

## ORIGINAL RESEARCH

# Risk Factors of Recurrent Anal Abscess in Patients with Type 2 Diabetes Mellitus; a 4-Year Retrospective study

Nasser Malekpour Alamdari<sup>1</sup>, Siamak Afaghi<sup>2</sup>, Farzad Esmaeili Tarki<sup>2</sup>, Mohammad Fathi<sup>3</sup>, Sara Besharat<sup>4</sup>, Fatemehsadat Rahimi<sup>1\*</sup>

1. Clinical Research and Development Center, Department of Surgery, Shahid Modarres Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

2. Research Institute of Internal Medicine, Shahid Modarres Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

3. Critical Care Quality Improvement Research Center, Shahid Modarres Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

4. Department of Radiology, Shahid Labbafinezhad Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

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**Abstract:** **Introduction:** Anal abscess is considered as a relatively common complication in type 2 diabetes mellitus (T2DM) patients. This study aimed to determine the risk factors of recurrent anal abscess in T2DM patients. **Methods:** In this 4-year retrospective cross-sectional study, T2DM patients hospitalized due to anal abscess in Shahid Modarres Hospital, Tehran, Iran from December 2016 to December 2020 were studied. The independent risk factors of disease recurrence were determined among demographic factors, underlying diseases, diabetes-related factors, clinical factors, laboratory parameters, abscess type, and culture using multivariate stepwise logistic regression analysis. **Results:** 203 patients were enrolled in the study. 58 (28.6%) patients had at least one re-occurrence of anal abscess during four years. The recurrent episodes had occurred more frequently in the first year after the initial treatment (55.2%). The prevalence of comorbidities such as metabolic syndrome, coronary artery disease, chronic kidney disease, end stage renal disease, and peripheral vascular disease was significantly higher amongst patients with abscess recurrence. The patients with recurrent anal abscess had statically significant poor glycemic control (HbA1C > 7.5), decreased levels of Estimated Glomerular Filtration Rate (e-GFR), and higher C-reactive Protein (CRP) upon the first admission. Presence of metabolic syndrome, HbA1c > 7.5%, WBC > 11.0 ×10<sup>9</sup>/L, and CRP > 5 mg/l were amongst the independent risk factors of recurrence. HbA1c > 7.5% was the greatest independent risk factor of anal abscess recurrence (OR=2.68, 95% CI: 1.37-5.25; p < 0.001). The area under the receiver operating characteristic (ROC) curve (AUC) of HbA1C, CRP, and WBC in predicting the risk of abscess recurrence was 0.81, 0.71, and 0.64, respectively. **Conclusion:** Th recurrence rate of anal abscess in this series was 28.6 %. It seems that in T2DM patients with uncontrolled diabetes who have metabolic syndrome and increased CRP and WBC in their routine tests, the probability of anal abscess reoccurrence is high.

**Keywords:** Diabetes mellitus; abscess; metabolic syndrome; leukocytosis; diabetes complications

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## 1. Introduction

Anal abscess is among the most prevalent anorectal diseases, and it is more frequent amongst the youth in their fourth

decade of life (1). Its incidence rate is 16-20 per 100,000 with a 15% risk of future fistula development (2). Surgical therapy aids in decompression and pain alleviation of the abscess, as well as in prevention of the development of Fournier's gangrene or pelvic sepsis (3); Whilst, treatment with antibiotics alone is regarded as ineffective, resulting in therapeutic failure, illness relapse, and the creation of a fistula (4). Some patients only experience a single episode of the illness, while other patients have recurring instances. It has been estab-

\*Corresponding Author: Fatemehsadat Rahimi; Clinical Research and Development Center, Department of Surgery, Shahid Modarres Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Tel: +989128303107, Email: trahimi@sbmu.ac.ir, ORCID: <https://orcid.org/0000-0001-8463-6214>.



lished that diabetes mellitus (DM) is related to occurrence of anal abscess (5). Also, the prevalence of anal abscess is recognized to be significantly more in cases afflicted with type 2 diabetes mellitus (T2DM), than those with type 1 diabetes mellitus (T1DM), indicating the fact that insulin resistance and metabolic syndrome associated with obesity and lifestyle is more important than autoimmune factors. It's probable that, like several other diabetes sequelae, anal abscess is related to lower glycemic control and hyperglycemia, although the link isn't apparent (5). Recurring anal abscess can last for months or years, and it's linked to a decline in the patient's condition and a decrease in their quality of life (6). Moreover, these repeated anal abscesses raise the health-care system's long-term expenses. Whilst some of the risk factors for occurrence of anal abscess, including high daily salt intake, active smoking, alcohol use, obesity, and DM have been recognized, there is presently a scarcity of information about which patient-related characteristics are most prognostic of anal abscess recurrence (6-8). Moreover, determining the risk factors might also aid one to further comprehend the pathogenesis of anal abscess. Hence, the initial goal of our study has been to evaluate the risk factors for recurrence of anal abscess among T2DM patients with treated initial anal abscess.

## 2. Methods

### 2.1. Study design and setting

This retrospective single-center cross-sectional study was conducted on medical records of T2DM patients hospitalized with the diagnosis of anal abscess in Shahid Modarres Hospital, Tehran, Iran, from December 2016 to December 2020. Shahid Modarres hospital is a tertiary and referral center of general surgery in the west of Tehran, conducting special clinical visit programs for the management and follow-up of T2DM patients under consideration of both general surgeons and internal medicine specialist teams. The study protocol was reviewed and approved by ethics committee of shahid Beheshti university of medical sciences (ethical number: IR.SBMU.MSP.REC.1398.956). All the patients who participated in this study, have provided a letter of consent to cooperate in this essay.

### 2.2. Participants

All adult T2DM patients with diagnosis of anal abscess during the study period were enrolled using census sampling method. Meeting one of the following criteria was considered as verification of diabetes mellitus during the initial admission: 1. A level of fasting plasma glucose (FPG) exceeding 126 mg/dL (7.0 mm/L), or 2. Hb A1C greater than 6.5%. Anal abscess was defined based on International Classification of Diseases, Eleventh Revision (ICD-11)(9).

Individuals infected with human immunodeficiency virus

(HIV) or afflicted with other immune-compromising conditions, including those with more than 2 mg/kg steroid drug intake/day, gastrointestinal malignancies, and Crohn's disease, and those who were expired during the first hospitalization or had incomplete medical documentation were excluded. All the patients received surgical treatment of incision and drainage with or without fistulotomy/ fistulectomy and antibiotic therapy as appropriate.

### 2.3. Data gathering

Potential risk factors of anal abscess recurrence were divided into 7 categories: 1. Demographic factors: age, gender, history of smoking and alcohol consumption, 2. Underlying diseases: metabolic syndrome, hypertension, dyslipidemia, end stage renal disease (ESRD), coronary artery disease (CAD), chronic kidney disease (CKD), and peripheral vascular disease, 3. Diabetes-related factors: diabetes duration, Hemoglobin A1c (HbA1c) levels, and diabetic foot ulcer, 4. Clinical status: presence of fever, length of hospitalization, and surgical site infection 5. Laboratorial findings: white blood cell count (WBC), estimated glomerular filtration rate (e-GFR), C-reactive protein (CRP), creatinine, and albumin, 6. Types of anal abscess: perianal, ischio-rectal, inter-sphincteric, supralelevator, as well as fistula formation, and 7. Microbiology based on abscess culture results. All data were gathered based on patients' electronic medical documents, extracted by two skilled medical researchers, and were double-checked before being entered into analysis.

### 2.4. Statistical analysis

SPSS version 25.0 (SPSS, Chicago, IL, USA) or R software version 3.6.3 were employed to carry out the statistical analysis. Data were analyzed using the Shapiro-Wilk test to confirm their normal distribution. Categorical and continuous variables were presented as case number (percentage) and mean  $\pm$  standard deviation, respectively. To compare the categorical variables, Chi-Squared or Fisher's exact test was utilized as appropriate. Independent t-test, or Mann-Whitney U test was used for comparison of means between continuous variables as necessitated. The mentioned potential risk factors for anal abscess have been assessed utilizing multivariate logistic regression test and indicated as Odds Ratio (OR) and 95% confidence interval. Moreover, the receiver operating characteristic (ROC) curves were drawn to find the predictive values of HbA1c, CRP, and WBC levels regarding anal abscess relapse. Two-sided p-value of less than 0.05 has been deemed statistically significant.



**Table 1:** Comparing the demographic, clinical, and laboratory parameters of diabetic patients with and without recurrent anal abscess

Characteristics	Recurrent anal abscess		P
	Yes (n = 58)	No (n = 145)	
<b>Demographic</b>			
Age (year)	45.9 ± 7.8	48.1 ± 8.3	0.08
Gender (male)	43 (74.1)	105 (72.4)	0.80
Active smoking (yes)	19 (32.7)	37 (25.5)	0.29
Smoking Pack-year	11.3 ± 5.7	9.9 ± 4.7	0.07
Alcohol consumption	7 (12.1)	19 (13.1)	0.84
<b>Comorbidities</b>			
Metabolic syndrome	22 (37.9)	25 (17.2)	0.001
Hypertension	46 (79.3)	127 (87.6)	0.13
Dyslipidemia	32 (55.2)	102 (70.3)	0.06
Coronary artery disease	34 (58.6)	53 (36.5)	0.001
Chronic kidney disease	29 (50)	48 (33.1)	0.02
End stage renal disease	10 (17.2)	9 (6.2)	0.01
Peripheral vascular disease	10 (17.2)	11 (7.6)	0.04
<b>Diabetes-related factors</b>			
Diabetes duration	13.0 ± 4.6	11.9 ± 6.1	0.21
HbA1C	6.0 ± 1.4	5.8 ± 1.5	0.38
Poor glycemic control (HbA1C>7.5)	42 (72.4)	61 (42.1)	0.001
Diabetic foot ulcer	7 (14.6)	9 (6.2)	0.16
<b>Clinical</b>			
Fever	53 (91.4)	136 (93.8)	0.54
Length of hospital stay (days)	12.3 ± 2.7	11.2 ± 6.6	0.22
Surgical site infection	3 (5.2)	9 (6.2)	0.77
<b>Laboratory findings</b>			
White blood cell (/mm <sup>3</sup> )	15.5 ± 7.9	13.1 ± 6.1	0.02
C-reactive protein (mg/dl)	7.9 ± 3.1	6.7 ± 3.5	0.02
E* <sub>g</sub> - glomerular filtration rate (ml/min)	88.3 ± 6.3	91.9 ± 10.7	0.02
Creatinine (mg/dl)	1.2 ± 1.3	1.0 ± 1.2	0.29
Albumin (g/l)	3.7 ± 1.6	4.0 ± 1.8	0.27

Data are presented as mean ± standard deviation or frequency (%). Hb: hemoglobin; \*: estimated.

**Table 2:** Comparing the abscess characteristics of diabetic patients with and without recurrent anal abscess

Characteristics	Recurrent anal abscess		P
	Yes (n = 58)	No (n = 145)	
<b>Anal abscess type</b>			
Perianal	34 (58.6)	91 (62.7)	0.58
Ischiorectal	13 (22.4)	24 (16.5)	0.32
Inter-sphincteric	5 (8.6)	21 (14.5)	0.26
Supralelevator	6 (10.3)	9 (6.2)	0.30
Formation of fistula	19 (32.7)	39 (26.9)	0.40
<b>Culture</b>			
Gram-positive and Gram-negative aerobic bacteria	7 (12.1)	13 (8.9)	0.50
Gram-positive aerobic bacteria only	9 (15.5)	25 (17.2)	0.46
Gram-negative aerobic bacteria only	6 (10.3)	11 (7.6)	0.52
Anaerobic bacteria only	2 (3.4)	4 (2.7)	0.79
Mixed aerobic and anaerobic flora	25 (43.1)	50 (34.5)	0.25
No culture result	9 (15.5)	42 (28.9)	0.07

Data are presented as frequency (%).

### 3. Results

#### 3.1. Baseline characteristics of studied cases

A total of 252 cases, diagnosed with anal abscess based on ICD-11 definition, were evaluated. 49 cases were excluded

and finally, 203 patients with T2DM who were hospitalized with the diagnosis of anal abscess for the first time were enrolled in the study (figure 1). The perianal type was the most



**Table 3:** Multivariate stepwise logistic regression analysis for independent risk factors of recurrent anal abscess in type 2 diabetes mellitus patients

Factor	Unit/level	OR	95% CI	P-value
HbA1C	> 7.5%	2.68	1.37-5.25	0.00
C- reactive protein	> 5 mg/L	2.04	1.05-3.94	0.01
White blood cells	>11.0 ×10 <sup>9</sup> /L	1.35	1.15-1.58	0.01
Metabolic syndrome	Presence vs Absence	1.99	1.02-3.85	0.04

Hb: hemoglobin; OR: odds ratio; CI: confidence interval.

common form of abscess. 58 (28.6%) patients had at least one re-occurrence of anal abscess in the following four years after initial treatment. The recurrence episodes had more frequently occurred during the first year after the initial treatment (55.2%) compared to second year (18.9%), third year (15.5%), and fourth year (10.3%) (Figure 2). Fistula formation was observed in 32.7% and 26.9% of patients with and without recurrence, respectively ( $p = 0.4$ ).

### 3.2. Risk factors of recurrence

Tables 1 and 2 compare the demographic, clinical, and laboratory parameters as well as abscess characteristics of diabetic patients with and without recurrent anal abscess.

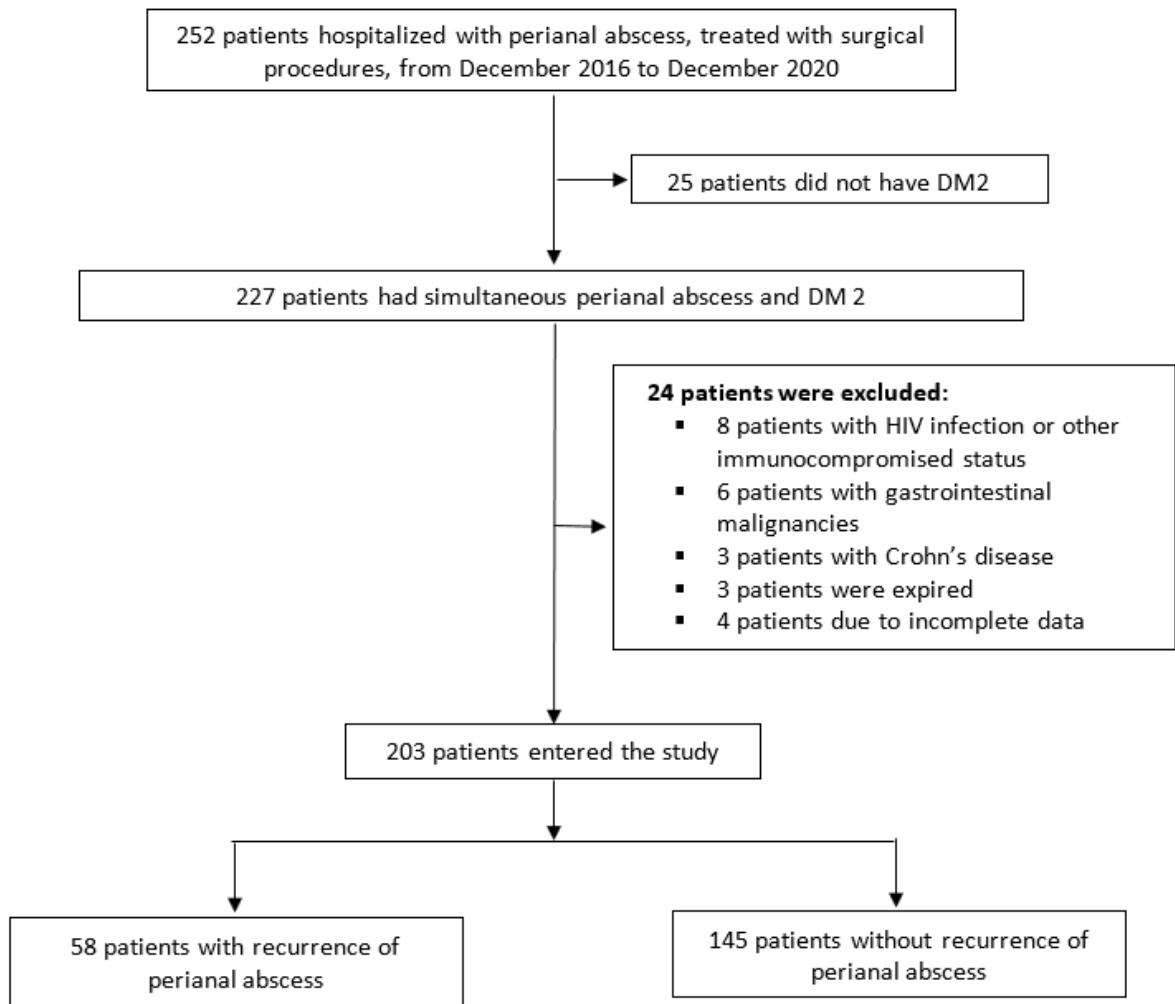
The mean age of patients with and without recurrence was  $45.9 \pm 7.8$  and  $48.1 \pm 8.3$  years, respectively ( $p = 0.08$ ). Also, both groups had similar sociodemographic characteristics in terms of male gender predominancy (47.1% vs. 72.4%,  $p = 0.80$ ), smoking (32.7% vs. 25.5%,  $p = 0.29$ ), severity of smoking ( $11.3 \pm 5.7$  vs  $9.9 \pm 4.7$  packyear,  $p = 0.07$ ), and alcohol consumption (12.1% vs 13.1%,  $p = 0.07$ ). The prevalence of metabolic syndrome, coronary artery disease, chronic kidney disease, end stage renal disease, and peripheral vascular disease comorbidities were significantly higher amongst patients with abscess re-occurrence.

The patients with recurrent anal abscess had statically significant poor glycemic control (HbA1C > 7.5), decreased levels of Estimated Glomerular Filtration Rate (e-GFR), and higher C-reactive Protein (CRP) upon the first admission. On microbiological evaluation, the mixed aerobic and anerobic bacteria flora was the most prevalent culture result ( $p = 0.25$ ).

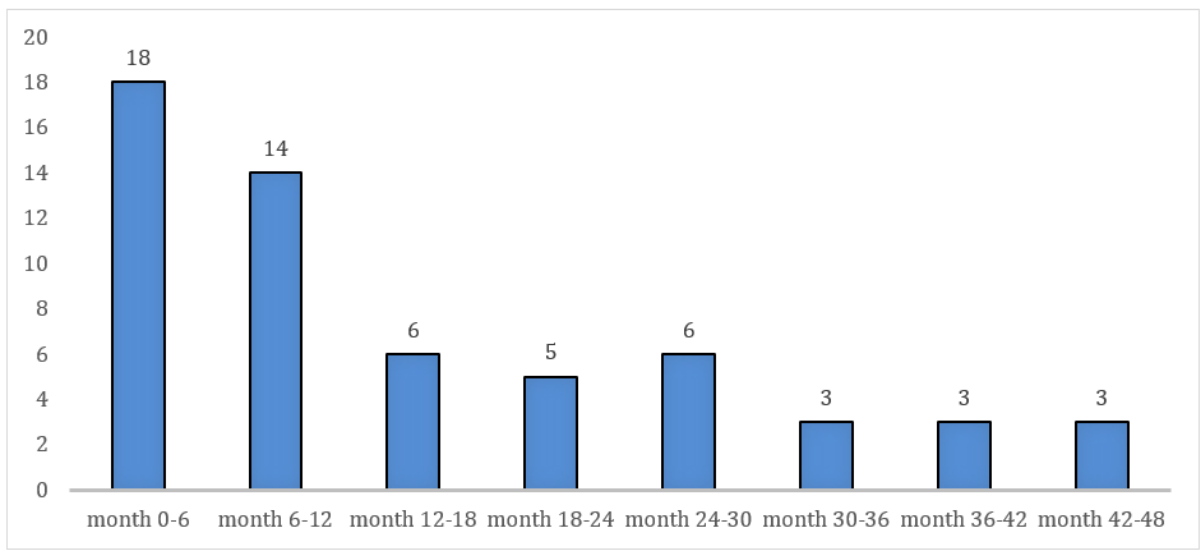
Based on the multivariate step-by-step logistic regression analysis on all potential predictors of perianal abscess recurrence (table 3), it was found that the independent risk factors were: presence of metabolic syndrome, HbA1c > 7.5%, WBC > 11.0 ×10<sup>9</sup>/L, and CRP > 5 mg/l. Amongst them, HbA1c > 7.5% as indicator of poor glycemic control was the most important independent risk factor of anal abscess recurrence (OR=2.68, 95% CI: 1.37-5.25;  $p < 0.001$ ). The area under the ROC curve (AUC) of HbA1C, CRP, and WBC in predicting the risk of abscess recurrence was 0.81, 0.71, and 0.64, respectively (figure 3).

## 4. Discussion

This 4-year retrospective single-center study of T2DM patients with an initial treated anal abscess demonstrated a high incidence for anal abscess recurrence (28.6%). As mentioned above, we discovered that amongst a wide range of possible risk factors, the ones consistently linked to recurring anal abscess were: 1. metabolic syndrome, 2. HbA1c > 7.5%, 3. WBC > 11.0 ×10<sup>9</sup>/L, and 4. CRP levels of more than 5 mg/l. Unfavorable glycemic control, described as having HbA1c levels of more than 7.5%, was recognized as the most prominent predisposing factor for abscess recurrence in the present study. These findings are supported by previous studies that stated HbA1c levels are markedly higher in those with relapse of both diabetic ulcer and anal abscess compared to those without re-occurrence (5, 10). Inadequate long-term blood glucose control may hinder healing of wounds, but it might also represent lower patient adherence to different preventative strategies, such as glycemic control self-monitoring and compliance with anal abscess treatment guidelines (11). Poor psychological support and patient education and may also be linked to a greater likelihood of anal abscess relapse (12). Additionally, we discovered that high CRP levels were an established risk factor for re-occurrence of anal abscess. Since the patients had no additional inflammatory or infectious disorders during our clinical evaluation, the increased CRP upon presentation was most likely due to infections. It was previously shown that increased amount of CRP was related to ensuing complications in a long-term analysis of peri-anal abscess (13-15). Although some studies have shown that higher CRP levels are linked to an elevated risk of sequelae and re-occurrence of the anal abscess, there have not been any formerly published evidence on the prognostic accuracy of CRP for anal abscess relapse. Eventually, we noticed that culture findings of patients with recurring anal abscess were identical to those of non-recurring patients. Abscess cultures frequently feature mixed anaerobic and aerobic microorganisms, as we discovered in our investigation. The skin and the gastrointestinal tract provide the majority of microorganisms in an anal abscess (16). Pepto streptococcus spp. and Bacteroides spp. were prevalent anaerobic pathogens in individuals, whereas Klebsiella

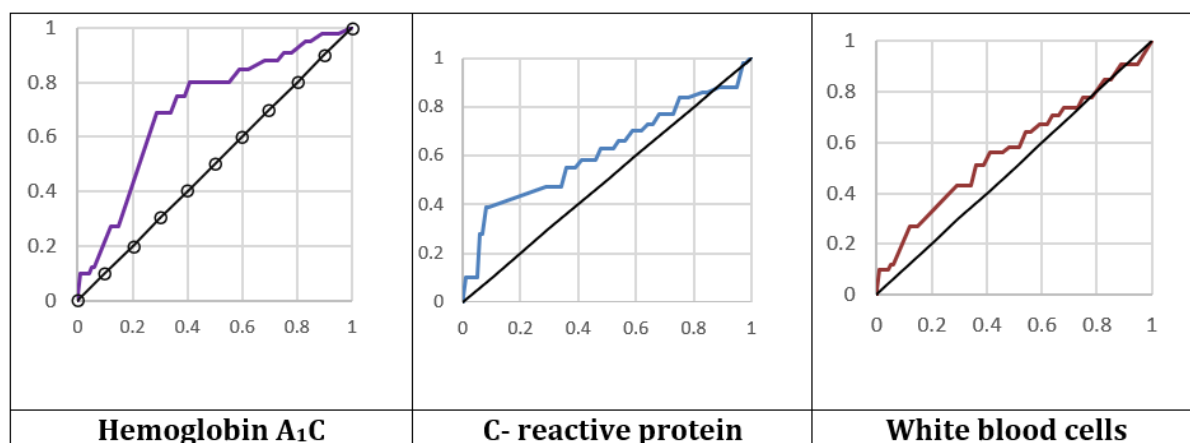


**Figure 1:** Flowchart of patients' enrollment in the study.



**Figure 2:** Frequency of perianal abscess recurrence in diabetes mellitus type 2 patients during 4-year follow-up.





**Figure 3:** Area under the receiver operating characteristic (ROC) curve (AUC) of hemoglobin A1C (AUC = 0.81), C- reactive protein (AUC = 0.71), and white blood cells (AUC = 0.64) in predicting the recurrence of perianal abscess in patients with type 2 diabetes mellitus.

pneumoniae, Staphylococci spp., and Escherichia coli, were prominent aerobic pathogens. T2DM patients are thought to have decreased adaptive and native immunity, according to current findings (17, 18). Hence, antibiotic treatment may be explored in all diabetic patients, even if post-surgical antibiotic therapy had a limited function in uncomplicated anal abscess. Both anaerobic and aerobic bacteria could be fully covered by empiric antibiotic therapy (19).

We propose that, given the considerable risk of recurring anal abscess, preventative programs focusing on cases recognized to be in the high-risk categories would be suitable. This might entail endeavors to inform individuals and the correspondent healthcare professionals on treatments found to be successful in avoiding anal abscess development and relapse. Reoccurrence of rectal abscess is not reported to increase the rate of mortality per se, but could remarkably increase morbidity and influence life quality of patients. This event could be even more important as we found that the majority of patients facing with anal abscess are in their youth (45.9 years  $\pm$  7.8). Of note, we found that the main risk factors of abscess recurrence are directly or indirectly related to metabolic disorders, such as obesity and uncontrolled plasma glucose levels. These variables are considerably preventable and manageable despite being extremely prevalent. Hence, the authors suggest that clinicians closely follow up patients with higher risk of abscess recurrence to better control their diabetes mellitus, diets, and physical activity in order to reduce the burden of anal abscess and the resulting health care expenses.

## 5. Strengths and limitations

Our study had some limitations: first, the relatively small number of included patients; second, the research being performed in a single center; and third, the retrospective ar-

rangement of the study were the main limitations. Only 48 T2DM patients with recurrence of anal abscess were identified during 4 years. Moreover, the addition of a tertiary center may have resulted in an unwanted selection bias. Indeed, we have to declare that our study could possibly face the following 2 concerns regarding study bias, if any, as the authors believe they did their best to prevent any bias: 1. Selection bias: The presence of missing data can result in selection bias during the course of the study; and 2. Confirmation bias: This may occur during the interpretation of study data when the authors, consciously or unconsciously, look for information or patterns in their data that confirm the ideas they already hold. Notwithstanding, to the best of our knowledge, this is the first-ever analysis focusing on the distinct risk factors of recurring anal abscess in T2DM patients, which evaluates their prognostic validity for anal abscess re-occurrence.

## 6. Conclusion

Our findings demonstrate a high rate of anal abscess recurrence within four years in diabetic patients with anal abscess. The presence of metabolic syndrome, elevated WBC count, an increased CRP (at the time of diagnosing the first anal abscess) and inadequate glycemic management, were independent risk factors for recurring abscess.

## 7. Declarations

### 7.1. Acknowledgments

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## 7.2. Authors' contributions

NMA: patient management, patient surgical management, data gathering, drafting, reviewing the article, SA: writing manuscript, data gathering, designation of figures, conducting statistical analysis, FET writing manuscript, data gathering, designation of figures, conducting statistical analysis, MF Final review, conceptualization, SB: patient management, patient disease diagnosis, data gathering, writing discussion, FR writing manuscript, data gathering, designation of figures, conducting statistical analysis, final review.

## 7.3. Funding and supports

This project did not have any sources of financial support.

## 7.4. Conflict of interest

No conflict of interest is declared by the authors of this study.

## 7.5. Sources of funding

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