Urinary PH as an Indicator of non-Alcoholic Fatty Liver Disease

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Abstract

Early discovery of NAFLD might be helpful to recognize those with possibly quiet reformist greasy liver malady. The point of the work is to explore the relationship between low pee pH and non-alcoholic greasy liver malady (NAFLD). This is a case control study, including 80 subjects isolated into two fundamental gatherings a solid benchmark group framed of 20 subjects without NAFLD shaped of 11 guys and 9 females with their ages went from 30 to 70 years, and an infected one shaped of 60 patients which partitioned into two subgroups: 30 diabetic patients framed of 16 guys and 14 females matured from 27 to 62 years, and 30 nondiabetic patients framed of 17 guys and 13 females matured from 34 to 70 years. all members were at that point going through mix of clinical, biochemical and imaging information to survey liver condition and glycemic state. Urinary PH was altogether lower in NAFLD cases than their controls, while 24 hours urinary proteins was higher among contemplated NAFLD cases yet not arrive at noteworthy level. affectability of urinary PH in discovery of NAFLD cases was 83.3% at cut-off 5.45, with capacity of avoidance of really negative cases without greasy liver by 37.6%. End: urinary pH can be utilized as a simple appropriate marker of essence of NAFLD, and it may help clinicians helpfully recognize patients at high danger of NAFLD in setting of mass screening of populace.

Keywords: Urinary PH, Non-Alcoholic, Fatty Liver.

1. Introduction

Nonalcoholic greasy liver illness (NAFLD) is a heterogeneous infection going from basic steatosis to nonalcoholic steatohepatitis (NASH) or hepatic fibrosis. The predominance of NAFLD has significantly expanded in the most recent years, being firmly identified with the corpulence pandemic [1].

Truth be told, it is assessed that roughly 25% of the populace overall is influenced by this condition, and NAFLD is presently the main source of constant liver infection. Its commonness in explicit gatherings, for example, patients with type 2 diabetes (T2D) or sullen corpulence is much higher, representing around 60 and 80% of these people, individually [2].

Albeit liver inclusion itself is significant and can prompt extreme grimness, just a couple of patients progress to cutting edge liver illness or liver-related passing. Subsequently, a hepatic-focused perspective could prompt oversight of different comorbidities which are frequently connected with this multisystemic malady and are fundamentally connected with its guess [3].

The pervasiveness of diabetes among the NAFLD and NASH patients is assessed to be 22.51% and 43.63%, separately, which is a lot higher than the commonness of diabetes in everybody (8.5%) [2].

It is firmly proposed that there is a complex bidirectional connection between the movement of NAFLD and the advancement of T2D, and their association could bring about an expansion in both hepatic and diabetic mortalities in patients with corresponding NAFLD and T2D [4].

As of late, a few investigations have indicated the relationship between pee pH and metabolic ailments: the 24-h pee pH is conversely connected with the weight record (BMI). Moreover, low pee pH is altogether connected with the midriff perimeter, homeostasis model appraisal of insulin obstruction (HOMAIR), fasting plasma glucose, hemoglobin A1c, fatty oils, high-thickness lipoprotein cholesterol, and metabolic disorder [5].

NAFLD was additionally connected with low pee pH in both genders, and the NAFLD pervasiveness essentially expanded as pee pH diminished. These outcomes were uncovered by Miyake et al., [6] which recommend that their discoveries may help clinicians advantageously recognize patients at high danger of NAFLD.

The point of the work is to research the relationship between low pee pH and non-alcoholic greasy liver infection (NAFLD).

2. Patients and methods

This study was performed in Internal Medicine Department inpatient ward and outpatient clinic in University hospital of Banha Egypt. This is a case control study including 80 subjects divided into two main groups a healthy control group formed of 20 subjects and a diseased one formed of 60 patients which is further subdivided into two equal subgroups diabetic and nondiabetic subgroups each has 30 patients who were selected from patients admitted inpatient ward, and in clinic unit during the period from August 2017 to January 2018.

2.1 Inclusion criteria

All participants were already undergoing combination of clinical, biochemical and imaging data to assess liver condition and glycemic state.

2.2 Exclusion criteria
- Patients less than 18 years.
- Patients who didn't give informed consent to participate in the study.

- Patient take any medication
- Patient take Ethanol and alcohol
- Patient with CKD or proteinuria
- Viral hepatitis C or B

Patients were allocated into two groups according to presence or absence of NAFLD as follows:

- **Group I:** 20 healthy subjects without NAFLD and deny exclusion criteria as a control group formed of 11 males and 9 females with their ages ranged from 30 to 70 years.
- **Group II:** 60 patients with proved NAFLD and denied exclusion criteria subdivided into two subgroups according to presence of DM.
- **Group IIa: 30** nondiabetic patients formed of 17 males and 13 females aged from 34 to 70 years.
- **Group IIb: 30** diabetic patients formed of 16 males and 14 females aged from 27 to 62 years.

All participants were subjected to:

- Full history taking focusing on history regarding data of smoking, alcohol habits and physical activity.
- Complete clinical examination and body weight and height were measured without shoes or heavy outer clothing for the calculation of the BMI (kg/m2). Blood pressure was measured using an automated sphygmomanometer while the subjects were in the seated position.
- Laboratory investigations: S. bilirubin, AST, ALT, total protein and S. albumin , S. creatinine and blood Urea , Fasting and post prandial blood glucose level, Urinary PH Midstream urine samples were collected in the morning and measured using dipstick testing, Lipid profiles Total cholesterol, LDL, HDL and Triglycerides, HbA1c.

- Abdomina US

Definition of NAFLD: Abdominal ultrasonography was performed on all participants by accredited medical technicians. Images were evaluated by a senior pathologist and gastroenterologist. NAFLD was diagnosed by the technician according to ultrasonography Liver brightness and liver contrast among the four known criteria (hepatorenal echo contrast, liver brightness, deep attenuation and vascular blurring) were used for diagnosing fatty liver [7].

2.3 Statistical analysis

Data were analyzed using IBM SPSS 23.0 for windows (SPSS Inc., Chicago, IL, USA) and NCSS 11 for windows (NCSS LCC., Kaysville, UT, USA). Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage. The following tests were done: Independent-samples t-test of significance was used when comparing between two means. Mann Whitney U test was used when comparing two means of not normally distributed data. Chi-square ($X2$) test of significance was used in order to compare proportions between two qualitative parameters. Fisher Exact test is a test of significance that is used in the place of chi square test in 2 by 2 tables, especially in cases of small samples.

3. Results

Regarding demographic and clinical data (age, sex, smoking and hypertension) there was no statistically significant difference among both cases and their controls except for BMI which showed significant increase in case group, Table (1).

Table (1) Demographic and clinical data of both studied groups.

Variables	Cases (N=60)		Controls (N=20)		t-test	P-value
Age (years)						0.37
Mean ±SD	46.5 ± 8.1		44.4 ± 11.2		0.895	NS
Body mass index						>0.001
Mean ± SD	26.9 ± 3.21		21.5 ± 2.52		4.54	S
	N	%	N	%	X^2	P-value
Sex						
Male	33	55	11	55	0.00	1.0
Female	27	45	9	45		NS
Smoking						
Smoker	17	28.3	5	25	0.083	0.77
Not	43	71.7	15	75		NS
Hypertension						
Yes	10	16.7	4	20	Fisher	0.73
No	50	83.3	16	80		NS

Total cholesterol, LDL and HDL levels were all higher among NAFLD cases, while TG level was not significantly higher among NAFLD cases Table (1).

Table (2) Difference in lipid profile among both studied groups.

Variables	Cases (N=60)	Controls (N=20)	t-test\ MW[#]	P-value
Cholesterol				
Mean ±SD	186.95 ± 28.9	158.1 ± 21.2	4.78	<0.001
Median	186	162		HS
Range	116-250	118-193		

Table (2) Continue

TG				
Mean ± SD	111.2 ± 52.3	85.3 ± 29.2	1.88[#]	0.06
Median	99	83		NS
Range	41-285	32-129		
LDL				
Mean ± SD	111.7 ± 12.6	69.2 ± 17.3	10.13	<0.001
Median	113	67		HS
Range	80-140	39-110		
HDL				
Mean ± SD	29.1 ± 11.7	48.5 ± 11.4	5.06[#]	<0.001
Median	29	49.5		HS
Range	4 -53	26-67		

HS: P-value<0.001 is high significant   NS: P-value>0.05 is not significant

Glycemic data (FBS, PPBS and Hb-A1c) levels were all higher among NAFLD cases Table (3).

Table (3) Difference in diabetic profile among both studied groups.

Variables	**Cases (N=60)**	**Controls (N=20)**	**t-test\ MW[#]**	**P-value**
FBS				
Mean ±SD	104.4 ± 31.4	78.62 ± 14.8	3.55	0.001
Median	94	82		S
Range	54-171	57-109		
PPBS				
Mean ± SD	198.4 ± 66.3	164.3 ± 22.4	2.2[#]	0.03
Median	188	162		S
Range	94-370	110-200		
HbA1c				
Mean ± SD	5.92 ± 1.01	5.27 ± 0.37	2.82	0.006
Median	5.85	5.35		S
Range	4.2-8.2	4.6-5.8		

S: P-value<0.05 is significant

Liver enzymes ALT and AST were significant higher in NAFLD group but   regarding creatinine level the groups matched Table (4).

Table (4) Difference in liver and kidney functions among both studied groups.

Variables	**Cases (N=60)**	**Controls (N=20)**	**t-test\MW[#]**	**P-value**
AST				
Mean ±SD	33.3±16	16.5 ± 8.4	4.145[#]	0.009
Median	21	16		S
Range	12- 42	3 – 30		
ALT				
Mean ± SD	44.2 ± 22	15.98 ± 7.04	3.634[#]	0.001
Median	27	15		S
Range	20 – 53	2 - 25		
Creatinine				
Mean ± SD	0.83 ± 0.13	0.79 ± 0.14	1.08	0.286
Median	085	0.8		NS
Range	0.5 – 1.2	0.5 – 1.0		

NS: P-value>0.05 is not significant

Urinary PH was significantly lower in NAFLD cases than their controls, while 24 hours urinary proteins was higher among studied NAFLD cases but not reach significant level Table (5).

Table (5) Difference in urinary PH and protein levels among both studied groups.

Variables	**Cases (N=60)**	**Controls (N=20)**	**t-test\MW[#]**	**P-value**
Urinary PH				
Mean ±SD	5.7 ± 0.24	6.2 ± 0.21	8.09	<0.001
Median	5.7	6.2		HS
Range	5.2 – 6.3	5.8 – 6.5		

Table (5) Continue

Urinary protein level (mg) Mean ± SD	154.02 ± 75.4	123.2 ± 24.8	1.26[#]	0.207
Median	128	121		NS
Range	90 - 420	81-200		

HS: P-value<0.001 is high significant   NS: P-value>0.05 is not significant

Sensitivity of urinary PH in detection of NAFLD cases was 83.3% at cut-off 5.45, with ability of exclusion of truly negative cases without fatty liver by 37.6%. Fig (1).
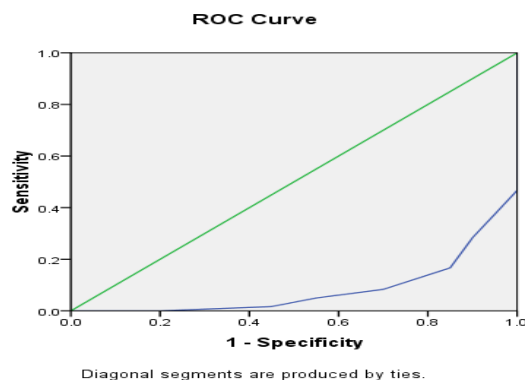

Fig (1) Receiver operating characteristics (ROC) curve for urinary PH in detection of NAFLD.

4. Discussion

The current examination shows a really basic differentiation among the two social occasions regarding lipid profile (cholesterol, LDL and HDL) levels which were all higher among NAFLD cases, while HDL level was not basically lower among NAFLD cases. Metabolic aggravations especially dyslipidemia is significantly regular in NAFLD. Lipid disrupting impacts are thought to develop in front of timetable inside the clinical course of NAFLD. Insulin-resistance (both hepatic and in the skeletal muscle or fat tissue) is the essential etiopathogenic factor for the lipoprotein inconsistencies in NAFLD [8].

Raised TG and low-thickness lipoprotein cholesterol (LDL-C) levels and Low degrees of high-thickness lipoprotein (HDL) cholesterol are essential in NAFLD. It has been suggested that standard lipid limits, for instance, non-HDL-cholesterol or especially the non-HDL-cholesterol to HDL-cholesterol extent, are free pointers of fortuitous NAFLD [8].

Maybe the greatest assessment for examination of lipoprotein profile in a NAFLD people was done in the Multi-Ethnic Study of Atherosclerosis accomplice on 3362 subjects has found that individuals with NAFLD (n=569) had raised combinations of greasy substances and decreased degrees of HDL-cholesterol (P<0.0001), anyway the examination fail to show contrasts in LDL-cholesterol (P=0.23) [9]. Our results concerning lipid profile resemble disclosures of a couple past examinations like [10].

Concerning low HDL level our results were against Nigam et al., 2013 which declared that between 120 NAFLD cases and 152 strong controls there was no basic difference in HDL levels in mg/dl (41.31±67.2 versus 41.98±66.54 separately with p regard 0.43).

As referred to before past its known effects on glucose homeostasis, insulin is apparently a key hormone in the rule of lipid absorption and insulin resistance is the rule factor for dyslipidemia in NAFLD [8], this reality maintained by our revelations in assessment among diabetic and non-diabetic NAFLD cases as there was an immense differentiation between the two subgroups as for (T.cholesterol, TG, and LDL)levels.

A meta-examination performed on 15 assessments, close by the data identifying with a general population of 336 patients. Data from lean (n=1966) and fat (n=5938) patients with NAFLD were researched as cases versus lean (n=9946) and bulky (n=6027) subjects without NAFLD filled in as controls; the meta-assessment found a vital stature in fasting glucose in lean and powerful cases with NAFLD more than cases without NAFLD what is important was 6.44±1.12 mg/dL with p value.000017 [11].

Our examination shows quantifiably basic difference among NAFLD and sound get-togethers concerning ALT, AST (table (7)), anyway between NAFLD subgroups the diabetic one has basically higher AST levels than non-diabetic.

ALT and AST are markers of liver injury and may be useful substitute extents of NAFLD. ALT is arranged in the hepatocellular cytosol, while AST is commonly inside the mitochondria. For sure, NAFLD

and NASH have been represented to be most ordinary explanations behind continually raised liver proteins and is regularly the tipping point for extra demonstrative appraisal [12]. In arrangement a progressing tremendous UK study found that NAFLD recognized by USG, was the most notable purpose behind odd liver natural science [13].

Furthermore a cross‑sectional office set up examination concerning 152 IGT and 158 starting late distinguished T2DM subjects developed some place in the scope of 30 and 69 years, close by 160 age and sexual direction facilitated non diabetic controls found that NAFLD was out and out associated with higher ALT and AST levels as ALT was 20.8±14 in non-NAFLD pack versus 44.2±22 in NAFLD one and with p regard 0.021. for AST 26±13 versus 33.3±16 independently with p regard 0.016, also levels of ALT and AST was higher in diabetic cases with NAFLD than non-diabetic with NAFLD as mean level of ALT was 45±22 versus 40.1±10 separately and AST mean level was 34±16 versus 30±7 exclusively (Sanyal et al., 2015). Instead of our results regular degrees of liver proteins have been displayed in subjects with the entire scope of NAFLD, and consequently ALT, AST have not been very significant in predicting NAFLD [14].

Concerning pH the examination showed a quantifiably high basic decrease among thought about NAFLD cases than their controls, as mean and standard deviation of pee pH was 5.7 ± 0.24 versus 6.2 ± 0.21 separately with p regard <0.001. our discovering maintained by an organization based cross sectional assessment that was held between April 2013 and March 2014, the records of 4,945 Japanese subjects who had experienced yearly prosperity tests were examined to perceive subjects who met the characteristic models for NAFLD, the individuals were masterminded reliant on pee pH, into four social affairs; a low pee pH was described as ≤5.5. Of the 3,411 subjects who qualified for enrollment, 1,028 met the suggestive principles for NAFLD. The results indicated that the inescapability of NAFLD was basically extended with decreasing pee pH in the two individuals (p<0.01 and p=0.02, separately). A multivariate examination, including changes for age, metabolic markers, and the renal limit, exhibited a basic connection between low pee pH and NAFLD in individuals (chances extent, 1.37; 95% assurance range, 1.01-1.85, p=0.04 and chances extent, 1.73; 95% sureness stretch, 1.15-2.62, p<0.01, independently) [6].

Our finding in like manner maintained with Okamura et al., 2018 that explored the connection between pee pH and event of NAFLD, in an enormous recorded assistant examination of 11,012 individuals (5503 men and 5509 women), the effect of pee pH on scene NAFLD was inspected. NAFLD was portrayed as having oily liver broke down by stomach ultrasonography. the individuals were divided into three social affairs according to pee pH; the most negligible get-together (pee pH ≤ 5.5), the middle get-together (pee pH = 6.0) and the most imperative get-together (pee pH ≥ 6.5). Cox relative dangers models was performed Over the center 6.8-year resulting length, 2023 individuals made NAFLD, and the harsh degrees were 20.3% (case/N = 1104/5447) at all pee pH gathering. (adjusted risk extent 1.48, 95% sureness range 1.31—1.66, P < 0.001). the assessment assumed that low pee pH predicts scene NAFLD and for shirking of event NAFLD, we should focus in extra on the presence of low pee pH [15].

Authenticity of pee pH as a pointer of nature of NAFLD was assessed by Receiver working ascribes (ROC) twist shows that affectability of urinary PH in distinguishing proof of NAFLD cases was 83.3% at cut-off 5.45, with limit of denial of truly negative cases without oily liver by 37.6%. Furthermore, ROC twist showed that affectability of urinary PH in partition among diabetic and non-diabetic NAFLD cases was half at cut-off 5.55, with limit of disallowance of truly negative cases without oily liver by 47.6%.

In the current assessment 24 hours urinary protein was higher in NAFLD cases anyway didn't show up at immense level (table 8) yet it was basically higher in NAFLD cases with diabetes than NAFLD without diabetes as showed up in table (14). This finding is maintained by a couple of assessments nitty gritty that the presence of NAFLD is immovably associated with an extended ordinariness and pace of CKD especially in diabetic patients with NAFLD, moreover, a continuous report proposed to investigate the relationship of nonalcoholic oily liver contamination (NAFLD) and its earnestness with the reduction in kidney work in patients with constant kidney ailment (CKD) revealed that patients with NAFLD had further degree of proteinuria than those without NAFLD (30.2 versus 23.5% independently, p=0.004) [16].

5. Conclusion

In conclusion our study results suggest strong association between presence of NAFLD and low urinary pH especially if accompanied with diabetes mellitus, and urinary pH can be used as an easy applicable indicator of presence of NAFLD, and it might help clinicians conveniently identify patients at high risk of NAFLD in setting of mass screening of population.

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