

Blood Sugar Trends in Patients with Diabetic Foot Ulcers: A Comparative Study before and after Amputation Surgery

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Abstract

Background: The diabetic foot is a chronic complication of diabetes. There is a strong relationship between glucose levels, the severity of diabetic foot ulcers (DFUs), and the need for amputation. This study aimed to evaluate the blood sugar (BS) trends before and after surgery in patients with DFU who had been amputated.

Methods: The adult patients who had undergone DFU-related amputation surgery between 2017 and 2020 in Imam Khomeini Hospital Complex, Tehran, Iran, were evaluated. The cases whose BS levels were charted at least three days before and after amputation were recruited. The main data, including hypoglycemia (defined as a blood glucose level < 70 mg/dl) and mean BS and fasting BS (FBS) levels, were recorded. The data were then analyzed and compared before and after amputation.

Results: Of 267 patients reviewed for inclusion criteria, 55 patients were included in the study. Twenty-eight patients (50.9%) were men, and the mean age was 60 years. The mean FBS before and after amputation was 229.5 and 181.3 mg/dl, respectively, and the mean BS before and after amputation was 227.3 and 197.8 mg/dl, respectively. The differences were significant ($P < 0.001$). Twelve patients (21.8%) before and 21 patients (36.4%) after amputation suffered from hypoglycemia ($P = 0.057$).

Conclusion: DFU-related amputation is associated with a significant decrease in blood glucose levels and inflammatory indexes. However, it can increase the risk of hypoglycemia during the first three days after the surgery.

Keywords: Diabetic Foot; Amputation; Ulcer; Blood Sugar

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Background

Diabetes mellitus (DM) is a main public health issue worldwide. The number of patients with diabetes has been estimated to increase from 171 million in 2000 to 366 million in 2030 (1). In 2002, the frequency of type II DM among Iranian people was estimated to be three million people (7.7%) (2). Every year, 2.5% of patients with diabetes develop diabetic foot ulcers (DFUs), of whom 15% suffer from ulcer-related complications (3, 4). The prevalence of DFUs in Iranian people with diabetes is approximately 6% (5).

DFUs are among the common complications of chronic DM, occurring in uncontrolled blood glucose levels (6). If not treated quickly, the ulcers result in infections, which may destruct the deep tissues and bones and necessitate amputation as the only treatment choice (7). DFUs are responsible for 50%-58% of non-traumatic amputations in the world annually. The treatment cost of DFUs is reported to be more than one billion dollars annually (7, 8).

The association of uncontrolled DM with postoperative complications and adverse outcomes has been established

in patients with diabetes undergoing surgery (9).

Therefore, the management of blood glucose in surgeries in patients with diabetes is crucial. However, the management protocols vary in different surgeries and are highly controversial (10). Currently, there is a lack of studies investigating blood glucose levels before and after DFUs-related amputations (11).

This study aims to evaluate and compare the blood glucose trends before and after surgery in patients with diabetes who have been amputated.

Methods

This retrospective cross-sectional study was conducted on patients with DFU in Imam Khomeini Complex Hospital, Tehran, Iran. The data from the patients with DFU admitted from 2017 to 2020 were extracted from the hospital's electronic record system. The patients included in this study were adult patients with DFU who underwent lower extremity surgery involving at least one toe amputation according to their surgical report and had their blood sugar (BS) regularly charted four times a day



for at least three days before and after amputation. The collected data were patients' demographic characteristics, past medical history, history of amputation, diabetic profile details and inflammatory lab indexes, details of the foot wound based on Wagner classification, amputation levels, medication history for controlling diabetes, and hypoglycemia (defined as a blood glucose level of < 70 mg/dl) (12).

For each patient, a BS chart comprising fasting BS (FBS), pre-dinner and pre-lunch BS, and postprandial blood glucose before bedtime was prepared based on the hospital recording chart. The mean BS and FBS were calculated for 72 hours before and after amputation and compared. The BS monitoring was performed by portable electronic devices (glucometer) at the patient's bedside.

The data were imported to a database Excel file, and data cleaning was conducted. Eventually, the descriptive and comparative analyses were carried out using SPSS software (version 20.0, IBM Corporation, Armonk, NY, USA). The normal distribution was confirmed by Kolmogorov-Smirnov test, and the general linear model (GLM) repeated measures analysis of variance (ANOVA) was used for the same measurements at different times on each patient's BS profile.

The study was approved by the Research and Ethics Committee of Tehran University of Medical Sciences with the code IR.TUMS.IKHC.REC1396.4894.

Results

Out of 267 patients with DFU who underwent amputation, 55 patients were included based on the inclusion criteria. Almost half of the patients ($n = 28, 50.9\%$) were men, the mean age was 60 years (38-87 years), and the mortality rate was estimated at 9.1%. Regarding blood glucose control methods, 17 patients (30.9%) had a history of using oral antihyperglycemic agents, 11 patients (20%) used insulin, and almost half of the patients (49.1%) had a combination of insulin and oral agents before hospitalization. The most common comorbidity was hypertension (HTN), which was observed in 32 patients (58.2%). The mean years of diabetes diagnosis were estimated at 14.5 years (1-30). The mean length of hospitalization was 20 days (6-66).

Wagner classification showed that 30 patients (54.5%) were in grade 3, 20 (36.4%) were in grade 4, and 5 (9.1%) were in grade 5 upon admission. Moreover, 14 patients (25.5%) had an amputation history. In terms of amputation level, 34 patients (61.8%) had a below-knee amputation, 14 (25.4%) had a metatarsal amputation, 5 (9.1%) had a thumb amputation, and 2 (3.7%) had a toe amputation.

The mean level of FBS before and after amputation was 229.55 and 181.30 mg/dl, respectively, and the mean level of BS before and after amputation was 227.38 and 197.85 mg/dl, respectively. The mean levels of FBS and BS were significantly lower ($P < 0.001$) after the amputation (Table 1 and Figure 1).

Variables	Three days before amputation	Three days after amputation	P-value
BS (mg/dl) (mean)	227.38	197.85	< 0.001
FBS (mg/dl) (mean)	229.55	181.30	< 0.001
Hypoglycemia [n (%)]	12 (21.80)	21 (36.40)	0.057
WBC count ($\times 10^3$ /ml)	17.30	8.90	0.001
CRP (mg/l)	92.83	34.66	0.001
ESR (mm/h)	112.53	51.44	0.001

BS: Blood sugar; FBS: Fasting blood sugar; WBC: White blood cell; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate

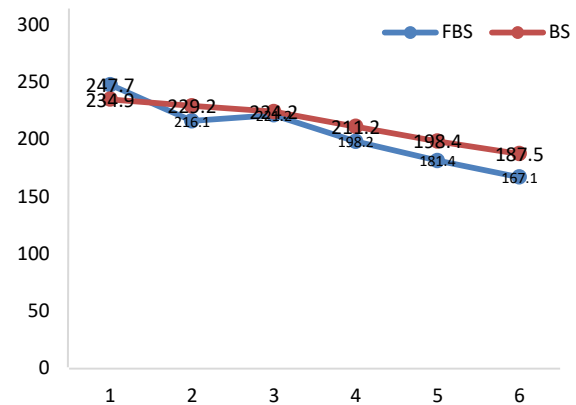


Figure 1. The comparison of mean blood sugar (BS) and fasting blood sugar (FBS) levels before and after the amputation

In addition, the differences between the mean white blood cell (WBC) counts, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) levels before and after the amputation were significant ($P = 0.001$) (Table 1).

The result of assessing the effects of and interactions between the patient's demographic and laboratory data, including gender, age (≤ 60 or above), duration of diabetes (12 years or above), HTN status (yes or no), length of stay (LOS) in hospital (< 20 days or above), diabetic ulcer (Wagner grades), and having fever ($> 38^\circ\text{C}$) on blood glucose indicated no statistically significant effect on FBS and BS trends before and after the surgery. In other words, the difference between pre and postoperative FBS and BS did not depend on patients' demographic and clinical data.

12 patients (21.8%) had hypoglycemia before amputation, and 21 patients (36.4%) suffered from hypoglycemia after amputation ($P = 0.057$).

Discussion

This study assessed the blood glucose levels and relevant factors in patients with diabetic foot before and after amputation. In the present study, the number of male patients admitted with complicated DFUs was higher than female ones (50.9%), similar to many previous studies, and due to the high prevalence of atherosclerosis in men (13-15). Moreover, the average time from the diagnosis of diabetes to admission for DFU was 14.5 years (1-30 years), contrary to similar studies with approximately ten years (16).

Preoperative hyperglycemia has a strong relationship with mortality rate in surgical procedures (9, 17). However, the preoperative BS controlled by insulin can improve a patient's survival rate (11). According to the guideline, the BS level in patients after surgery is considered between 140 to 180 mg/dl (18). However, despite the higher level of post-amputation BS in the present study (197.85 mg/dl), the rate of postoperative hyperglycemia increased.

The hypoglycemic and hyperglycemic conditions negatively affect diabetic patients' outcomes admitted in hospital (19). The most important cause of hypoglycemia in hospitalized patients with DM is decreased calorie intake (20). The main concern is that the symptoms of hypoglycemia usually develop very quickly and can even lead to death (11). Therefore, according to the study outcomes, controlling the fluctuating levels of blood glucose, especially in post-amputation hypoglycemia, can be a necessary therapeutic action.

In most cases, increased inflammatory markers in patients with DFUs are strongly in favor of the infection. The high serum levels of ESR has also reported to be significantly associated with osteomyelitis (21). According to our findings, the postoperative decrease in mean blood glucose was accompanied by a dramatic drop in leukocytosis, ESR, and CRP. The levels of CRP and ESR significantly declined in patients with infected DFUs after therapeutic management (22). Besides, there is a significant reduction in the inflammatory process in the patients receiving effective treatment, including infection source control after diabetic foot amputation.

Conclusion

Amputation can be an important way to control hyperglycemia in DM patients with DFU. Although DFU-related amputation is associated with a dramatic drop in inflammatory indexes, it can increase the risk of hypoglycemia during the first three days after the surgery.

Conflict of Interest

The authors declare no conflict of interest in this study.

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References

- Lantion-Ang LC. Epidemiology of diabetes mellitus in Western pacific region: Focus on Philippines. *Diabetes Res Clin Pract.* 2000;50(Suppl 2):S29-S34. doi: [10.1016/S0168-8227\(00\)00176-5](https://doi.org/10.1016/S0168-8227(00)00176-5). [PubMed: [11024581](https://pubmed.ncbi.nlm.nih.gov/11024581/)].
- Larejani B, Zahedi F. Epidemiology of diabetes mellitus in Iran. *Iran J Diabetes Lipid Disord.* 2001;1(1):1-8. [In Persian].
- Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. *Diabetes Care.* 2004;27(5):1047-53. doi: [10.2337/diacare.27.5.1047](https://doi.org/10.2337/diacare.27.5.1047). [PubMed: [15111519](https://pubmed.ncbi.nlm.nih.gov/15111519/)].
- Dunstan DW, Zimmet PZ, Welborn TA, de Courten MP, Cameron AJ, Sicree RA, et al. The rising prevalence of diabetes and impaired glucose tolerance: The Australian Diabetes, Obesity and Lifestyle Study. *Diabetes Care.* 2002;25(5):829-34. doi: [10.2337/diacare.25.5.829](https://doi.org/10.2337/diacare.25.5.829). [PubMed: [11978676](https://pubmed.ncbi.nlm.nih.gov/11978676/)].
- Esteghamati A, Larijani B, Aghajani MH, Ghaemi F, Kermanchi J, Shahrami A, et al. Diabetes in Iran: Prospective Analysis from First Nationwide Diabetes Report of National Program for Prevention and Control of Diabetes (NPPCD-2016). *Sci Rep.* 2017;7(1):13461. doi: [10.1038/s41598-017-13379-z](https://doi.org/10.1038/s41598-017-13379-z). [PubMed: [29044139](https://pubmed.ncbi.nlm.nih.gov/29044139/)]. [PubMed Central: [PMC5647418](https://pubmed.ncbi.nlm.nih.gov/PMC5647418/)].
- Katsilambros N, Tentolouris N, Tsapogas P, Dounis E. Atlas of the diabetic foot. Hoboken, NJ: Wiley; 2003. p. 25-6.
- Abolhasani F, Mohagerie Tehrani MR, Tabatabaei O, Larijani B. Burden of diabetes and its complications in Iran in year 2000. *Iran J Diabetes Lipid Disord.* 2005;5(1):35-48. [In Persian].
- Mayfield JA, Reiber GE, Sanders LJ, Janisse D, Pogach LM. Preventive foot care in people with diabetes. *Diabetes Care.* 1998;21(12):2161-77. doi: [10.2337/diacare.21.12.2161](https://doi.org/10.2337/diacare.21.12.2161). [PubMed: [9839111](https://pubmed.ncbi.nlm.nih.gov/9839111/)].
- Frisch A, Chandra P, Smiley D, Peng L, Rizzo M, Gatcliffe C, et al. Prevalence and clinical outcome of hyperglycemia in the perioperative period in noncardiac surgery. *Diabetes Care.* 2010;33(8):1783-8. doi: [10.2337/dci10-0304](https://doi.org/10.2337/dci10-0304). [PubMed: [20435798](https://pubmed.ncbi.nlm.nih.gov/20435798/)]. [PubMed Central: [PMC2909062](https://pubmed.ncbi.nlm.nih.gov/PMC2909062/)].
- Duggan EW, Carlson K, Umpierrez GE. Perioperative Hyperglycemia Management: An Update. *Anesthesiology.* 2017;126(3):547-60. doi: [10.1097/ALN.0000000000001515](https://doi.org/10.1097/ALN.0000000000001515). [PubMed: [28121636](https://pubmed.ncbi.nlm.nih.gov/28121636/)]. [PubMed Central: [PMC5309204](https://pubmed.ncbi.nlm.nih.gov/PMC5309204/)].
- Wallace CR. Postoperative management of hypoglycemia. *Orthopaedic Nursing.* 2012;31(6):334-5. doi: [10.1097/NOR.0b013e318276c1d6](https://doi.org/10.1097/NOR.0b013e318276c1d6).
- American Diabetes Association. Standards of medical care in diabetes-2015 abridged for primary care providers. *Clin Diabetes.* 2015;33(2):97-111. doi: [10.2337/diaclin.33.2.97](https://doi.org/10.2337/diaclin.33.2.97). [PubMed: [25897193](https://pubmed.ncbi.nlm.nih.gov/25897193/)]. [PubMed Central: [PMC4398006](https://pubmed.ncbi.nlm.nih.gov/PMC4398006/)].
- Kahn R. Diabetes technology--now and in the future. *Lancet.* 2009;373(9677):1741-3. doi: [10.1016/S0140-6736\(09\)60960-0](https://doi.org/10.1016/S0140-6736(09)60960-0). [PubMed: [19465215](https://pubmed.ncbi.nlm.nih.gov/19465215/)].
- Levy MJ, Valabhji J. The diabetic foot. *Surgery (Oxford).* 2008;26(1):25-8. doi: [10.1016/j.mpsur.2007.10.013](https://doi.org/10.1016/j.mpsur.2007.10.013).
- Larijani B, Afshari M, Darvishzadeh F, Bastanagh MH, Pajuhi M, Baradar Jalili R, et al. Lowe limb amputation in pateint with diabetic foot ulcer: A 22 year review. *Iran Red Crescent Med J.* 2006;8(3):21-4.
- Kalish J, Hamdan A. Management of diabetic foot problems. *J Vasc Surg.* 2010;51(2):476-86. doi: [10.1016/j.jvs.2009.08.043](https://doi.org/10.1016/j.jvs.2009.08.043). [PubMed: [19853400](https://pubmed.ncbi.nlm.nih.gov/19853400/)].
- Umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, Kitabchi AE. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Endocrinol Metab.* 2002;87(3):978-82. doi: [10.1210/jcem.87.3.8341](https://doi.org/10.1210/jcem.87.3.8341). [PubMed: [11889147](https://pubmed.ncbi.nlm.nih.gov/11889147/)].
- Sudhakaran S, Surani SR. Guidelines for Perioperative Management of the Diabetic Patient. *Surg Res Pract.* 2015;2015:284063. doi: [10.1155/2015/284063](https://doi.org/10.1155/2015/284063). [PubMed: [26078998](https://pubmed.ncbi.nlm.nih.gov/26078998/)]. [PubMed Central: [PMC4452499](https://pubmed.ncbi.nlm.nih.gov/PMC4452499/)].
- Peled S, Pollack R, Elishoov O, Haze A, Cahn A. Association of inpatient glucose measurements with amputations in patients hospitalized with acute diabetic foot. *J Clin Endocrinol Metab.* 2019;104(11):5445-52. doi: [10.1210/je.2019-00774](https://doi.org/10.1210/je.2019-00774). [PubMed: [31246256](https://pubmed.ncbi.nlm.nih.gov/31246256/)].
- Braithwaite SS, Buie MM, Thompson CL, Baldwin DF, Oertel MD, Robertson BA, et al. Hospital hypoglycemia: Not only treatment but also prevention. *Endocr Pract.* 2004;10(Suppl 2):89-99. doi: [10.4158/EP.10.S2.89](https://doi.org/10.4158/EP.10.S2.89). [PubMed: [15251646](https://pubmed.ncbi.nlm.nih.gov/15251646/)].
- Senneville E, Lipsky BA, Abbas ZG, Aragon-Sanchez J, Diggle M, Embil JM, et al. Diagnosis of infection in the foot in diabetes: A systematic review. *Diabetes Metab Res Rev.* 2020;36(Suppl 1):e3281. doi: [10.1002/dmrr.3281](https://doi.org/10.1002/dmrr.3281). [PubMed: [32176440](https://pubmed.ncbi.nlm.nih.gov/32176440/)].
- van Asten SA, Nichols A, La Fontaine J, Bhavan K, Peters EJ, Lavery LA. The value of inflammatory markers to diagnose and monitor diabetic foot osteomyelitis. *Int Wound J.* 2017;14(1):40-5. doi: [10.1111/iwj.12545](https://doi.org/10.1111/iwj.12545). [PubMed: [26634954](https://pubmed.ncbi.nlm.nih.gov/26634954/)]. [PubMed Central: [PMC7949900](https://pubmed.ncbi.nlm.nih.gov/PMC7949900/)].