Journal of Diabetes and Its Complications 26 (2012) 501–505

Contents lists available at SciVerse ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: WWW.JDCJOURNAL.COM

# Incidence of genital infection among patients with type 2 diabetes in the UK General Practice Research Database ☆

Ishan Hirji [a,*], Susan W. Andersson [b], Zhenchao Guo [a], Niklas Hammar [c], Andres Gomez-Caminero [a]

[a] Bristol-Myers Squibb Co., USA
[b] Bayer Pharma AG, Germany
[c] AstraZeneca R&D, Sweden

ARTICLE INFO

*Article history:*
Received 29 November 2011
Received in revised form 21 June 2012
Accepted 22 June 2012
Available online 25 July 2012

*Keywords:*
Type 2 Diabetes
Genital Infections
Vaginitis
Balanitis
GPRD

ABSTRACT

The objective of this population-based study was to evaluate the incidence of vaginitis (females) and balanitis (males) among a cohort of type 2 diabetes patients and compare this risk to patients without diabetes. The study population included 125,237 female patients and 146,603 males identified from GPRD. All patients were followed for 1-year from their study index date for the first record of an infection or a censored event. Among patients with diabetes the incidence of vaginitis was 21.0/1000PY (95% CI 19.8–22.1) with the risk being 1.81 (95% CI 1.64–2.00) greater that patients without diabetes. The incidence of balanitis among diabetes patients was 8.4/1000PY (95% CI 7.8–9.1) with a relative risk of 2.85 (2.39–3.39) compared to patients without diabetes. Additional analyses were performed by HbA1c level. Results from this large population-based study indicate that patients with diabetes are at an increased risk of being diagnosed with infections of the genital tract and patients with poorly controlled diabetes have higher risks.



## 1. Background

Individuals with type 2 diabetes are prone to higher occurrence of certain infections, compared to individuals without diabetes (Joshi, Caputo, Weitekamp, & Karchmer, 1999; Muller et al., 2005; Benfield, Jensen, & Nordestgaard, 2007; Lisboa et al., 2010). Diabetes is considered a risk factor for vaginal infections and balanitis (Bohannon, 1998; de Leon, Jacober, Sobel, & Prevalence, 2002; Fakjian, Hunter, Cole, & Miller, 1990; Edwards, 1996). Although vulvovaginal candidiasis is the second most common infection of the female genital tract, there is a paucity of population-based studies on the occurrence of genital infection in women with diabetes making comparison to other studies difficult (Bohannon, 1998; de Leon et al., 2002; Nyirjesy & Sobel, 2003). Prior epidemiological studies evaluating balanitis also report higher infection rates among patients with diabetes compared to patients without diabetes (Fakjian et al., 1990; Drivsholm, 2005). However, most studies of genital infection have rather small sample sizes, examine specific sub-populations and/or rely on self-reported or survey data to quantify rates of infection (de Leon et al., 2002; Goswami et al., 2000; Grigoriou et al., 2006; Shah & Hux, 2003). The objective of this study was to estimate background incidence rates of genital infection (vaginitis in women and balanitis in men) among patients with and without type 2 diabetes in a large population-based cohort.

## 2. Methods

This study was conducted using the General Practice Research Database (GPRD). The GPRD constitutes one of the world's largest computerized databases of anonymized longitudinal medical records of patients enrolled with a general practitioner (GP) in the United Kingdom. The age and gender distribution of the population served by the GPRD physicians parallels that of the general UK population (García Rodríguez & Pérez Gutthann, 1998). For this study, data from approximately 6.5 million patients involving nearly 500 primary care practices were available. Patient data that were evaluated included demographic and clinical information as well as prescriptions issued. Clinical diagnoses were determined using the Oxford Medical Indexing System (OXMIS) and Read codes. Treatments were identified based on prescriptions generated from GPs.

### 2.1. Cohort identification

Patients with type 2 diabetes were identified between January 1, 1990 and December 31, 2007 based on a combination of OXMIS/Read codes and oral anti-diabetes (OAD) treatment (2 OXMIS/Read codes of type 2 diabetes or 1 OXMIS/Read code plus one OAD or 2 continuous OAD treatments). Patients were excluded if their medical records indicated a diagnosis of Type 1 diabetes (1 OXMIS/Read code

☆ Disclaimer: I. Hirji, Z. Guo and A. Gomez-Caminero are employees of Bristol-Myers Squibb Co., S Andersson is an employee of Bayer Pharma AG., N Hammar is an employee of Astra Zeneca R&D.

* Corresponding author. 5 Research Parkway, Wallingford, CT 06492, USA.
*E-mail address:* ishan.hirji@bms.com (I. Hirji).

1056-8727/$ – see front matter © 2012 Elsevier Inc. All rights reserved.
doi:10.1016/j.jdiacomp.2012.06.012

**Table 1**
Demographic characteristics of the vaginitis and balanitis cohorts within the GPRD.

| | Vaginitis cohort (N = 125,237) | | Balanitis cohort (N = 146,603) | |
|---|---|---|---|---|
| | Females with diabetes n = 62,537 | Females without diabetes n = 62,700 | Males with diabetes N = 73,383 | Males without diabetes N = 73,220 |
| Age (years) | | | | |
| Mean (SD) | 64.1 (14.4) | 64.3 (14.3) | 61.4 (12.6) | 61.2 (12.9) |
| Median | 65 | 66 | 62 | 62 |
| Diabetes at index date n (%) | | | | |
| Newly diagnosed | 55,498 (88.7%) | n/a | 65,266 (88.9%) | n/a |
| Previously diagnosed diabetes | 7039 (11.3%) | n/a | 8117 (11.1%) | n/a |
| Prior genital infection n (%) | | | | |
| Vaginitis (females) | 1366 (2.2%) | 359 (0.6%) | n/a | n/a |
| Balanitis (males) | n/a | n/a | 1159 (1.6%) | 141 (0.2%) |
| Patients receiving diabetes treatments, n (%) | 28,829 (46.1%) | n/a | 33,377 (45.5%) | n/a |

of type 1 diabetes, patients <25 years with insulin as their initial treatment, or patients receiving exclusive insulin therapy for 3 months). Eligible patients included those aged ≥18 years with a minimum of 90 days of follow-up, based on the index date. The index date was the date of the first type 2 diabetes diagnosis or the date of the first record of an OAD in the database. Newly diagnosed diabetes patients included those cases identified after 6 months of registration within the database. A random sample of patients without diabetes was matched to patients with diabetes based on age, gender and index year using a previously published propensity score method (Parsons, 2001). The patients without diabetes were identified as those who did not have a record of diabetes during their registration period and who had at least one patient record in the database.

### 2.2. Study outcome identification

Clinical diagnoses of genital infection were determined using OXMIS and Read codes. A comprehensive list of vaginitis and balanitis codes was compiled based on key diagnostic codes (vaginitis, vulvitis, vaginosis, and balanitis) as well as related symptoms and laboratory coding. Manual reviews by independent clinical investigators were conducted to identify codes that were clinically relevant and would accurately reflect a clinical diagnosis of vaginitis or balanitis.

### 2.3. Statistical analysis

Analyses for vaginitis among women and balanitis among men were conducted separately. Wilcoxon's rank sum and Pearson's chi-squared tests were used to compare age and study index year for the patients with and without diabetes. Incidence rates (IR) of infection per 1000 person-years (PY) and corresponding 95% confidence intervals (CI) were calculated. For vaginitis and balanitis respectively, the incidence rate was defined as the number of new infection cases divided by the total number of PY of follow-up. Person-time calculations for patients ended at first occurrence of one of the following: (1) First vaginitis (females) OR balanitis (males) event; (2) Transferring out of GP practice; (3) Last data collection for practice; (4) Death; or (5) End of 1-year follow-up (1 year from index date). For patients with and without diabetes, incidence rates were stratified by age categories (18–39, 40–49, 50–59, 60–69, 70+ years) and history of genital infection (recorded in a period of up to 6 months prior to the index date).

Hazard ratios (denoted relative risk [RR]) of genital infection for diabetes vs non-diabetes patients were estimated using Cox-proportional hazards regression. Covariates adjusted for in the multivariate analysis included age, index year and history of genital infection. Correspondingly, risk estimates of infection were calculated among patients with and without diabetes respectively for each age category, controlling for index year and history of infection.

As a sub-analysis, IR and RR estimates were calculated for both treated and non-treated diabetes patients to evaluate the association between the risk of vaginitis and balanitis and level of diabetes control. HbA1C levels were used to classify level of diabetes control as: 'poor control' defined as HbA1C measure >8.0% or switch to, or add-on of insulin if no valid HbA1c measure was available in the database and 'fair control' defined as no HbA1c measure >8.0% during the study period. Treated patients were identified as such if they had a diabetes treatment regimen (including oral anti diabetes treatments and/or insulin) recorded within either 30 days of an infection event or at time of censoring.

This study was approved by the GPRD Independent Scientific Advisory Committee. Data extraction and statistical analyses were performed using SAS® version 9.1 (Cary, NC, USA).

## 3. Results

The study population comprised 125,237 female patients evaluable for vaginitis and 146,603 male patients evaluable for balanitis over the one year study period. Approximately 89% of all diabetes patients were newly diagnosed at the study index date. Prior history of vaginitis was observed in 1366 (2.2%) of the female diabetes patients and 359 (0.6%) of the female patients without diabetes; 1159 (1.6%) of the male diabetes patients and 141 (0.2%) of the male patients without diabetes had a previous balanitis history.

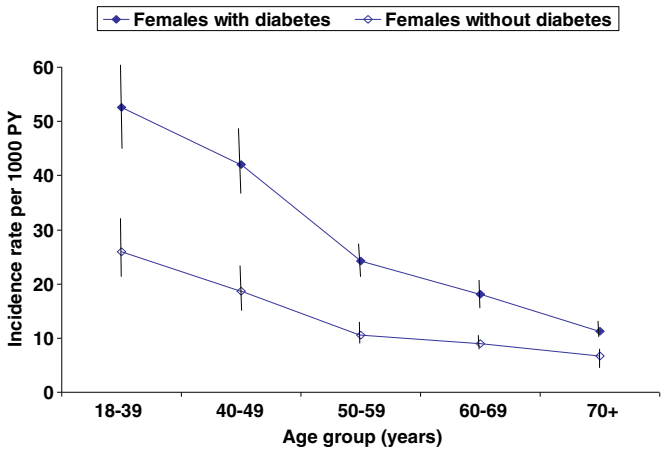


**Fig. 1.** Incidence rates (per 1000 person-years) of vaginitis by age groups among female diabetes and nondiabetes patients.