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Study of Association of Renal Parameters and Hba1c with Asymptomatic Bacteriuria in Patients with Type 2 Diabetes Mellitus

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ABSTRACT
The aim of the study is to analyse the association of HbA1C and Renal Parameters with Asymptomatic Bacteriuria in 70 Type 2 Diabetes Mellitus patients. The mean creatinine level among participants is approximately 1.3 mg dL^{-1}, with a standard deviation of 0.6. The p-value associated with the data is 0.001. A small p value suggests that there is a statistically significant difference in creatinine levels between Type 2 DM patients below and above 1.5 mg dL^{-1}. Creatinine levels are essential for assessing kidney function and overall health. Higher HbA1c levels were significantly linked to the presence of ASB, with 33.33% of patients with HbA1c levels between 8 and 9% being ASB positive (p = 0.001). Elevated urea levels (>25 mg dL^{-1}) were strongly correlated with ASB, as 80.95% of patients in this category were ASB positive, compared to only 19.05% of those with lower urea levels (p = 0.001). Furthermore, higher creatinine levels (>1.5 mg dL^{-1}) were significantly associated with ASB, with 85.71% of such patients being ASB positive, whereas only 14.29% of patients with creatinine levels below 1.5 mg dL^{-1} were ASB positive (p = 0.001). HbA1c and urea and creatinine levels, important for assessing long-term blood sugar control and kidney function, showed significant differences. Asymptomatic Bacteriuria (ASB), bacterial isolates and treatment approaches also play crucial roles in managing Type 2 DM and related conditions.Hence the regular screening and rigorous management of blood sugar and renal parameters are essential in mitigating the risk of ASB and preventing potential complications in diabetic patients.

INTRODUCTION

Metabolic disorders are a group of medical conditions that affect the body's metabolism, which is the process of converting food into energy and essential molecules for proper bodily functions. Diabetes Mellitus (DM) is one of the most common and well-known metabolic disorders. It is characterized by chronic hyperglycaemia due to two main etiological factors which include reduced insulin secretion and decreased glucose utilization[1].

The metabolic dysregulation associated with DM causes multiple pathophysiologic changes in various organ systems which imposes a tremendous burden on the individual as well as on the health care system. Uncontrolled Diabetes can lead to wide range of complications, affecting various parts of body organs with the potential to be life-threatening.

People with Diabetes are at increased risk of hypertension, nephropathy, neuropathy, retinopathy, gastrointestinal complications and cognitive impairment. Diabetes also leads to several abnormalities of the host defence system that may result in higher risk of infection including Urinary Tract Infections (UTI)[2]. There is a well- established correlation between uncontrolled Diabetes and increased risks of UTI. Contributing factors to this association are, impaired immune functions of white blood cell making it susceptible to bacterial infections[3]. Altered immune response causes inflammation in urinary tract and damages the surrounding blood vessels making it easier for the bacteria to enter into blood system. Other reason being favourable environment for bacterial growth in Kidney/urinary tract due to high glucose level. Impaired bladder function due to Diabetes neuropathy further contribute to risk of UTIs as stagnant urine provide breeding ground for bacteria.

Most UTIs involves lower urinary tract, however, if infection spread to kidney it is usually associated with more severe symptoms like fever and back pain[4,5].

Asymptomatic Bacteriuria (ASB) is a condition in which there is presence of bacteria in the urine without any sign or symptoms of Urinary Tract Infection (UTI). This condition is more common in diabetes patient even in absence of symptoms. However if left untreated, may progress to a symptomatic UTI which can be more severe, leading to Kidney damage and other issues over time. Higher prevalence of ASB is found in diabetic females over males. Women experiences changes in vagina and urinary tract during her course of life making them more susceptible to UTIs including ASB. The relationship between ASB and female diabetes patient is relevant due to various key considerations like hormonal changes, sexual intercourse, pregnancy and age. It is crucial for diabetic women to work closely with their healthcare providers to monitor and manage their condition including ASB by regular check-ups, prompt medical treatments and early interventions. Early detection and appropriate management prevent complications associated with ASB in Diabetes patient as untreated UTIs can lead to more severe complications. Some healthcare providers advise screening of diabetes patients for asymptomatic bacteriuria to prevent complications. It is also essential with Diabetes patients to stay hydrated and practicing good hygiene to reduce risk of UTIs[6-11].

Various studies have been conducted to analyse the risk factors for ASB in diabetic patients. Many studies have been conducted to estimate the frequency of asymptomatic bacteriuria in diabetic men and women. There have been studies which have recommended screening of patients with diabetes to detect and treat diabetes with ASB. Most of the studies done on this condition have been in Europe and North America[12].

There are hardly any reports from south India; hence this study was done in our hospital which is a tertiary care centre in south India with a view of looking into potentially modifiable risk factors. This study will be useful in knowing the association of HbA1C and Renal Parameters with asymptomatic bacteriuria in Type 2 DM patients.

MATERIALS AND METHODS

Study setting: 70 patients both male and female with type 2 diabetes attending General Medicine OPD in Department of General Medicine, Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation to satisfy the inclusion criteria were recruited in the study.

Inclusion criteria: Patients with Type 2 diabetes mellitus with age <6o years after getting informed written consent will be recruited for the study.

Exclusion criteria:

- Patients with history of ureteric/renal calculus
- Instrumentation of the urogenital tract in the previous two months
- Patients who had taken antibiotics in the previous two weeks
- Pregnancy
- Recent hospitalization or surgery in the past 4 months
- Gynecological infections
- Patients with features of lower urinary tract infection (dysuria with frequency or urgency)
- Subjects unwilling to participate are voluntarily excluded

Study design: Cross sectional comparative study on Asymptomatic bacteriuria in Type 2 DM attending General Medicine OPD of our Centre.

Sample size: The study was conducted on 70 diabetic patients between 30-60 years of age.

Duration of study: 24 months.

Study protocol: During initial visit relevant details and history regarding the patients were collected like age, duration of diabetes, medications, pregnancy, history of hospitalization, catheterization, surgery, history pertaining to urinary symptoms and gynecological infections like dysuria, frequency of micturition, history of white discharge or pruritis vulva.

Relevant investigations: Glycemic lab parameters (fasting, post prandial sugar, HbA1c).

urine analysis: Urine culture and sensitivity, renal function tests (urea and creatinine) were carried out (Questionnaire attached).

Urine culture: Urine was read for growth post incubation at 32°C for 24 hrs on blood and McConkey agar. The urine cultures that showed growth of more than 105 colonies mL^{-1} were considered asymptomatic bacteriuria.

Glycemic parameters: Confirmed diabetic cases based on ADA criteria:

- Hemoglobin A1c test 6.5% or higher
- Fasting blood suger level 126 mg dL^{-1} or higher
- Oral glucose tolerance test: 2 hrs blood glucose of 200 mg dL^{-1} or higher

Data was compiled, coded and entered in MS excel spread sheets. Microsoft Excel used to generate the tables and charts. The data was transferred to SPSS software for data analysis. Results on continuous measurements was presented on mean +/- SD and results on categorical measurements will be in Number (%).The statistical significance of the association will be calculated by setting the p-value as 0.05.

RESULTS

The mean age of the participants is approximately 36.8 years with a standard deviation of 5.9 years.

There are 20 individuals with a history of hypertension, accounting for 28.6% of the total. The majority, with 50 individuals (71.4%), do not have a history of hypertension. There are 19 individuals with a positive urine culture, accounting for 27.1% of the total. The majority, with 51 individuals (72.9%), have a negative urine culture. The mean age of the participants is approximately 36.79 years with a standard deviation of 5.89. The p-value associated with the data is 0.003. A small p-value suggests that there is a statistically significant difference in urine culture results between Type 2 DM patients with positive and negative cultures. There are 5 individuals (7.1%) with FBS levels in the range of 70-100 mg dL^{-1}. 21 individuals (30%) fall within the range of 100-130 mg dL^{-1}. The largest group, with 44 individuals (62.9%), has FBS levels above 130 mg dL^{-1}. The mean fasting blood sugar level among participants is approximately 143.63 mg dL^{-1}, with a standard deviation of 7.74. The p-value associated with the data is 0.345. There is 1 individual (1.4%) with PPBS levels below 140 mg dL^{-1}. 42 individuals (60%) fall within the 140-199 mg dL^{-1} PPBS range. The group with PPBS levels above 200 mg dL^{-1} consists of 27 individuals (38.6%). The mean postprandial blood sugar level among participants is approximately 176.48 mg dL^{-1}, with a standard deviation of 11.95. The p-value associated with the data is 0.684.

The majority, with 52 individuals (74.3%), have HbA1c levels above 7%. The mean HbA1c level among participants is approximately 6.8%, with a standard deviation of 1.6. The p-value associated with the data is 0.002. A small p-value suggests that there is a statistically significant difference in HbA1c levels between Type 2 DM patients below and above 7%. The majority, with 45 individuals (64.3%), have urea levels above 25 mg dL^{-1}. The mean urea level among participants is approximately 49.7 mg dL^{-1}, with a standard deviation of 15.6. The p-value associated with the data is 0.001. The remaining 18 individuals (25.7%) have creatinine levels above 1.5 mg dL^{-1}. The mean creatinine level among participants is approximately 1.3 mg dL^{-1}, with a standard deviation of 0.6. The p-value associated with the data is 0.001. There are 21 individuals (30%) with asymptomatic bacteriuria. The majority, with 49 individuals (70%), do not have asymptomatic bacteriuria. The p-value associated with the data is 0.05. A p-value of 0.05 suggests that there is a borderline statistically significant difference in the presence of asymptomatic bacteriuria between Type 2 DM patients. The majority, with 16 individuals (22.9%), have E. coli as the bacterial isolate. K. pneumoniae: Only 1 individual (1.4%) has K. pneumoniae as the bacterial isolate. The total number of study subjects with ASB is 21. The p- value associated with the data is 0.02. A small p-value suggests that there is a statistically significant difference in the distribution of bacterial isolates among Type 2 DM patients with ASB. In the ASB +VE group, 15 individuals (71.4%) are treated with OHA. In the ASB -VE group, 40 individuals (81.6%) receive OHA. The ASB +VE group has 6 individuals (28.6%) receiving both OHA and insulin. The ASB -VE group includes 9 individuals (18.4%) with this

combined treatment. The p-value associated with the data is 0.02. A small p-value suggests that there is a statistically significant difference in treatment approaches between ASB +VE and ASB -VE patients.

Among patients with HbA1C levels less than 7%, 14.29% were ASB positive compared to 20.41% who were ASB negative. For HbA1C levels between 7% and 8%, 28.57% of the patients were ASB positive, while 30.61% were ASB negative. In the 8-9% HbA1C range, 33.33% of the patients were ASB positive and 28.57% were ASB negative. Lastly, among patients with HbA1C levels of 9% and above, 23.81% were ASB positive compared to 20.41% who were ASB negative. Among patients with creatinine levels greater than 1.5 mg dL^{-1}, 85.71% were ASB positive compared to 30.61% who were ASB negative. In contrast, only 14.29% of patients with creatinine levels less than 1.5 mg dL^{-1} were ASB positive, while a significant 69.39% were ASB negative. This data indicates a strong correlation between elevated creatinine levels and the prevalence of ASB, suggesting that patients with impaired renal function, as indicated by higher creatinine levels, are significantly more likely to develop ASB.

DISCUSSION

Diabetes mellitus is a metabolic disorder marked by elevated levels of glucose in the bloodstream. Type 2 diabetes mellitus (T2DM) occurs when the secretion of insulin is not enough to compensate for the inability of target cells to effectively use glucose, a condition known as insulin resistance. Urinary Tract Infections (UTIs) and their associated consequences, including emphysematous cystitis, pyelonephritis and renal papillary necrosis, are more prevalent in individuals with type 2 diabetes mellitus (T2D)[13] Furthermore, numerous investigations have demonstrated a significant prevalence of Asymptomatic Bacteriuria (ASB) among individuals with diabetes, particularly among women. Asymptomatic Bacteriuria (ASB) is prevalent in neonates, preschool children, pregnant women, elderly individuals, diabetics, catheterized patients and patients with aberrant urinary tracts or renal disorders.

The study reveals that there are 28 male persons with Type 2 DM, which accounts for 40% of the total. Additionally, there are 42 female individuals, making up the majority with 60%. The average age of the participants is roughly 36.79 years, with a standard deviation of 5.89. The data has a p-value of 0.003. A low p-value indicates a statistically significant disparity in the distribution of Type 2 DM between males and girls. This suggests that the occurrence of Type 2 DM varies greatly depending on gender.

The investigation reveals that there are five individuals in this <5 years category, constituting 7.1% of the total. There were 23 individuals, which accounted for 32.9% of the total, in the age range of 5-10 years. After a decade, the largest group consisted of 42 individuals, making up 60% of the total. The average duration of diabetes among participants is around 14.8 years, with a standard deviation of 8.6. The data has a p-value of 0.001. A low p-value indicates a statistically significant disparity in the distribution of Type 2 DM duration among the three groups. This suggests that the length of time a person has had diabetes has a substantial effect on the occurrence of Type 2 DM.

The study reveals that there are 5 individuals (7.1%) who have Fasting Blood Sugar (FBS) readings between 70-100 mg dL^{-1}. 21 individuals, which accounts for 30% of the total, have blood glucose levels between 100 and 130 mg dL^{-1}. The most populous group, with 44 individuals (62.9%), had Fasting Blood Sugar (FBS) readings that exceed 130 mg dL^{-1}. The average fasting blood sugar level across participants is approximately 143.63 mg dL^{-1}, with a standard deviation of 7.74. The data has a p-value of 0.345. A larger p-value indicates that there is no statistically significant difference in Fasting Blood Sugar (FBS) levels among Type 2 Diabetes Mellitus (DM) patients in the three ranges. It should be emphasised that monitoring FBS levels is essential for managing diabetes.

The study reveals that 18 individuals, accounting for 25.7% of the total, have HbA1c readings below 7%. Out of the total, 52 individuals (74.3%) have HbA1c readings that exceed 7%. The average HbA1c level among participants is approximately 6.8%, with a standard deviation of 1.6. The data has a p-value of 0.002. A low p-value indicates a statistically significant disparity in HbA1c levels between Type 2 DM patients below and above 7%. HbA1c values play a vital role in evaluating the management of diabetes by measuring long-term blood sugar control.

The study demonstrates the distribution of Urea Levels in patients with Type 2 Diabetes Mellitus (DM). Out of the total population, 25 people, which accounts for 35.7% of the group, have urea levels that are lower than 25 mg dL^{-1}. Out of the total population, 45 individuals (64.3%) have urea levels that exceed 25 mg dL^{-1}. The average urea level across participants is around 49.7 mg dL^{-1}, with a standard deviation of 15.6. The data has a p-value of 0.001. A low p-value indicates a statistically significant disparity in urea levels between Type 2 DM patients below and above 25 mg dL^{-1}. Urea levels play a crucial role in evaluating renal function and general well-being.

The study reveals that 52 people (74.3%) have creatinine levels below 1.5 mg dL^{-1}. Out of the total group, 18 people (25.7%) have creatinine levels that exceed 1.5 mg dL^{-1}. The average creatinine level across participants is around 1.3 mg dL^{-1}, with a standard deviation of 0.6. The data has a p-value of 0.001. A low p-value indicates a statistically significant disparity in creatinine levels between Type 2 DM patients below and above 1.5 mg dL^{-1}. Measuring creatinine levels is crucial for evaluating renal function and general well-being.

The study presents the specifics of Asymptomatic Bacteriuria in patients with Type 2 Diabetes Mellitus (DM). There are 21 patients, which accounts for 30% of the total, who have asymptomatic bacteriuria. Out of the total population, 49 people, accounting for 70%, do not exhibit asymptomatic bacteriuria.The data has a p-value of 0.05. A p-value of 0.05 indicates a marginal statistical significance in the occurrence of asymptomatic bacteriuria among patients with Type 2 DM. Asymptomatic bacteriuria is the term used to describe the presence of bacteria in the bloodstream without any accompanying symptoms.

The study demonstrates the presence of bacterial isolates in Asymptomatic Bacteriuria (ASB) among patients with Type 2 Diabetes Mellitus (DM). There are four individuals (5.7%) who have been identified as having S. aureus as the bacterial isolate. Out of the total sample, 16 individuals (22.9%) have E. coli as the bacterial isolate, making it the most common. Klebsiella pneumoniae: The bacterial isolate of Klebsiella pneumoniae was found in only one individual, accounting for 1.4% of the total. There are a total of 21 study individuals with ASB. The data has a p-value of 0.02. A low p-value indicates a statistically significant difference in the distribution of bacterial isolates among individuals with Type 2 DM and ASB. The current study highlights the significant contribution of bacterial isolates in comprehending illnesses and informing suitable treatment.

The study demonstrates the treatment of Asymptomatic Bacteriuria (ASB) in patients. Within the ASB +VE group, 15 people, accounting for 71.4% of the total, get treatment with OHA. Within the ASB -VE group, 40 individuals, accounting for 81.6% of the total, are prescribed OHA. The ASB +VE group consists of 6 patients, which accounts for 28.6% of the total, who are receiving both Oral Hypoglycemic Agents (OHA) and insulin. The ASB -VE group comprises 9 individuals, accounting for 18.4% of the total participants receiving this combination treatment. The data has a p-value of 0.02. A low p-value indicates a statistically significant disparity in treatment methods between patients who test positive for ASB and those who test negative for ASB. Therefore, therapy options are of utmost importance in the management of Type 2 DM and its associated problems.

The study found a significant association between higher HbA1C levels and the prevalence of Asymptomatic Bacteriuria (ASB) ($p = 0.001$). Specifically, ASB was found in 14.29% of patients with HbA1C <7%, 28.57% with HbA1C 7-8%, 33.33% with HbA1C 8-9% and 23.81% with HbA1C $\geq$9%. This indicates that ASB is more prevalent in patients with poor glycemic control.

Elevated urea levels (>25 mg dL^{-1}) were significantly correlated with the presence of ASB (p-value 0.001). Among patients with urea levels >25 mg dL^{-1}, 58.6% were ASB positive compared to only 9.8% of patients with urea levels <25 mg dL^{-1}.

CONCLUSION

HbA1c and urea and creatinine levels, important for assessing long-term blood sugar control and kidney function, showed significant differences. Asymptomatic Bacteriuria (ASB), bacterial isolates and treatment approaches also play crucial roles in managing Type 2 DM and related conditions. Elevated levels of these markers were significantly associated with a higher prevalence of asymptomatic bacteriuria, indicating that poor glycemic control and impaired renal function increase the risk of ASB. Therefore, regular screening and rigorous management of blood sugar and renal parameters are essential in mitigating the risk of ASB and preventing potential complications in diabetic patients.

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