	t=9.3
Hba1c	8.4 ± 0.2	7.4 ± 0.1	0.0001	t=4.06

LDL-C level inference, there was no statistical difference between the two groups, as the HDL-C recorded lower test result compared to the TG level with their P<0.001, which is less compared to the standard urine pH <5.5. At the same time HOMA IR index was higher in group with urine pH <5.5 and P<0.04. Comparatively, even the mean for HbA1c proved to be lower than the urine pH >5.5 in the subjects (p<0.0001).

DISCUSSION

A number of physiological and metabolic changes are involved in the Metabolic Syndrome, with various components, including abdominal obesity, hypertension, dyslipidemia and hyperglycemia clinically recognized [15]. This feature cluster is strongly associated with type 2 diabetes, coronary artery disease, and raised cardiovascular and all-cause mortality [16]. Recently, there was a link between low urinary pH (pH <5.5) and diabetes and insulin resistance [17]. Obesity, another metabolic syndrome feature, also has low urinary pH [18]. According to the results obtained in this study, urine pH <5.5 are therefore associated with most of the metabolic syndrome components. Production and excretion of ammonia buffer urine help in balancing the acidic and basic content of the urine. The parameters that proved statistically significant were the elevated TGs and fasting glucose levels. The subjects who had insulin resistance registered reduced production of ammonia forms the proximal tubules of kidney excretion. The acidic urine pH also due to increase absorption of sodium due to hyperinsulinemia [19]. The results obtained coincided with the previously done researches as there was a strong correlation between the low urine pH and

hyperglycemia presented in the study as well that the insulin resistance in participants was probably due to lower pH in their urine. Recently, a group of researchers suggested from Japan, and both showed that the incidence of metabolic syndrome in diabetes type 2 patients was due to reduced urine pH values [20]. Therefore, our most comprehensive study that can help determine the strong relation between urine pH and insulin resistance. A notable limitation for the study was that the urine samples used were collected on the spot rather than 24-hour samples of urine. The assumption we made was that the spot urine correlated with the 24-hour urine samples [21]. The best approach to measure urine pH is by using the pH electrode as it is the simplest and noninvasive way to determine insulin resistance level.

CONCLUSION

This study's result proved that fasting low urine pH approach can be used to project the insulin resistance and metabolic syndrome among diabetic patients.

DISCLOSURE STATEMENT

There was no conflict of interest in this study.

ETHICAL COMMITTEE APPROVAL

The study was approved by institutional ethical committee.

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