

Is Type 1 Diabetes Mellitus More Prevalent Than Expected in Transgender Persons? A Local Observation



Justine Defreyne, MD,¹ Dirk De Bacquer, PhD,² Samyah Shadid, MD, PhD,¹ Bruno Lapauw, MD, PhD,¹ and Guy T'Sjoen, MD, PhD³

ABSTRACT

The International Diabetes Federation estimates that approximately 0.4% of the Belgian population is diagnosed with type 1 diabetes mellitus, which is similar to other industrialized countries. The prevalence of transgenderism is estimated at 0.6% to 0.7% of all adults in Western populations. In this study, we evaluated whether there was an increased prevalence of type 1 diabetes mellitus in transgender people in the local cohort. Medical records of transgender patients were analyzed retrospectively. From January 1, 2007 until October 10, 2016, 1,081 transgender patients presented at a tertiary reference center to start hormonal treatment. Nine of these 1,081 patients were previously diagnosed with type 1 diabetes mellitus and 1 was diagnosed with latent autoimmune diabetes in adults. A 2.3-fold higher prevalence of type 1 diabetes mellitus was observed in transgender patients. We concluded that type 1 diabetes mellitus was more prevalent in transgender patients than one would expect from population prevalences. This could be a spurious result in a local cohort, because a causal relation seems unlikely, but our finding might encourage other centers to investigate this putative association. **Defreyne J, De Bacquer D, Shadid S, et al. Is Type 1 Diabetes Mellitus More Prevalent Than Expected in Transgender Persons? A Local Observation. Sex Med 2017;5:e215–e218.**

Copyright © 2017, The Authors. Published by Elsevier Inc. on behalf of the International Society for Sexual Medicine. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Key Words: Transgender; Type 1 Diabetes Mellitus; Epidemiology

INTRODUCTION

At the Ghent University Hospital outpatient endocrine clinic (Ghent, Belgium), recognized as a tertiary referral center for transgender care, we perceived a relatively high prevalence of type 1 diabetes mellitus in transgender individuals seeking gender-affirming hormonal treatment. However, there is no known association between type 1 diabetes mellitus and transgenderism.

In Belgium, the prevalence of type 1 diabetes mellitus in the Belgian population is estimated at 0.4% by the International Diabetes Federation (IDF), which is similar to the prevalence rate of type 1 diabetes mellitus in the Netherlands (0.48%).¹ Exact incidence rates are unknown, because newly diagnosed cases are not systematically documented in Belgium.

Previous studies on the prevalence of transgenderism reported mainly on the prevalence of transgender persons looking for gender-affirming care, which led to an underestimation of the prevalence of transgenderism.² In a recent study by Van Caenegem et al,² the overall prevalence of transgenderism in Flanders, Belgium was estimated at 0.6% to 0.7% of all adults.

Theoretically, the options for gender affirmation include social, psychological, hormonal, and surgical transitioning, although decisions regarding gender-affirmative therapy should be made for the individual. Options for gender-affirming hormonal treatment include testosterone administration (intramuscular injections or gel applications) in transmen and estrogens (orally or transdermally administered) and antiandrogens in transwomen.

Given the relatively low prevalence of transgenderism and type 1 diabetes mellitus, combined prevalence in one person is expected to be rare. Therefore, we evaluated whether the number of transgender persons with the comorbidity of type 1 diabetes mellitus was higher than expected in our center.

METHODS

To evaluate a possible association between type 1 diabetes mellitus and transgenderism in our local cohort, medical

Received March 13, 2017. Accepted June 5, 2017.

¹Department of Endocrinology, Ghent University Hospital, Ghent, Belgium;

²Department of Public Health, Ghent University, Ghent, Belgium;

³Department of Endocrinology and Center for Sexology and Gender, Ghent University Hospital, Ghent, Belgium

Copyright © 2017, The Authors. Published by Elsevier Inc. on behalf of the International Society for Sexual Medicine. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<http://dx.doi.org/10.1016/j.esxm.2017.06.004>

records of transgender persons were analyzed retrospectively. To investigate whether the difference between expected and observed numbers of transgender persons presenting with type 1 diabetes mellitus was significant, a χ^2 statistical test ($[(\text{observed} - \text{expected})^2 / \text{expected}]$) was performed using IDF estimates.

RESULTS

From January 1, 2007 until October 10, 2016, 1,081 transgender persons and 372 patients with type 1 diabetes mellitus presented at the endocrinology department of our hospital. We found that 9 of 1,081 transgender persons were previously diagnosed with type 1 diabetes mellitus and 1 person was previously diagnosed with latent autoimmune diabetes of adulthood, a form of type 1 diabetes mellitus that develops later in adulthood (Table 1). Of these transgender individuals, eight (80%) were transwomen (male-to-female transgender persons) and two (20%) were transmen (female-to-male transgender persons). Their mean age was 36.7 years (range = 19–53 years) and mean age at diagnosis of type 1 diabetes mellitus was 15.7 years (range = 3–29 years). Five transgender persons recalled their first feelings of gender incongruence at a mean age of 6.8 years (range = 4–13 years). For two persons, this information was not found in the medical records, one did not recall, and two persons responded that they felt this way since “early childhood.” The reported trans-persons started gender-affirming hormonal therapy at mean age of 29.4 years (range = 19–50 years). The expected number of persons previously diagnosed with type 1 diabetes mellitus presenting for transgender care was 4.32 ($1,081 \times 0.4\%$). The calculated χ^2 statistic of 7.47 ($P = .006$) indicated that the higher prevalence of type 1 diabetes mellitus in transgender individuals (0.92%) was highly significant (2.3 times higher; Figure 1).

DISCUSSION

We found an increased number of transgender persons with type 1 diabetes mellitus at our center compared with the expectation based on the combined prevalence of transgenderism and type 1 diabetes mellitus in Western populations. Because not all transgender persons wish or search for gender-affirming hormonal treatment, this number could be an understimation.²

The predominant effector mechanism of type 1 diabetes mellitus is autoimmunity, although the primary cause is unknown.³ There are case reports describing other autoimmune diseases in transgender persons, although those researchers correlated their observations with the administered hormonal therapy, whereas in our patients type 1 diabetes mellitus was already prevalent before initiation of hormonal therapy.^{4,5}

A possible pathophysiologic mechanism behind the observed correlation between type 1 diabetes mellitus and transgenderism is difficult to fathom, if only because the etiology of transgenderism remains unclear. Etiologic theories include atypical

Table 1. Characteristics of transgender persons with a history of type 1 diabetes mellitus presenting at the Ghent University Hospital Department of Endocrinology

Patient ID	Desired gender	Birth year	Age at onset of gender dysphoria (y)	Age at		Insulin therapy	HbA _{1c} (%)	C-peptide (nmol/L)	Height (cm)	Weight (kg)	BMI (kg/m ²)
				onset of T1DM (y)	start of CSHT (y)						
1	Female	1991	13	14	23	Basal bolus	9.4		181	60	18.31
2	Female	1983	Unknown	9	20	Basal bolus	9		182	78	23.5
3	Female	1963	6	3	37	Basal bolus	7		178		
4*	Male	1972	4	29	22	Basal bolus	6		170	61	21.1
5	Female	1990	7	14	20	Basal bolus	10	0.10	186.5	90.5	26
6	Female	1979	Unknown	11	31	Basal bolus	8.7		188	118.5	33.5
7	Female	1981	“Early childhood”	25	27	Basal bolus		<0.03	169.8	91.8	31.8
8	Female	1997	4	12	19	Basal bolus			171	49	16.8
9	Female	1966	“Early childhood”	14	50	Basal bolus	6.7		172	67.6	22.9
10	Male	1982	Unknown	29	34	Insulin pump	7.1	0.01	168	71	25.2

BMI = body mass index; CSHT = cross-sex hormone therapy; HbA_{1c} = hemoglobin A_{1c}; T1DM = type 1 diabetes mellitus.

*Patient was diagnosed with latent autoimmune diabetes in adults.

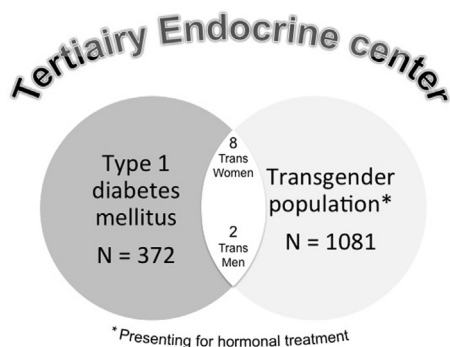


Figure 1. Venn diagram of the transgender population with type 1 diabetes mellitus (January 1, 2007 through October 10, 2016) at Ghent University Hospital.

gender development during childhood and parental and familial, genetic, and biological factors.⁶ Because the incidence of type 1 diabetes mellitus is known to peak during puberty,³ a time when serum sex hormone levels increase, one could hypothesize a correlation between the administration of cross-sex hormones in transgender persons and the occurrence of type 1 diabetes mellitus. However, the trans-persons in our study cohort had known type 1 diabetes mellitus before they initiated cross-sex hormone therapy. So far, no studies have shown autoimmunity to be a cause for gender dysphoria.

Another possible explanation for the correlation between type 1 diabetes mellitus and gender dysphoria might be that the prolonged psychological stress of the gender dysphoria—mostly present at a young age in our cohort—is a precipitating factor for type 1 diabetes mellitus. Several studies have provided evidence for an association between psychological stress and type 1 diabetes mellitus.^{7–13} Many transgender persons experience mental health issues and chronic stress (often called “minority stress”) owing to internalized stigma, victimization, social rejection, and lack of social support.^{14–16} This chronic psychoneurotic distress decreases markedly after the initiation of gender-affirming hormonal therapy.^{17–19} Emotional problems such as depression and anxiety are frequently reported in trans-children and trans-adolescents,²⁰ with ostracism and peer victimization as risk factors accounting for co-occurring general psychopathology in gender non-conforming children and adolescents.²¹

Different types of stress are known to cause excessive release of stress hormones (cortisol, catecholamines), which can increase insulin requirements and increase stress on pancreatic β -cells. Another hypothesis is that stress accelerates the autoimmune destruction of pancreatic β -cells by affecting the immune system.²²

To date, to our knowledge, there is no literature on the management of type 1 diabetes mellitus in transgender patients. We recommend transgender patients seek care for their type 1 diabetes mellitus in a center where health care providers treat transgender persons with respect and dignity, independent of their personal views of gender incongruence.

As for the strengths and weaknesses of this study, there might be a selection bias. The reported transgender persons visited a diabetologist close to their home for the management of type 1 diabetes mellitus. None of them were treated for type 1 diabetes mellitus in our hospital. However, the fact that a trans-person is seen by a peripheral endocrinologist for follow-up of type 1 diabetes mellitus can increase the possibility that this person would be referred to an endocrinologist specialized in transgender care.

CONCLUSIONS

Type 1 diabetes mellitus seemed more prevalent in transgender patients visiting a tertiary endocrinology center than one would expect from population prevalence. This could be a spurious result in a local cohort, because a causal relation seems unlikely and a pathophysiologic mechanism is difficult to fathom, but our findings might encourage other centers to investigate this association in larger cohorts.

ACKNOWLEDGMENTS

We thank our multidisciplinary diabetes care team and the Center for Gender and Sexology, particularly all endocrinology residents, who made a valuable contribution to the transgender care and diabetes care outpatient clinic. In addition, we thank Dr Peggy Joosen for her help with the collection of the data.

Corresponding Author: Justine Defreyne, MD, Department of Endocrinology, Ghent University Hospital, De pintelaan 185, Ghent, Oost-Vlaanderen 9000, Belgium. Tel: 00329 332 57 25; Fax: 00329 332 38 97; E-mail: justine.defreyne@ugent.be

Conflicts of Interest: The authors report no conflict of interest.

Funding: None.

STATEMENT OF AUTHORSHIP

Category 1

(a) Conception and Design

Justine Defreyne; Guy T’Sjoen

(b) Acquisition of Data

Justine Defreyne; Dirk De Bacquer; Samyah Shadid; Bruno Lapauw; Guy T’Sjoen

(c) Analysis and Interpretation of Data

Justine Defreyne; Dirk De Bacquer; Samyah Shadid; Bruno Lapauw

Category 2

(a) Drafting the Article

Justine Defreyne; Dirk De Bacquer; Samyah Shadid; Bruno Lapauw; Guy T’Sjoen

(b) Revising It for Intellectual Content

Guy T’Sjoen

Category 3

(a) Final Approval of the Completed Article

Justine Defreyne; Dirk De Bacquer; Samyah Shadid; Bruno Lapauw; Guy T'Sjoen

REFERENCES

1. International Diabetes Federation. IDF diabetes atlas. 7th ed. Brussels, Belgium: International Diabetes Federation; 2015.
2. Van Caenegem E, Wierckx K, Elaut E, et al. Prevalence of gender nonconformity in Flanders, Belgium. *Arch Sex Behav* 2015;44:1281-1287.
3. Maahs DM, West NA, Lawrence JM, et al. Epidemiology of type 1 diabetes. *Endocrinol Metab Clin North Am* 2010;39:481-497.
4. Tangpricha V, Afdhal N, Chipkin S. Auto-immune hepatitis in a male-to-female transsexual treated with conjugated estrogens. *Int J Transgend* 2001;5. Available at: https://www.atrria.nl/eazines/web/IJT/97-03/numbers/symposium/ijtvo05no03_03.htm. Accessed July 26, 2017.
5. Pakpoor J, Wotton CJ, Schmierer K, et al. Gender identity disorders and multiple sclerosis risk: a national record-linkage study. *Mult Scler* 2016;22:1759-1762.
6. Cohen-Kettenis PT, Gooren LJ. Transsexualism: a review of etiology, diagnosis and treatment. *J Psychosom Res* 1999;46:315-333.
7. Chida Y, Hamer M. An association of adverse psychosocial factors with diabetes mellitus: a meta-analytic review of longitudinal cohort studies. *Diabetologia* 2008;51:2168-2178.
8. Sipetić SB, Vlajinac HD, Kocev NI, et al. The Belgrade childhood diabetes study: a multivariate analysis of risk determinants for diabetes. *Eur J Public Health* 2005;15:117-122.
9. Robinson N, Lloyd CE, Fuller JH, et al. Psychosocial factors and the onset of type 1 diabetes. *Diabet Med* 1989;6:53-58.
10. Robinson N, Fuller JH. Role of life events and difficulties in the onset of diabetes mellitus. *J Psychosom Res* 1985;29:583-591.
11. Dahlquist G, Blom L, Lönnberg G. The Swedish Childhood Diabetes Study—a multivariate analysis of risk determinants for diabetes in different age groups. *Diabetologia* 1991;34:757-762.
12. Littorin B, Sundkvist G, Nyström L, et al. Family characteristics and life events before the onset of autoimmune type 1 diabetes in young adults: a nationwide study. *Diabetes Care* 2001;24:1033-1037.
13. Virk J, Ritz B, Li J, et al. Childhood bereavement and type 1 diabetes: a Danish National Register Study. *Paediatr Perinat Epidemiol* 2016;30:86-92.
14. Hendricks M, Testa R. A conceptual framework for clinical work with transgender and gender nonconforming clients: an adaptation of the minority stress model. *Prof Psychol Res Pract* 2012.
15. Robles R, Fresán A, Vega-Ramírez H, et al. Removing transgender identity from the classification of mental disorders: a Mexican field study for ICD-11. *Lancet Psychiatry* 2016;3:850-859.
16. Marshall E, Claes L, Bouman WP, et al. Non-suicidal self-injury and suicidality in trans people: a systematic review of the literature. *Int Rev Psychiatry* 2016;28:58-69.
17. Heylens G, Verroken C, De Cock S, et al. Effects of different steps in gender reassignment therapy on psychopathology: a prospective study of persons with a gender identity disorder. *J Sex Med* 2014;11:119-126.
18. Colizzi M, Costa R, Pace V, et al. Hormonal treatment reduces psychobiological distress in gender identity disorder, independently of the attachment style. *J Sex Med* 2013;10:3049-3058.
19. Fisher AD, Castellini G, Ristori J, et al. Cross-sex hormone treatment and psychobiological changes in transsexual persons: two-year follow-up data. *J Clin Endocrinol Metab* 2016;101:4260-4269.
20. Zucker KJ, Bradley SJ, Owen-Anderson A, et al. Demographics, behavior problems, and psychosexual characteristics of adolescents with gender identity disorder or transvestic fetishism. *J Sex Marital Ther* 2012;38:151-189.
21. de Vries AL, Steensma TD, Cohen-Kettenis PT, et al. Poor peer relations predict parent- and self-reported behavioral and emotional problems of adolescents with gender dysphoria: a cross-national, cross-clinic comparative analysis. *Eur Child Adolesc Psychiatry* 2016;25:579-588.
22. Wilcox G. Insulin and insulin resistance. *Clin Biochem Rev* 2005;26:19-39.