

# Glycosylated Hemoglobin Level Changes Following Total Knee Arthroplasty in Type II Diabetic Patients: A Retrospective Cohort Study

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## ABSTRACT

**Objectives:** Total knee arthroplasty (TKA) has dramatically improved the quality of life of patients with end-stage arthritis, improving both their physical activity and functioning level. There are sufficient data illustrating the postoperative complications of patients with diabetes undergoing TKA. However, no satisfactory data exist illustrating the relationship of TKA on the glycosylated hemoglobin (HbA1c) levels in patients with type II diabetes postoperatively, which is the aim of this study. **Methods:** This retrospective cohort chart review study was conducted in King Abdulaziz Medical City, Riyadh, Saudi Arabia, where 308 individuals were included after applying the inclusion/exclusion criteria. The primary outcome was to establish if any association exists between type II diabetic patients and postoperative drop in HbA1c levels compared with nondiabetic patients. **Results:** The overall mean age was 65.5 years, and 67% of the total sample were patients with diabetes. Furthermore, 76% of the whole sample underwent unilateral knee surgery. The overall mean for pre- and post-HbA1c were 7.08 and 7.04, respectively. **Conclusions:** In our sample, there were more diabetic patients needing TKA than nondiabetic. It was also noticed that diabetic patients have a higher chance of undergoing bilateral TKA than unilateral when compared to nondiabetic patients, with both results being statistically significant. In addition, postoperative HbA1c level was significantly reduced in diabetic patients who underwent bilateral TKA when compared to diabetic patients who underwent unilateral TKA.

**Keywords:** Diabetes mellitus type II, glycosylated hemoglobin, hemoglobin A1c, Saudi Arabia, total knee arthroplasty

## INTRODUCTION

Since its introduction in the early 1970's, knee arthroplasty has dramatically improved the quality of life of patients suffering from end-stage arthritis, it has also been shown to be one of the most cost-effective procedures in modern medicine.<sup>[1]</sup> In addition, it is associated with an increase in both the physical activity and functioning level of patients, which were measured subjectively by patients' report and objectively by an increase in the knee society score and function score.<sup>[2]</sup> In the United States, >700,000 knee arthroplasty surgeries have been performed in 2012 and > 75,000 in the United Kingdom. These numbers have been increasing every year in developed countries.<sup>[3-5]</sup> The vast majority of total knee arthroplasty (TKA) procedures is performed for osteoarthritis (OA), which is the most common form of arthritis.<sup>[6]</sup> Due to the high prevalence of OA in older age groups, this procedure is frequently done

for people whom are older than 65 years old.<sup>[7]</sup> Because of this rise in this particular population, they usually present with other comorbidities, diabetes mellitus (DM) in particular. OA and DM have been linked to aging and currently about 50% of type II diabetic patients are over 60 years of age.<sup>[8]</sup> Moreover, the estimated prevalence of DM in patients who undergo TKA and total hip arthroplasty (THA) in the United States is >8%.<sup>[9]</sup> Sufficient data exist to illustrate that diabetic

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Received : 02-01-2018

Revised : 25-01-2018

Accepted : 17-03-2018

Published Online : 09-05-2018

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**How to cite this article:** AlTurki A, AlTawayjri I, AlTahan H, Khan A, AlMalki M. Glycosylated hemoglobin level changes following total knee arthroplasty in Type II diabetic patients: A retrospective cohort study. J Musculoskelet Surg Res 2018;2:57-61.

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patients undergoing TKA have shown significant increases in common surgical and systemic complications in addition to mortality during the initial hospital stay.<sup>[9-11]</sup> Such data have shown that diabetic patients undergoing total joint arthroplasty have a higher incidence of infection than patients without diabetes in addition to having a significantly increased risk of pneumonia, stroke after primary arthroplasty. Moreover, previous studies have reported higher rates of infection and wound complications in patients with DM undergoing TKA compared with patients without DM.<sup>[12]</sup> On the other hand, there are no satisfactory data illustrating the effect of TKA on blood glucose levels in the diabetic population postoperatively.<sup>[13]</sup>

The main aim of this study was to investigate the relationship between TKA and glycosylated hemoglobin (HbA1c) level in the diabetic population. It is hypothesized that patients undergoing joint arthroplasty will become more active and experience lower HbA1c levels.

## MATERIALS AND METHODS

### Study design, setting, and subjects

This retrospective cohort chart review study was carried out at the National Guard Health Affairs, Riyadh (Saudi Arabia). The inclusion and exclusion criteria are as follow:

#### Inclusion criteria

Patients aged 18 years or above and underwent a primary TKA for OA with a diagnosis of type II DM on dietary, oral, or insulin treatment. Total eligible individuals estimated to reach 500 patients since 2006 in our facility.

#### Exclusion criteria

1. Type 1 diabetes
2. Patients with other chronic diseases such as congestive heart failure, chronic liver disease, renal failure, and liver failure
3. Patients undergoing Revision TKA.

The participants who had undergone TKA were identified using chart review from electronic medical records, and only the first primary replacement was the index surgery. Collected information were included demographics and all inpatient and outpatient diagnoses in addition to HbA1c laboratory results.

Total included eligible participants were 308 after applying the exclusion criteria.

### Outcome, exposure, and potential confounder variables

Preoperative HbA1c indicates levels before surgery within 5–7 days, and postoperative levels were taken 6 months after the surgery.

Based on the literature review and surgeons input, the potential confounders such as age and gender were adjusted for.

### Biases and sample size

Appropriate statistical methods were used to take into account the correlation of observations (due to bilateral TKA in a

patient, simultaneously or sequentially). The estimated sample size was 350 with expected drop rate of 10%. It was based on a paired *t*-test using 10% difference in their standard deviation (SD) for preoperative and postoperative HbA1c level after surgery and considering a minimally clinically significant result to lower the pre-TKA level by 1%.

### Statistical analyses

Descriptive statistics for demographic and clinical characteristics were measured as mean or median with SDs for continuous variables and as count and percentages for categorical variables. The preoperative and postoperative HbA1c levels were estimated using Pearson correlation. Paired *t*-test was used for preoperative and postoperative observations to see the effect of HbA1c measurements. Chi-square or Fisher's exact test was used to compare categorical variables between diabetic and nondiabetic patients. The general linear model, generalized estimation equation, and MIXED model statistical methods were applied to assess the effect of HbA1c levels for the covariates such as age, gender, DM, OA, and TKA.  $P < 0.05$  was considered statistically significant. The statistical software packages: Statistical Analysis software (SAS) version 94 was used for data analysis (SAS institute, North Carolina, United States) was used for data analysis.

### Ethical considerations

The study was approved by the ethics committee of the Internal Review Board of the King Abdullah International Medical Research Centre, Riyadh, Saudi Arabia.

## RESULTS

### Demographic and clinical characteristics

The overall mean age (mean + SD) was  $65.5 \pm 8.8$  years. The female and males were distributed as 77% and 23%, whereas the diabetic and nondiabetic participants were distributed as 67% and 33%, respectively. Bilateral and unilateral knee surgeries were distributed as 24% and 76%, respectively. The overall mean preoperative and postoperative HbA1c levels were  $7.08 \pm 1.51$  and  $7.04 \pm 1.52$ , respectively. When compared between diabetic and nondiabetic participants, the pre-and post-operative HbA1c levels showed a statistically significant difference. The overall nondiabetic versus diabetic, demographic, and clinical characteristics are presented in Table 1.

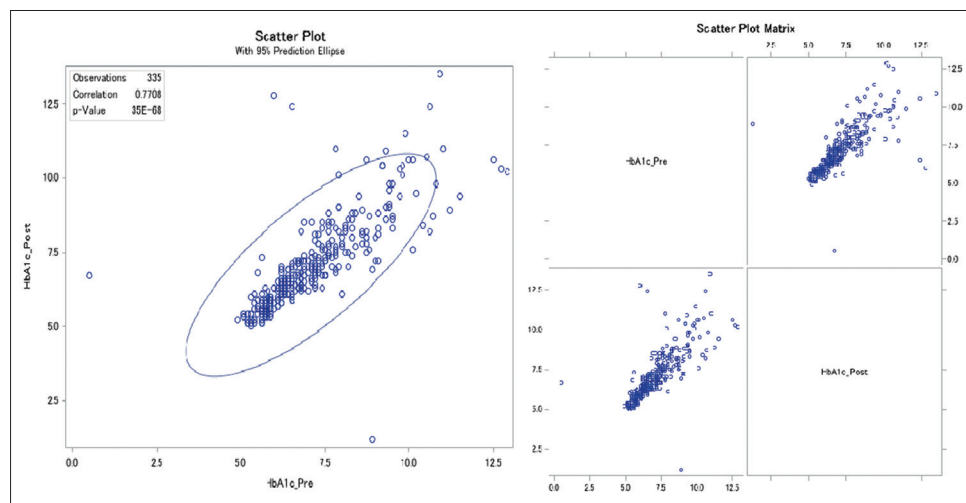
### Univariate and multivariate association of diabetes after total knee arthroplasty

The correlation between pre-and post-operative HbA1c level was 77%, which is statistically significant ( $P < 0.05$ , 95% confidence interval). Scatter diagram for pre-and post-operative HbA1c levels are shown in Figure 1, and the correlation between pre-and post-operative HbA1c level is 68%, which is also statistically significant ( $P < 0.05$ ). Figure 2 shows the regression line for pre-and post-operative HbA1c level at different age categories. The slope line in red shows that older participants have a steeper slope than other age

**Table 1: Basic demographics and clinical characteristics**

Characteristics	Overall	Nondiabetic	Diabetic	P
Age	65.47±8.78	65.5±8.8	65.5±8.7	0.0015***
Gender (%)				
Male	72 (23.4)	21 (6.8)	51 (16.56)	0.8056
Female	236 (76.6)	78 (25.3)	158 (51.3)	
Side-of-surgery (%)				
Unilateral	233 (75.64)	70 (22.72)	163 (52.92)	0.2886
Bilateral	75 (24.35)	30 (9.74)	45 (14.61)	
Reason (osteoarthritis) (%)				
Yes	306 (99.35)	98 (38.81)	208 (67.53)	0.0039***
No	2 (0.64)	2 (0.64)	0	
HbA1c				
Pre	7.08±1.51	5.8±0.38	7.74±1.43	0.0015***
Post	7.04±1.52	5.75±0.4	7.71±1.46	0.0015***

\*\*\* $P < 0.01$ . Age, and HbA1c levels are presented as: Mean±SD. SD: Standard deviation, HbA1c: Glycosylated hemoglobin



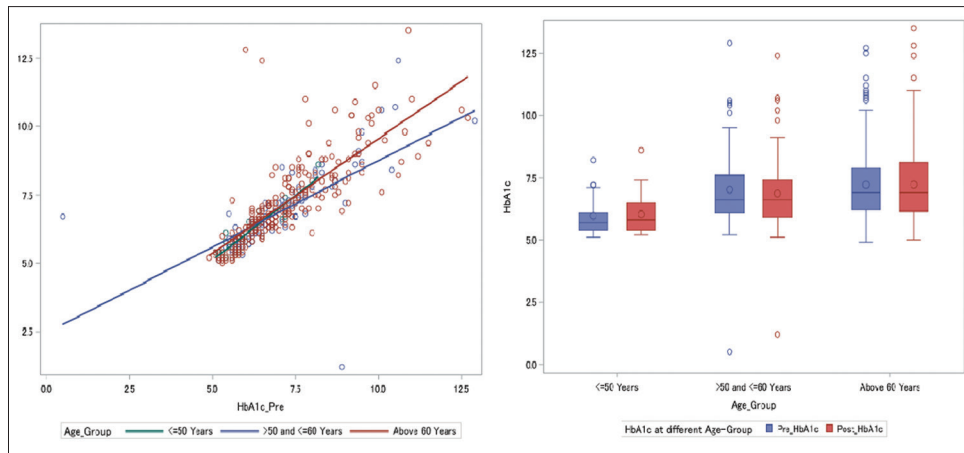
**Figure 1:** Correlation is 77% with 95% prediction ellipse between pre-operative and post-operative glycosylated hemoglobin levels shown in left, and right figure scatter plot is shown

categories, and slope line in blue for other age categories are overlapped, whereas the box plot also shows that postoperative HbA1c level is higher for older population. Moreover, Figure 3 shows HbA1c levels between nondiabetic versus diabetic participants. It shows that HbA1c levels at different age groups get elevated among diabetic participants, whereas it remains almost consistent among nondiabetic participants. Similarly, the mean slope line is higher for diabetic participants. Furthermore, there was no evidence of an association between gender and diabetes ( $P = 0.8056$ , odds ratio of 1.0669). The variable was regrouped as: OA versus others, and this variable versus diabetic and nondiabetic participants shows that there is a statistically significant association between these two variables using ( $P < 0.05$ ). Moreover, paired  $t$ -test was performed and showed no statistically significant difference between pre-and post-operative HbA1c levels ( $t = 0.33$ ,  $P = 0.7403$ ). Furthermore, the analysis of covariance was modeled for the pre-and post-operative HbA1c along with the covariates such as Gender and TKA, which was significant

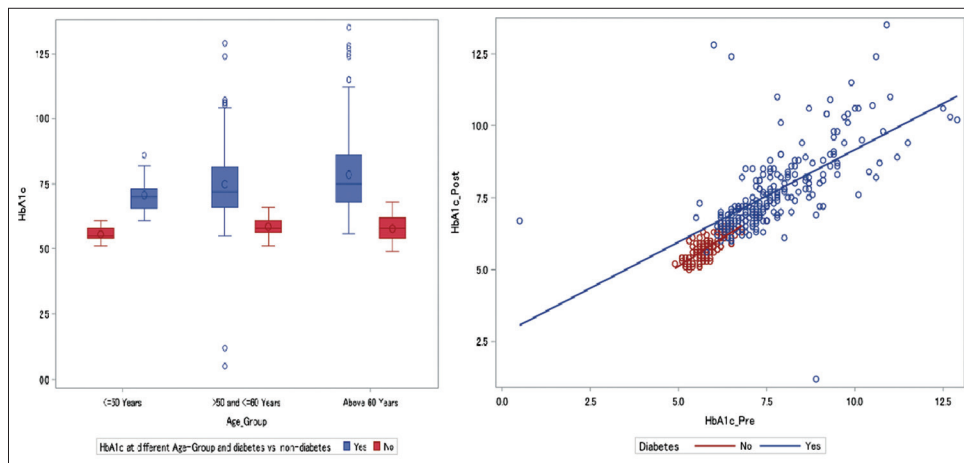
overall ( $P < 0.05$ ). A group test statistic for the equality of means is reported for both equal and unequal variances. The equality of variances test indicates a significant difference between unilateral and bilateral surgery side ( $F = 2.15$  and  $P < 0.05$ ).

## DISCUSSION

In the present study, we compared multiple variables in diabetic and nondiabetic patients. Our results could not illustrate any association between gender and DM which is consistent with a previous systematic review.<sup>[17]</sup> There is no statistically significant difference between diabetic and nondiabetic participants in relation to having unilateral or bilateral TKA. However, our study shows that diabetic participants have higher chances of undergoing TKA when compared to nondiabetic participants. In addition, diabetic patients have a higher chance of undergoing bilateral TKA than unilateral when compared to nondiabetic patients, with both results being statistically significant. Additionally, the



**Figure 2:** The slope is steeper (regression line) for participants above 60-year-old as well as higher values after postoperative glycosylated hemoglobin levels



**Figure 3:** The glycosylated hemoglobin levels are constant at different age groups among nondiabetic participants have lower slope shown in red color

level of HbA1c postoperatively was significantly reduced in diabetic patients who underwent bilateral TKA when compared to diabetic patients who underwent unilateral TKA as illustrated in the figures earlier. This significant reduction in postoperative HbA1c levels in bilateral TKA is probably attributed to the greater degree of improvement in clinical outcomes for Oxford Knee Score, Knee Society Score-Functional, and Objective scores and short form 36 (SF-36) as compared to unilateral TKA, as demonstrated by Lim JB.<sup>[14]</sup>

OA was the leading cause of TKA in our study population. It was also highly prevalent amongst diabetic participants compared to nondiabetic participants, which is consistent with a previous local study.<sup>[15]</sup> Louati *et al.* have also illustrated in a systematic review that OA is highly frequent amongst diabetic patients, indicating a possible association between the two diseases, while another prospective study identified a significant association between OA and DM.<sup>[16,17]</sup> When it comes to HbA1c levels in diabetic patients, our study shows no significant difference between the mean pre-and post-operative levels (7.74 and 7.71, respectively). Multiple factors could

be hindering our proposed theory, including the presence of other diseases such as metabolic syndrome, which has shown to be associated with a decrease in physical activity levels and cardiorespiratory fitness.<sup>[18]</sup> Another factor is whether patients had undergone proper postoperative physiotherapy treatment which could not be accurately measured in our study, as part of the treatment includes home physiotherapy which is not easily assessed and measured. Although a prospective study showed that diabetes by itself is associated with poor functional outcome, Artz *et al.* illustrated that proper physiotherapy treatment post-TKA can lead to improvement in the physical function of patients in the first 3–4 months and can extend up to 6 months.<sup>[3,19]</sup>

There are multiple limitations to our study. First, there are other factors, which haven't been measured that could possibly affect the results, including the quality and type of therapy (insulin vs. no insulin), postoperative rehabilitation and physiotherapy, and the presence of metabolic syndrome. Second, patients body mass index levels were not obtained pre-and post-operatively to observe any change, which could have been translated to a likely increase in physical performance.

## CONCLUSIONS

In our sample, there were more diabetic patients needing TKA than nondiabetic. It was also noticed that diabetic patients have a higher chance of undergoing bilateral TKA than unilateral when compared to nondiabetic patients, with both results being statistically significant. Additionally, postoperative HbA1c level was significantly reduced in diabetic patients who underwent bilateral TKA when compared to diabetic patients who underwent unilateral TKA.

We highly recommend further extensive prospective research looking at the effect of TKA on postoperative HbA1c in diabetic patients while putting into account other variables and confounding factors mentioned in our limitations.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

### Authors contributions

AA contributed in conducting the research, choosing the study design and providing research materials. IA conducted the research, collected the data in addition to analyzing it and edited the manuscript. MA collected the data, analyzed it, and contributed in manuscript writing and editing. AK contributed in choosing the study design, analyzing data and editing the manuscript. HA contributed in analyzing the data and editing the manuscript. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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