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UNDERSTANDING THE COMPLEX RELATIONSHIP BETWEEN DIABETES, HBA1C LEVELS, AND PENILE PROSTHESIS INFECTIONS: A COMPREHENSIVE ANALYSIS AND CLINICAL IMPLICATIONS

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Objectives: To investigate the relationship between glycated hemoglobin levels and the incidence of infection in patients undergoing penile prosthesis implant surgery, in order to determine if glycated hemoglobin can serve as a reliable predictor for postoperative infections.

Methods: A prospective comparison research was conducted comparing diabetic and non-diabetic individuals who underwent penile prosthesis implantation to compare patients who developed or did not develop a prosthetic infection.

Results: In total, 100 patients with full records were included in this study. Patients were divided into two groups: non-diabetic (control) and diabetic group (each with 50 patients). The non-diabetic group had a median age of 55 years (range 39-72) whereas the diabetic group had a median age of 57 years (range 35-70). Preoperative HbA1c levels were 4.8% with SD ± 0.66% (range 3.5-6%) for the median and 8.5% with SD ± 0.61% (range 7–10.1%) for the mean respectively. The incidences of postoperative infection were 4% and 6%, respectively. All infections occurred at the skin level, with no prosthetic device infection or device explantation required. As a result, there was no relationship between HbA1c levels and postoperative infection rates; p-value = 0.32.

Conclusions: We found that preoperative haemoglobin A1c level alone does not increase the risk of postoperative infection significantly. Just with the use of preventive measures and special technique strategies infection can be eradicated.

Keywords: Erectile dysfunction; penile prosthesis; infection; HGBA1C; diabetic patients; malleable prosthesis.

INTRODUCTION

Diabetes mellitus is a well-established contributor to erectile dysfunction (ED).[1] Unlike ED associated with other medical conditions, diabetes-induced ED is multifaceted, stemming from vascular, neurogenic, and myogenic dysfunctions.[2] Penile prosthesis implant surgery stands as a widely recognized treatment option for men experiencing erectile dysfunction when conservative therapies have proven ineffective. However, akin to any surgical procedure, concerns about postoperative complications, particularly infection, remain pertinent. Infection following penile prosthesis implant surgery can result in substantial morbidity, necessitate device removal, and demand revision surgery, underscoring the critical importance of identifying reliable predictors to inform preoperative risk assessment and preventive strategies.[3-5]

Extensive research has explored the influence of glycated hemoglobin (HbA1c) levels on the risk of postoperative infection across various surgical interventions, with a particular focus on patients with diabetes mellitus. HbA1c, a measure reflecting long-term glucose control, serves as a widely adopted indicator of glycemic status. Elevated HbA1c levels have been linked to compromised wound healing, heightened infection rates, and adverse surgical outcomes across several surgical specialties.[6]

Nonetheless, the debate surrounding HbA1c's role as a predictor of infection following penile prosthesis implant surgery remains inconclusive. While some studies have suggested a substantial connection between elevated HbA1c levels and increased infection rates, others have failed to consistently establish this correlation. This discordant body of evidence underscores the necessity for further investigation to elucidate the relationship between HbA1c levels and the risk of postoperative infection, particularly within the specific context of penile prosthesis implant surgery.[7]

This comparative study seeks to augment existing literature by scrutinizing the link between glycated hemoglobin levels and the incidence of infection in patients undergoing penile prosthesis implant surgery. Through the evaluation of a patient cohort and the analysis of their HbA1c levels alongside postoperative infection rates, this study aims to provide valuable insights into the viability of HbA1c as a dependable predictor for postoperative infections within this unique surgical domain. The discoveries stemming from this research hold the potential to refine preoperative risk assessment strategies, enhance patient selection criteria, and inform preventative measures to mitigate the occurrence of postoperative infections in individuals undergoing penile prosthesis implant surgery.

METHODS

Study Design and Population:

This prospective comparative study was conducted in the andrology unit of our urology department and included all eligible patients with erectile dysfunction (ED) between January 2022 and January 2023. Ethical approval was obtained from the Medical Research Committee, and informed written consent was obtained from all patients.

Case Identification and Data Collection:

Out of a total of 235 patients with ED in the andrology unit, 100 patients met the inclusion criteria for this study after being categorized into diabetic and non-diabetic groups. Exclusion criteria comprised the absence of a primary penile prosthesis implant (PPI) requirement, HbA1c levels exceeding 11 due to poorly managed diabetes and hyperinsulinemia, which elevated the risk of wound-healing issues, and concurrent PPI and artificial urinary sphincter implantation. Data retrieved from patients' medical records encompassed patient demographics, penile prosthesis type and size, corporal dimensions, relevant laboratory results (including HbA1c), and post-surgery complications, including infections, within a 6-month follow-up period.

Procedures:

In this study, four experienced surgeons specialized in penile prosthesis surgery participated in the procedures. Patients received preoperative instructions emphasizing genital hygiene and care. Surgical anesthesia options included spinal or general anesthesia, with the exclusion of intrathecal (IT) morphine. External genital hair was removed before surgery, followed by a chlorhexidine scrotal wash lasting 10 minutes. Patients received peri-operative infusions of two antibiotics: ceftazidime 1,000 mg intravenously twice daily, commencing no later than one hour before surgery.

A peno-scrotal midline single vertical incision was made to create an entry point for prosthesis insertion into both corpora cavernosa. The Dartos layer was gently dissected, beginning with the urethra and progressing laterally to expose both corporal bodies. One precaution taken to reduce infection risk was the use of a fresh scalpel for corporotomy until the spongy corporal tissue was clearly defined. Metzenbaum scissors were then utilized to distribute this tissue and create the plane for both proximal and distal corporal dilatation.

To prevent contact between the penile prosthesis components and the skin, fresh surgical gloves and sterile drapes were applied immediately before insertion. Continuous irrigation of the corpora cavernosa during surgery was carried out using saline containing gentamicin (80 mg gentamicin in 2 ml saline).

Prosthesis sizing was performed according to measurements, avoiding aggressive overextension of the penis, with a recommendation that the prosthetic implant not extend beyond the proximal one-third of the glans penis to minimize the risk of perforation. In cases where adequate hemostasis was achieved before the procedure concluded, a drain was unnecessary, and urethral catheterization was not required.

Subsequently, a multi-layered surgical closure was performed using 2-0 vicryl to close the corporotomy and the deep dartos layer with a gathering stitch, while a 3-0 monocryl stitch was used for the more superficial dartos layer and skin closure in a simple, interrupted fashion.

Post-surgery, patients received amoxicillin and clavulanate (1000 mg/tablet, two times a day for 10–14 days) and ceftazidime (1000 mg/intravenous, two times a day starting on the second post-operative day for 7 days). Paracetamol was administered for post-operative discomfort management. Maintaining a surgical procedure duration of no more than 20 to 30 minutes and a post-operative hospital stay of 4 to 6 hours aimed to reduce the risk of hospital-acquired infections.

Strict blood glucose management following surgery, not exceeding 180 mg/dl,

was a pivotal measure in infection prevention and the cornerstone of the process.

Statistical Analysis:

Quantitative data are presented as mean ± standard deviation (SD), while qualitative variables are described using numerical and percentage representations. The correlation between qualitative variables was assessed using the Chi-squared test or Fisher exact test, depending on sample sizes. Quantitative variables were analyzed using either the unpaired t-test or the Mann-Whitney U test, considering the data distribution. Relationships between two quantitative variables, such as age and HbA1c, were evaluated using Pearson and Spearman correlation coefficients. Statistical analyses were conducted using software from the Centers for Disease Control and Prevention (CDC) and SPSS, version 25.0. Statistical significance was assumed at $P \leq 0.05$.

RESULTS

In total, the study enrolled 100 patients with complete records, who were categorized into two groups: diabetic and non-diabetic, each comprising 50 patients. The median age for the non-diabetic group was 55 years (range: 39–72), while for the diabetic group, it was 57 years (range: 35–70). Preoperative HbA1c values had a median of 4.8% with a standard deviation (SD) of 0.66% (range: 3.5–6%) for the non-diabetic group and a median of 8.5% with an SD of 0.61% (range: 7–10.1%) for the diabetic group. All penile prostheses (PP) used in the study were of the malleable type, specifically the Tube® (Promedon) malleable devices. Surgical procedures employed a vertical midline peno-scrotal approach for both corpora cavernosa. A surgical procedure duration mean was 23.7 min with SD ± 3.3.

The postoperative infection rates for the non-diabetic and diabetic groups were 4% and 6%, respectively. Notably, all infections were confined to the skin, with no instances of infection affecting the prosthetic device or necessitating device explantation. Consequently, there was no discernible association between HbA1c levels and postoperative infection rates, with a p-value of 0.32. The hospital stay in our study not exceeding the 6 hours to prevent any hospital acquired infections with mean 5.6 hour and SD ± 0.65.

(Table 1) presents a comprehensive dataset comparing patient demographics and comorbidities between individuals who experienced infections and those who did not. In (table 2) factors affect postoperative complication .The results of multivariate analysis did not indicate a statistically significant association between a history of complications related to diabetes mellitus and infection or explantation rates.

Table (1): Patient demographics and comorbidities

Variables	Summary statistics
Age (year) NO(100)	
Mean± S.D.	**56.28±10.19**
Median (IQ range)	**59(35:72)**
Marital state	
Married	**97 (97%)**
Not married	**3 (3%)**
Diabetes mellitus	
Non diabetic	**50 (50%)**
Diabetic	**50 (50%)**
Hypertension	
Not hypertensive	**51(51%)**
Hypertensive	**49 (49%)**
Coronary artery disease	
No	**72 (72%)**
Yes	**28 (28%)**
HgbA1c% of diabetic patients	
Mean± S.D.	**8.45±0.62**
Median (IQ range)	**8.45(7:10.1)**
PSA	**2.0996±1.12**
Mean± s.d.	**2.065(0.16:3.82)**
Median (iq range)	
Penile dopplar finding	**9 (9%)**
Arterial insufficiency	**5(5%)**
Peyronie's disease	**86(86%)**
Venous leak	

PSA; prostate specific antigen -SD; standard deviation – HGB; hemoglobin

Table (2): factors affect postoperative complication.

Variables	CONTROL Non diabetic (N.= 50)	CASES Diabetic (N.=50)	P-value
Age (year)			
Mean± S.D.	**54.78±8.95**	**57.78±11.19**	***
	53.5(39:72)	**60(35:70)**	0.096
Hgb%A1c			
Mean± S.D	**4.826±0.66**	**8.45±0.62**	
Median (IQ range).	**4.9(3.5:6)**	**8.45(7:10.1)**	*** <0.001
Hypertension			
Not hypertensive(51)	**34(68%)**	17(34%)	0.001*
Hypertensive(49)	**16 (32%)**	33(66%)	
Coronary artery disease			
No (72)	**41 (82%)**	31(62%)	0.044*
Yes (28)	**9 (18%)**	19(38%)	
Penile dopplar finding			
Arterial insufficiency(9)	**4 (8%)**	**5 (10%)**	0.856
Peyronie's disease(5)	**3(6%)**	**2(4%)**	
Venous leak (86)	**43(86%)**	**43(86%)**	
Total postoperative complications			
No (87)	**44(88%)**	43(86%)	0.015*
yes(13)	**6 (12%)**	7(14%)	
Total postoperative complications			
No (87)	**44(88%)**	**43(86%)**	
Superficial wound infection(5)	**2(4%)**	**3(6%)**	0.015*
UTI(7)	**4 (8%)**	**3 (6%)**	
Others(1)	**0(0%)**	**1(2%)**	
Patient satisfaction			
Not satisfied (13)	**7 (14%)**	**6 (12%)**	**1.000**
Satisfied (87)	**43(86%)**	**44(88%)**	

***P-value was calculated by Fisher's Exact Test**
**** P-value was calculated by independent sample T-Test**
***** P-value was calculated by Mann-Whitney Test**
P-value less than 0.05 is statistically significant

Figure 1: chlorhexidine scrotal wash was performed to all genital organs from umbilicus to the knee for 10 min.

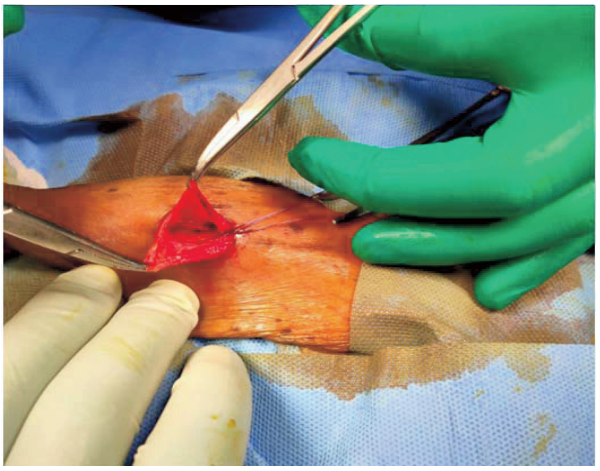

Figure 2: The Dartos layer gently dissected in the midline to expose both right and left corporeal bodies

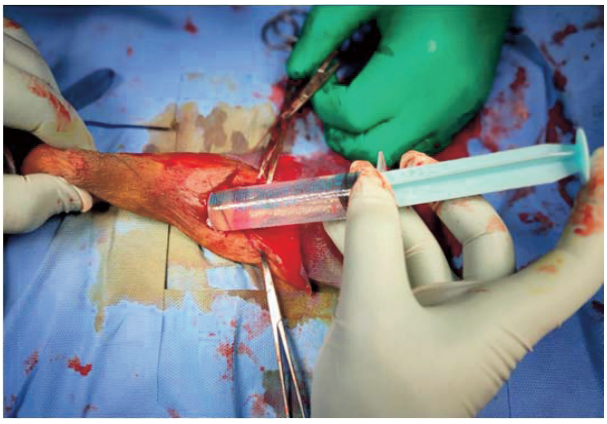

Figure 3: irrigation of the corpora cavernosa using saline containing gentamicin 80 mg ampules

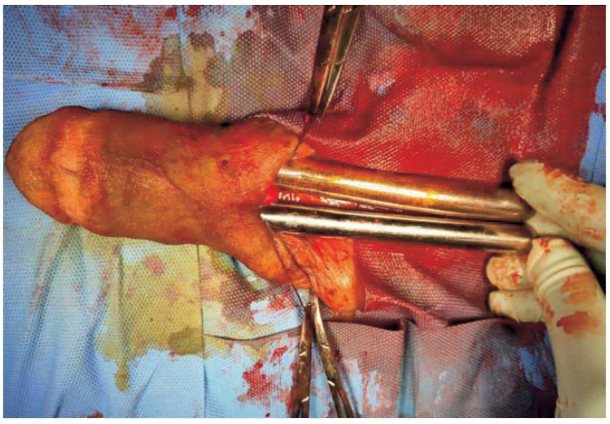

Figure 4: dilatation of both corpora and taking the maximum size and girth, prosthetic implant go no farther than the proximal one-third of the glans penis

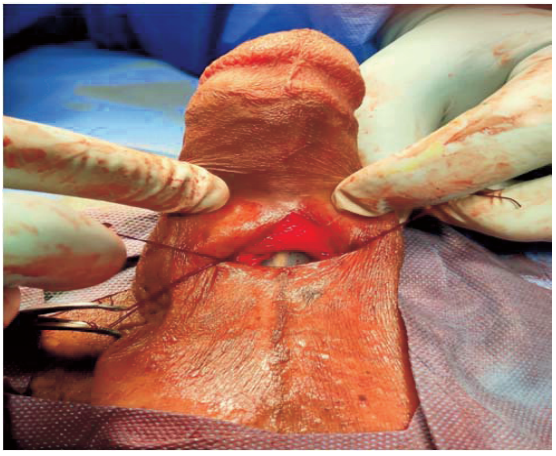

Figure 5: hemostasis and closure over the prosthetic implant without drain

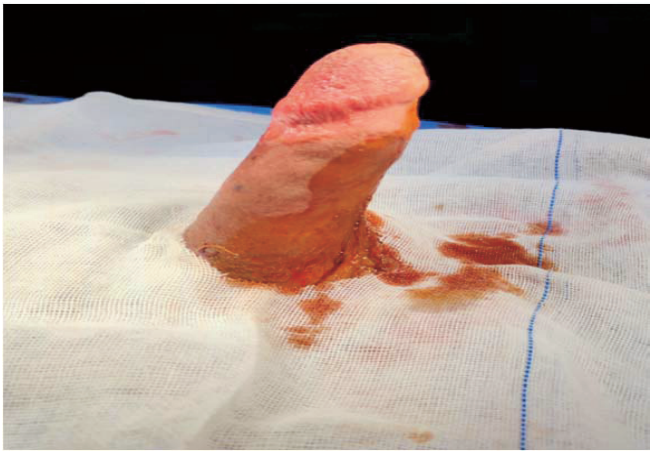

Figure 6: surgical closure with final result from lateral view.

DISCUSSION

In prosthetic urology, infection following penile prosthesis implantation is a significant and worrisome complication. Such infections can result in notable penile shortening and scarring of the corporal bodies, leading to patient dissatisfaction with subsequent penile prosthesis reinsertion.[9] These outcomes not only profoundly affect patients' overall health and well-being but also place a substantial financial and social burden on the healthcare system. The timing, presentation, symptoms, and underlying microbiology of penile prosthesis infection (PPI) can vary considerably, with infections manifesting shortly after implantation or even years later. Clinical presentations range from severe local infection symptoms complicated by sepsis to more subtle symptoms requiring thorough clinical investigation.[10]

Recent technological advancements have contributed to a notable reduction in PPI infection rates. These include the use of Antimicrobial Coated implant components,[11] innovative skin preparation solutions like chlorhexidine,[12] and the adoption of a 'no touch' surgical approach.[8] As a result, the incidence of PPI infection now typically falls within the range of 1% to 3%.[13]

We may be entering a new era of rigorous patient management encompassing preoperative, intraoperative, and postoperative phases. This involves selecting the appropriate device type, ensuring comprehensive antibiotic coverage, irrigating corporal bodies with antibiotics for precise control of post-operative prosthetic infection.

In 2018, Habous et al. conducted a comprehensive multicenter study involving 904 individuals who underwent penile prosthesis surgery between 2009 and 2015.

Their findings indicated that patients who developed infections had significantly higher HbA1c levels compared to those who did not (9.5% vs. 7.8%; $p < 0.001$).[14] Furthermore, there was a clear association between elevated HbA1c levels and increased infection rates when patients were stratified based on their HbA1c levels. However, not all recent studies have observed a consistent correlation between high HbA1c levels and infection risk. A more recent systematic review, spanning from 1960 to 2014, suggested that infection rates in patients with diabetes mellitus were not statistically different from those reported in the general population.[15]

Additional studies, such as one by Osman et al., examined 875 patients who had undergone primary penile prosthesis implantation in a retrospective data analysis from 2003 to 2018. This study found no significant link between preoperative HbA1c levels and surgical infection.16

Similarly, Canguven et al. conducted a retrospective chart review from 2012 to 2016, identifying 300 patients who had received penile prosthesis implants. Only two individuals developed infections, and both had diabetes with HbA1c values of 9%. Intriguingly, not only was HbA1c not correlated with penile prosthesis infection, but the penile prosthesis infection group actually exhibited a lower mean HbA1c than the non-infected group (7.0% ± 0.14 vs. 7.6% ± 1.9).

Despite some conflicting data, the literature largely concurs that diabetes increases the risk of implant infection.[18]

In our study, infection rates were 4% in the non-diabetic group and 6% in the diabetic group, with a p-value of 0.32. This lack of statistical significance, when considering other risk factors and patient variables, suggests that HbA1c levels alone may not serve as a reliable predictor of infection. Traditional treatments for PPI infection typically involve complete device removal with extensive irrigation of contaminated areas or the Mulcahy salvage and washout procedure followed by implant replacement.[19] While these treatments have demonstrated efficacy in appropriately selected patients, they can lead to corporal fibrosis and scarring, making repeat implantation challenging. Aside from the emotional and financial toll on both patients and physicians, the cost of treating PPI infection has been estimated to be more than six times the initial implant cost.[20] Consequently, urologic surgeons seek dependable and clinically effective methods for identifying patients at high risk of PPI infection. Reducing risk factors in such patients can significantly lower the risk of device infection. Beyond diabetes mellitus itself, the management of diabetes in these individuals has emerged as a pivotal factor in understanding the relationship between diabetes and PPI.

Our study has certain limitations. Firstly, its single-center design, coupled with the involvement of expert implant surgeons, raises concerns about the generalizability of the findings. The relatively small patient cohort might introduce potential bias into the results, and the limited sample size may impact the statistical power and robustness of the analyses.

Our study protocol deviates from widely accepted guidelines;[22] however, this is offset by several factors that contribute to a lower infection incidence: (a) intra and post-operative prophylactic antibiotics, (b) the use of a single type of malleable PPI, (c) the 'no touch' technique, (d) avoidance of urethral catheterization intra- and post-operatively, and (e) dedicated postoperative patient follow-up by a specialized team. Despite these limitations and deviations from conventional practices, our study suggests that diabetic patients can undergo penile implant surgery with an acceptable risk of device infection, thus negating the need for extensive pre-operative diabetes management.

CONCLUSIONS

This study underscores that diabetic patients undergoing penile implant surgery may experience infection rates similar to those in non-diabetic patients when strict intraoperative sterile procedures and post-operative prophylaxis and care are standardized. Furthermore, the study indicates that an HbA1c cut-off of 8.5-9% in patients with infections is not predictive of infection occurrence and therefore may not serve as a useful predictive tool in this context.

Limitation:

One limitation of this study is the small sample size. With a larger sample size, we may have been able to detect smaller differences between the groups.

Declarations:

Ethical approval and consent to participate.

Yes, ethical approval obtained from Medical Research Committee of sohag university

faculty of medicine, and informed written consent from all the patients was obtained.

Consent for Publication.

Yes. Obtained directly from patient of legal age.

Availability of data and material.

The data that supports the findings of this study are available from the corresponding author upon reasonable request.

Competing interests.

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Authors Contribution.

Conceptualization and study design done by HM and AR, generation and collection of data done by AM and ER, data analysis and manuscript preparation manuscript review done by EW and EM

All authors have read and approved the manuscript

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List of Abbreviations:

(HbA1c) Haemoglobin A1C
(ED) Erectile dysfunction
(PBG) Preoperative blood glucose
(PPI) Penile prosthesis implant
(CDC) Disease Control and Prevention

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