

# Prediction Score for Urinary Tract Infection among Diabetes Mellitus Patients in a Tertiary Care Hospital at Dakar, Senegal

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## Abstract

**Background:** Urinary Tract Infection (UTI) in diabetes mellitus patients can cause acute complications of diabetes and thus be life-threatening. The objective of this study was to propose a prediction score for UTI in diabetes mellitus patients hospitalized in the department of medicine at the Military Principal Hospital of Dakar.

**Methods:** We conducted a retrospective cross-sectional study from January 1, 2016, to December 31, 2019, including diabetes mellitus patients hospitalized in the study setting. We randomly sampled the study population in learning and validation datasets, and we built a prediction score for UTI from a multivariate logistic regression model. The Receiver Operating Characteristics (ROC) curve and its Area Under the Curve (AUC) was used to determine the discriminating power of the score.

**Results:** We enrolled 573 diabetes mellitus patients with a mean age of  $63 \pm 14$  years and a male to female ratio of one, divided into two subgroups: a learning and a validation subgroup of 372 (65%) and 201 (35%), respectively. The prevalence of UTI was 27%. After a multivariate logistic regression, independent associated factors with UTI were: female gender (OR=1.9; 95%CI [1.1-3.3]), UTI history (OR=3.7; 95%CI (1.4-9.7)), diabetic neuropathy (OR=1.8; 95%CI (1-3.2)), urinary symptom (OR=6.9; 95%CI (3.6-13.3)), positive CRP (OR=2.9; 95%CI (1.5-5.7)) and anemia (OR=1.8; 95%CI (1-3.2)). The AUC was 77.8% (95% CI (72.8%-82.9%)), 71.9% (95%CI (63.7%-78.8%)) and 75.8% (95%CI (71.2%-79.7%)) on the learning, validation and total dataset, respectively.

**Conclusion:** A valid prediction score for UTI may help in its early diagnosis and prevent acute complications of diabetes mellitus.

**Keywords:** Urinary tract infection; Diabetes mellitus; Prediction score; Dakar

## Key Summary Points

- Urinary tract infection is common in diabetes mellitus patients and can lead to glycemic imbalance
- Urinary tract infection in diabetes mellitus patients can be in link with a number of factors such as: female gender, history of urinary tract infection, diabetic neuropathy, CRP and haemoglobin levels
- A valid prediction score of urinary tract infection can help in its early diagnosis in diabetic patients
- A web application can make it easier for physicians to use this prediction score

## Introduction

According to World Health Organization (WHO), diabetes mellitus is a chronic disease that occurs when the pancreas does not produce enough insulin or when the human organism is unable to use insulin effectively [1]. It represents a major public health issue regarding its high morbidity and mortality. According to the International Diabetes Federation (IDF), the number of adults with diabetes mellitus reported in 2019 was around 463 million corresponding to 9.3% of the world population from 20 to 79 years of age. This prevalence will tend towards 10.2% by 2030 in this same age group. Around 90% of these patients suffer from type 2 diabetes mellitus [2]. Around 212.4 million people in the world are at risk to have the disease but remain undiagnosed [2]. The majority of these populations live in low and middle-income countries. In Africa, 3.9% of the population lives with diabetes mellitus, however 59.7% of these diabetes mellitus patients are undiagnosed. Diabetes and its complications lead to the death of 4.2 million adults from 20 to 79

years of age in 2019, worldwide. Most of these deaths occur among the working population under the age of 60 years in Africa [2,3]. When not properly managed, diabetes mellitus can progress to serious infectious, vascular or metabolic complications. The vulnerability of the immune system of the diabetes mellitus patients exposes them to an increased risk of occurrence of potentially serious infections. Urinary Tract Infections (UTI) are the most frequent after those of the pulmonary tract [4,5]. Furthermore, urinary tract infection often occurs in diabetes mellitus patients with unusual clinical presentation. Urinary upper tract involvement is frequent and can lead to acute pyelonephritis and renal abscess [6]. The prevalence of pyelonephritis is, thus, 20 to 30 times higher in diabetes mellitus patients over 44 years of age compared to non-diabetic patients [7]. Some severe UTIs, such as emphysematous pyelonephritis or renal papillary necrosis are almost present in diabetes mellitus patients exclusively [8,9]. UTI is also one of the main infectious causes of glycemic imbalance or diabetic decompensation [10]. Some studies have evaluated the risk factors for UTI in diabetes mellitus patients with often controversial results [3,5,11] and they are

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rarely carried out in Africa. We conducted this study to identify the factors associated with UTI in diabetes mellitus patients at the Military Principal Hospital of Dakar (Senegal) and to subsequently propose a prediction score for UTI in this chronic health condition.

## Materials and Methods

### Patients and study design

We conducted a retrospective descriptive and analytical study covering the period from January 1, 2016, to December 31, 2019. Our study population concerned all diabetes mellitus patients hospitalized in the medical department (including infectious and tropical diseases, pulmonology, gastroenterology and internal medicine) at the Military Principal Hospital of Dakar during the study period. All admitted diabetes mellitus patients who were more than 16 years of age were included in our study. We did not include in the study, patients whose medical records were incomplete and patients who had less than 24 hours of hospitalization.

### Data collection

Data were collected from hospital registers, medical records and patient's laboratory data. The sampling method was exhaustive taking into account all hospitalized diabetes mellitus patients. A tested questionnaire was created, and a trained investigator was in charge of collecting data such as: socio-demographic characteristics (including age, sex, address), history of UTI, diabetes mellitus characteristics (including the type of diabetes, duration of diabetes, anti-diabetic treatment), other comorbidities (including hypertension, HIV infection, chronic kidney disease, prostatic disease), lifestyle (including alcohol consumption, smoking and marital status), clinical features and laboratory data.

### Study definitions

We have adopted the following operational definitions for a better data analysis. UTI was defined as the presence of urinary tract symptoms such as, polyuria, dysuria, burning voiding or urinary incontinence with significant leukocyturia ( $\geq 10^4$  cells/mm<sup>3</sup>) and/or significant bacteriuria. Bacteriuria was considered significant when it was  $\geq 10^3$  CFU/mL for *Escherichia coli* and *Staphylococcus saprophyticus* or  $\geq 10^3$  CFU/mL in men and  $10^4$  CFU/mL in women for other pathogens. We defined diabetic neuropathy as either any neuropathic pain or other sensory disorder present in a patient that cannot be attributed to any other cause. Anemia was defined as a hemoglobin level  $<12$ g/dL or  $<13$  g/dL in female patients or in male patients, respectively. Positive CRP was defined as a CRP rate  $>6$  mg/L.

### Data management and statistical analysis

Data were recorded in EPI INFO software (version 7.2.2.6), exported to Excel (version 15.13.3), and analyzed using R software (version 4.0.3). R shiny packages were used to create a web application of the finale score. According to the distribution, quantitative variables were represented using either mean  $\pm$  Standard Deviations (SD) or medians and their Interquartile Ranges (IQR). Qualitative variables were represented using frequency and percentages.

To create a prediction score of the presence or the absence of UTI (which was the dependent variable) in diabetes mellitus patients, we randomly divided the study population into two subgroups: a learning

subgroup for the model building and an internal validation subgroup which represented 65% and 35% of the total population, respectively. Bivariate and then multivariate analysis were performed in the learning subgroup to compare patients with or without UTI. We performed a logarithmic transformation of quantitative independent variables that did not have a normal distribution. The means of independent variables were compared using either Student's t-test or Wilcoxon Mann Whitney test according to their distribution and variance homogeneity. The proportions were compared using Pearson chi-squared test, Pearson's Chi-squared test with Yates' continuity correction or Fisher's exact test. A multivariate logistic regression was subsequently performed and all the independent variables with p-values  $<0.2$  in the bivariate analysis were introduced in the multivariate model. A backward stepwise method was used to identify the factors independently associated with UTI. Hosmer Lemeshow's adequacy test and interactions checking between independent variables were performed to validate the final model with statistically significant level of 0.05. We subsequently train the final model with the selected independent variables from the backward stepwise method, using a 10 fold cross-validation. At the end of this analysis, the beta coefficients of the statistically significant independent variables in the final model were used to create the UTI prediction scoring system in diabetes mellitus patients. The Receiver Operating Characteristics (ROC) curve was built with its Area under the Curve (AUC) to appreciate the discriminating power of the score. The validation of the learning score was performed in the validation dataset and in the full dataset. We selected the probabilities cut-off of 75% and 25% as the boundaries of high and low probabilities of UTI, respectively. Patients between these two cut offs were considered to be at intermediate risk to have UTI. For each cut-off point, sensitivity, specificity, positive and negative predictive values of the score were calculated.

### Ethical considerations

Ethical approval for the study was not requested because its non-interventional design limited exclusively to an exploitation of medical records. However, prior to the study, permission was obtained from the medicine departmental heads. Additionally, data collected were recorded in a secure database; anonymity and confidentiality of the patients were preserved.

## Results

### Epidemiological characteristics of the study population

We enrolled 573 diabetes mellitus patients divided into two subgroups: a learning subgroup of 372 patients (65%) and a validation subgroup of 201 patients (35%). The epidemiological characteristics of the patients are represented in Table 1. Of the 573 patients included, there were as many men as women. Their mean age was  $63 \pm 14$  years and the most represented age group was 60 to 80 years (53.8%). Diabetes mellitus was mainly type 2 (95%) and the mean duration of the disease was around  $11 \pm 9$  years. At the admission, they were already under anti-diabetic therapy in 94% of cases and most of them (50%) were under oral anti-diabetic treatment. Patients were married in 84% of cases and for the most part in a polygamist regime (54.4%). More than half of the patients had high blood pressure. The prevalence of Urinary Tract Infection (UTI) was almost similar in all three samples and was estimated at 27%.

Characteristics	Total population	Learning group	Validation group
	N=573*	N=372*	N=201*
Age (years)	63 (14)	63 (13)	62 (14)
Sex			
Male	286 (50%)	198 (53%)	88 (44%)
Female	287 (50%)	174 (47%)	113 (56%)
Marital status			
Married	482 (84%)	314 (84%)	168 (84%)
Single	21 (3.7%)	13 (3.5%)	8 (4.0%)
Divorced	10 (1.8%)	8 (2.2%)	2 (1.0%)
Widowed	60 (10.5%)	37 (9.9%)	23 (11%)
Type of diabetes mellitus			
Type 1	26 (5%)	17 (5%)	9 (4%)
Type 2	547 (95%)	355 (95%)	192 (96%)
Duration of diabetes mellitus (years)	11 (9)	11 (9)	10 (9)
HbA1C (%)	9.9 (3.3)	10.0 (3.3)	9.75 (3.24)
Under anti-diabetic treatment	539 (94.1%)	349 (93.8%)	190 (94.5%)
Diabetic neuropathy	137 (24%)	93 (25%)	44 (22%)
Alcohol consumption	19 (3.3%)	13 (3.5%)	6 (3.0%)
Smokers	72 (12.6%)	54 (14.5%)	18 (9%)
Decoction	28(4.9%)	20(5.4%)	8(4%)
History of UTI	37 (6.5%)	26 (7.0%)	11 (5.5%)
High blood pressure	322 (56%)	212 (57%)	110 (55%)
Chronic kidney disease	101 (18%)	63 (17%)	38 (19%)
HIV	4 (0.7%)	2 (0.5%)	2 (1.0%)
Prostatic disease (reported to men)	46 (16%)	29 (14.7%)	17 (19.3%)
Urinary infection	157 (27%)	100 (27%)	57 (28%)

Note: \* Mean (Standard Deviation); n (%).

Table 1: Baseline characteristics of patients with diabetes mellitus at the military principal hospital of Dakar from January 1, 2016, to December 31, 2019.

### Clinical and biological characteristics of diabetes mellitus patients with urinary tract infection

The clinical and biological characteristics of diabetes mellitus patients with urinary tract infections in the three subgroups are represented in the Table 2. Fever was present in 10.8% (17/157) of cases. Of those who had glycosuria (27%) or ketonuria (14%) in the urine dipstick test, the level varied between 1+ and 4+. The most common urinary tract symptoms were pollakiuria (22%), followed by dysuria, voiding burning and urinary incontinence present in 15% of patients for each of these symptoms. Regarding the labs data, anemia and positive CRP were present in 69% and 82% of cases, respectively. The cause of the urinary tract infection was unknown in a quarter of patients.

Characteristics	Study population	Learning group	Validation group
	N=157*	N=100*	N=57*
Temperature	36.98 (0.77)	37.03 (0.84)	36.88 (0.64)
Ketonuria	22 (14%)	10 (10%)	12 (21%)
Glycosuria	42 (27%)	26 (26%)	16 (28%)
Pollakiuria	34 (22%)	28 (28%)	6 (11%)
Dysuria	24 (15%)	19 (19%)	5 (8.8%)
Voiding burning	24 (15%)	15 (15%)	9 (16%)
Urinary incontinence	23 (15%)	14 (14%)	9 (16%)
Cloudy urine	6 (3.8%)	5 (5.0%)	1 (1.8%)
Low back pain	4 (2.5%)	2 (2.0%)	2 (3.5%)
Ureteric pain	8 (5.1%)	4 (4.0%)	4 (7.0%)
Hemoglobin level (g/dL)	11.00 (2.14)	10.96 (2.19)	11.07 (2.06)
CRP (mg/L)	93 (110)	84 (101)	108 (124)

Glomerular filtration rate (GFR) (liter/min)	73 (36)	74 (37)	71 (34)
Cytobacteriological examination of urine (CBEU)			
Positive	134 (85%)	82 (82%)	52 (91%)
Sterile	23 (15%)	18 (18%)	5 (9%)

Note: \* Mean (Standard Deviation); n (%).

Table 2: Clinical and biological characteristics of diabetes mellitus patients with UTI at the military principal hospital of Dakar from January 1, 2016, to December 31, 2019.

### Bivariate analysis

The bivariate analysis performed in the learning subgroup showed that the factors significantly associated with the presence of UTI in diabetes mellitus patients were female gender (p=0.004), the presence of diabetic neuropathy (p=0.007), the presence of a urinary tract infection history (p<0.001), the presence of at least one urinary tract symptom (p<0.001), an increase in CRP (p<0.001) a low Hemoglobin level (p<0.001) and the absence of anti-diabetic therapy at the time of hospitalization (p=0.007). There was no statistically significant link between the other independent variables and urinary tract infection (Table 3).

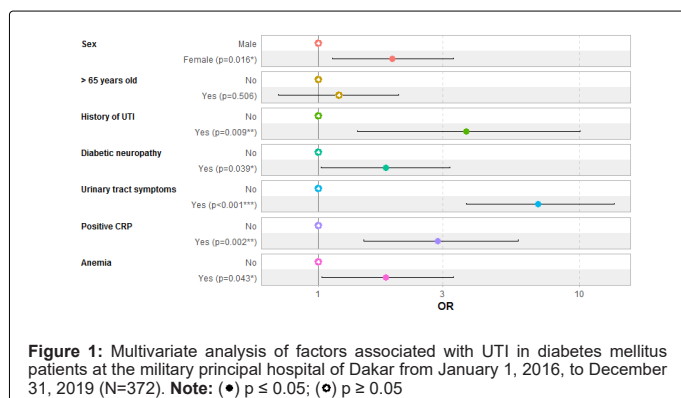
Characteristics	UTI		p-value
	Yes , N = 100 *	No , N = 272 *	
Age (years)	64 (14)	62 (13)	0.3
Sex			0.004
Male	41 (21%)	157 (79%)	
Female	59 (34%)	115 (66%)	
Marital status			0.4
Married	82 (26%)	232 (74%)	
Single	2 (15%)	11 (85%)	
Divorced	2 (25%)	6 (75%)	
Widowed	14 (38%)	23 (62%)	
Type of diabetes mellitus			0.8
Type 1	5 (29%)	12 (71%)	
Type 2	95 (27%)	260 (73%)	
Duration of diabetes mellitus (years)	11 (9)	10 (9)	0.4
Without antidiabetic treatment			0,007
Yes	12(52%)	11(48%)	
No	88(25%)	261(75%)	
HbA1C (%)	10 (3.3)	10 (3.3)	0.5
Diabetic neuropathy			0.007
Yes	35 (38%)	58 (62%)	
No	65 (23%)	214 (77%)	
Alcohol consumption			0.5
Yes	2 (15%)	11 (85%)	
No	98 (27%)	261 (73%)	

History of UTI			<0.001
Yes	17 (65%)	9 (35%)	
No	83 (24%)	263 (76%)	
High blood pressure			0.3
Yes	61 (29%)	151 (71%)	
No	39 (24%)	121 (76%)	
Urinary tract symptom **			<0,001
Yes	39 (59%)	27 (41%)	
No	61 (20%)	245 (80%)	
Hemoglobin level (g/dL)	11 (2.2)	12 (2.4)	<0.001
Log(CRP) (mg/L)	4 (1.6)	3(1.9)	<0.001
Log(GFR)(liters/min)	4 (0.7)	5 (0.6)	0.075
<b>Note:</b> * Mean (Standard Deviation) ; n (%),**pollakiuria, dysuria or voiding burning			

**Table 3:** Bivariate analysis of factors associated with UTI in diabetic mellitus patients at the military principal hospital of Dakar from January 1, 2016, to December 31, 2019.

### Multivariate analysis

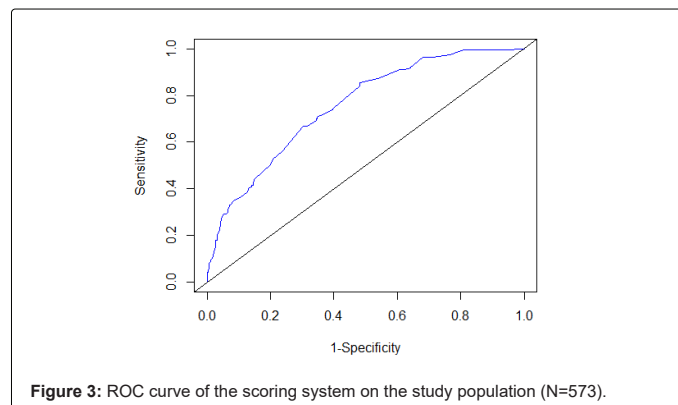
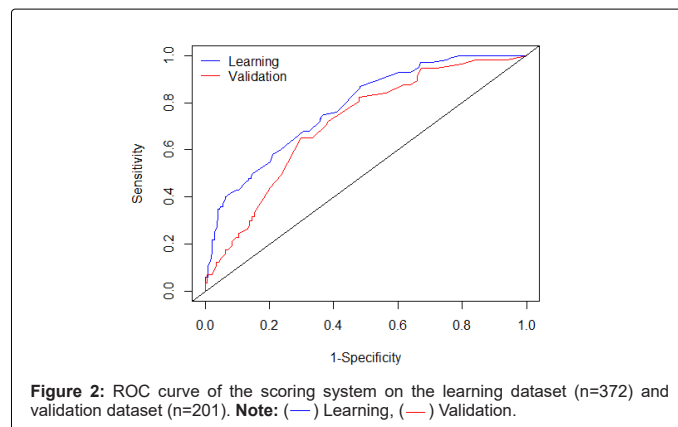
After adjusting for potential confounding factors by a multivariate logistic regression, female gender (OR=1.9; 95% CI (1.1-3.3); p=0.016), presence of a UTI history (OR=3.7; 95% CI (1.4-9.7); p=0.009), the presence of diabetic neuropathy (OR =1.8; 95% CI (1-3.2); p=0.04), the presence of a urinary tract symptoms (pollakiuria, dysuria or voiding burning) (OR=6.9; 95%CI (3.6-13.3); p<0.001), positive CRP (OR=2.9; 95% CI (1.5-5.7); p=0.002) and the presence of anemia (OR=1.8; 95% CI (1-3.2); p=0.04) were independent associated factors of the presence of urinary tract infection (Figure 1).



### Prediction score building and internal validation

The scoring system equation from the learning model was: UTI\_D\_Score= - 3.3 + 0.65\*sex (female=1, male=0) + 0.18\*(age>65) (Yes=1, No=0) + 1.3\*history of UTI (Yes=1, No=0) + 0.6\*diabetic neuropathy (Yes=1, No=0) + 1.9\*urinary tract symptoms (pollakiuria, dysuria or voiding burning) (Yes=1, No=0) + 1.1\*Positive CRP (Yes=1, No=0) + 0.6\*Anemia (Yes=1, No=0). Although the age variable is not statistically significant in the final multivariate model, we decided to include it in the scoring system with its beta coefficient because it is an important independent biological variable in the occurrence of health issues. The AUC of this prediction score was 77.8% (95%CI (72.8%-82.9%)) (Figure

2). The probability of 17.2% corresponded to the threshold probability defined as the maximum value of the sum of sensitivity (87%) and specificity (51%). By applying the model on the validation group and on the full group, the AUCs were 71.9% (95%IC (63.7%-78.8%)) and 75.8% (95%IC (71.2%-79.7%)), respectively (Figures 2 and 3).



### Predictive value of the scoring system

We considered arbitrarily that a score ≥ +1 corresponds to a high probability of UTI (≥ 75%) and a score ≤ -1 corresponds to a low probability of UTI (≤ 25%). At the cut-off value of +1, the specificity is 98%; at the cut-off value of -1, the sensitivity is 72% (Table 4).

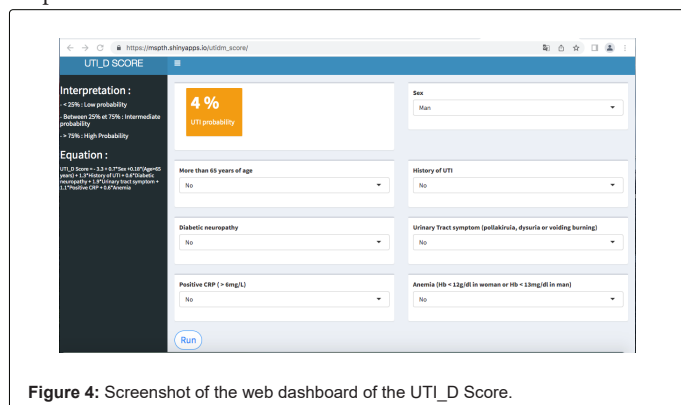
	Low cut-off	Intermediate	High cut-off
Threshold score	≤ -1	Between -1 and +1	≥ +1
Probabilities	≤ 25%	Between 25% and 75%	≥ 75%
Classification score	0.66		0.75
Specificity	0.64		0.98
Sensitivity	0.72		0.13
Positive predictive value	0.42		0.75
Negative predictive value	0.86		0.75

**Table 4:** Model performance criteria at probability thresholds.

### Web application building

We have built a web application to make it easier for physicians to use the score (Figure 4): [https://mspth.shinyapps.io/uti\\_dm\\_score/](https://mspth.shinyapps.io/uti_dm_score/). it is a web dashboard that includes a header containing the title of the score

“UTI\_D SCORE”, a left sidebar containing both the interpretation of the threshold probabilities and the score equation, and a body containing the different items of the score, the run button and the UTI probability result. When the different items of a diabetes mellitus patient are entered in the dashboard body, the run button should be pressed, and then the probability of UTI will be automatically generated. A red color code is used to highlight probabilities >75% and an orange color code for probabilities <75%.



## Discussion

In the present cross-sectional study, we reported a prevalence of UTI in diabetes mellitus patients of 27%. After a multivariate logistic regression with a backward stepwise method, the independent associated factors with UTI were: female gender, history of UTI, presence of diabetic neuropathy, presence of current urinary tract symptoms (pollakiuria, dysuria or voiding burning), anemia and positive CRP. We used the selected independent variables in the final model which were: sex, age, history of UTI, diabetic neuropathy, urinary tract symptoms, and CRP and hemoglobin level to suggest a scoring system that may help diagnose UTI in diabetes mellitus patients. This score, which we call ‘UTI\_D score’, uses easily reachable clinical and laboratory parameters with a satisfactory discriminating power (AUC of the ROC curve=77.8%). We believe that by using the probability thresholds that we have proposed, this score can help to make an early diagnosis of UTI in diabetes mellitus patients by considering the upper cut off (75% i.e. UTI\_D score=+1) and would avoid wrongly prescribing antibiotics in diabetes mellitus patients who do not have UTI by considering the lower cut off (25% i.e. UTI\_D score=-1). Patients between 25% and 75% should undergo further investigations to establish a correct diagnosis. The predictors of UTI we identified are consistent with those identified by many other authors. In our study, female diabetes mellitus patients were nearly twice more likely to have a UTI than male diabetes mellitus patients. The link between female gender with UTI is frequently noted in the studies assessing risk factors of UTI. In a Portuguese cohort of type 2 diabetes patients in 2020, Carrondo found a statistically significant association between female gender and the occurrence of UTI (OR=2.2; 95% CI (1.77-2.84)) (12). A similar observation was made by Li Y.M in 2020 in a Shanghai study in stroke patients with OR of 4 (13). This link is mainly explained by the anatomical configuration of the female urinary tract. The female urethra is shorter than that of men (3-4 centimeters vs 20 centimeters). It is also close to the vagina and perineum which are often colonized with enteric bacteria.

The presence of a UTI history appeared to be significantly associated with UTI occurrence in our study with an adjusted OR of 3.7 and a 95% CI (1.4-9.7). This finding is similar to that of Nabi in India in 2021, who reported a significant link (p-value <0.05) between the presence of

history of UTI in the previous year and the occurrence of a new event of UTI (14). Ikahelmo in Finland also reported that patients with a history of UTI were 7 times more at risk to have a new event of UTI (15). This increased risk may be due to several reasons. First, damage from a previous infection in the urinary tract can diminish its natural ability to resist a number of pathogens, making it more vulnerable to bacterial colonization. Additionally, an increase in antibiotic resistance after an event of UTI may also increase the risk of UTI relapse. Our study showed that the probability of UTI was almost twice higher in patients with diabetic neuropathy than in patients without diabetic neuropathy. This association may be related to an autonomic neuropathy involving the urinary tract that can lead to an incomplete emptying of the bladder and thus promote bacterial growth. Some authors have suggested that UTI in diabetes mellitus patients with neurogenic bladder dysfunction may have increased risk of UTI (10,16). Having one of the three urinary tract symptoms (pollakiuria, dysuria or voiding burning) was strongly associated with UTI in our patients (OR=6.9; 95% CI (3.6-13.3)). In an Ethiopian diabetes mellitus cohort in 2020, Alemu also reported that current urinary tract symptoms were independently associated with UTI (OR=2.702, 95% CI: (1.102, 6.624)) (17).

These symptoms are the most present in UTIs as showed in the Gninkoun CJ’s study in Beninese patients (3). Diabetes mellitus patients who had a positive CRP or anemia in our study had increased probability of UTI compared to diabetes mellitus patients who did not, with ORs of 2.9 and 1.8, respectively. Mushi MF underlined in a Tanzanian study that positive CRP (>6 mg/l) significantly predicted the presence of significant bacteriuria due to gram-negative enteric bacteria with OR of 4 in pediatric patients (18). Hemoglobin level was also among the predictive factors of UTI score in stroke patients in the study of Li with a beta coefficient of -0.049 (13). These significant links may be explained by the non-specific inflammatory syndrome, including an increase of CRP and anemia, which is noted in any bacterial infection.

## Limitations of the study

Despite the fact that the predictors of UTI that we found are broadly similar with those reported in literature, our scoring system has some limitations. The main issue is that the study was built from retrospective data, which did not allow us to have complete information on all the patients included and led to poorer precision on the data collected. Additionally, because of the retrospective design of the study, other factors that may be associated with the occurrence of UTIs such as socio-economic level, cultural characteristics, patient sexual activity or urinary catheter carriage could not be taken into account in our analysis. Our prediction score is also from single-center data and does not allow for a statistical inference. It should be applied to an independent diabetes mellitus patient’s cohort from another health care center for an external validation.

## Conclusion

UTI remains frequent in diabetes mellitus patients. It can be predicted by a number of factors such as sex, history of UTI, diabetic neuropathy, urinary tract symptoms, CRP and hemoglobin level. Physicians must always give priority to their clinical analysis for a proper management of their patients. Nevertheless, a valid prediction score for UTI in diabetes mellitus patients may help in its early diagnosis and thus prevent acute complications of diabetes.

## Conflict of Interests

The authors declare no conflicts of interest regarding the publication of this paper.

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