Skin diseases in the Da Qing Diabetes Study: a cross-sectional study

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Abstract

Background: The prevalence of skin diseases and diabetes mellitus (DM) are prominent around the world. The current scope of knowledge regarding the prevalence of skin diseases and comorbidities with type 2 DM (T2DM) is limited, leading to limited recognition of the correlations between skin diseases and T2DM.

Methods: We collected 383 subjects from the Da Qing Diabetes Study during the period from July 9th to September 1st, 2016. The subjects were categorized into three groups: Normal glucose tolerance (NGT), impaired glucose tolerance (IGT), and T2DM. The prevalence and clinical characteristics of skin diseases were recorded and investigated.

Results: In this cross-sectional study, 383 individuals with ages ranging from 53 to 89-year-old were recruited. The overall prevalence of skin diseases was 93.5%, and 75.7% of individuals had two or more kinds of skin diseases. Additionally, there were 47 kinds of comorbid skin diseases in patients with T2DM, of which eight kinds of skin diseases had a prevalence >10%. The prevalence of skin diseases in NGT, IGT, and T2DM groups were 93.3%, 91.5%, and 96.6%, respectively; stratified analysis by categories showed a statistically significant difference in "disturbances of pigmentation" and "neurological and psychogenic dermatoses". The duration of T2DM also significantly associated with the prevalence of "disturbances of pigmentation" and "neurological and psychogenic dermatoses". Subsequently, the prevalence of "disturbances of pigmentation" was higher in males than females in NGT ($P < 0.01$) and T2DM ($P < 0.01$) groups. In addition, the difference in the prevalence of "disturbances of pigmentation" was also significant in NGT and T2DM groups ($P < 0.01$).

Conclusions: There was a high prevalence of skin diseases in the Da Qing Diabetes Study. To address the skin diseases in the Da Qing Diabetes Study, increased awareness and intervention measures should be implemented.

Keywords: Skin diseases; Type 2 diabetes mellitus; Prevalence; Comorbidities

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Introduction

Skin is the largest organ in the human body, and it is the first line of defense against various foreign objects. When the skin is infected, there is a large variation in the symptoms and severity of the disease in which some arise to certain situational causes, while others may be genetic. Skin diseases are one of the most common diseases among the general population which can cause a great deal of misery, suffering, incapacity, economic loss, and lead to major public health issues. Disability secondary to skin conditions is substantially prevalent worldwide, in which skin conditions contributed 1.79% to the global burden of disease from 306 diseases and injuries in 2013.[1] In China, the years lived with disability (YLDs) of skin and subcutaneous diseases rank ninth, and YLDs per 100,000 population was 499 in 2017.[2] In 2013, there are reports that quantify the economic burden of 24 skin disease categories in the United States. Half of these categories are associated with mortality, non-melanoma skin cancer, and melanoma accounted for 60% of skin disease-related deaths, and an estimate of $75 billion was spent on skin diseases.[3-5]

Diabetes mellitus (DM) is a debilitating, life-threatening, widespread endocrine disease, which affects a variety of systems and organs including the skin, accounting for the death of 5 million people worldwide in 2015. According to the estimations, 415 million adults currently suffer from DM, and this number is expected to rise to 642 million by 2040.[6] Type 2 DM (T2DM) is the most common type of DM, accounting for around 90% of all DM cases. Interestingly, there are 30% to 97% of patients with DM who may have pathological lesions that arise in the skin or have concurrent dermatological disorders worldwide.[7,8] Moreover, skin diseases found in patients with DM frequently occur before the DM diagnosis, thus playing an important role in the initial recognition of underlying DM.[9] A study has also indicated that abnormal skin findings in the toe webs show an increased risk of occult DM, and thus it may serve as an additional sign of undiagnosed DM.[10] Consistent with these studies, we found that some skin diseases coexist with T2DM in the clinic. In this study, we attempted to explore the prevalence of skin diseases and their related affected factors in the Da Qing Diabetes Study.

Methods

Ethical approval

The study was approved by the Ethics Committee of China-Japan Friendship Hospital (No. 2016-35). Written informed consent was obtained from all participants before data collection.

The Da Qing Diabetes Study

The Da Qing Diabetes Study was a follow-up study since 1986, in 33 clinics in Da Qing, China. These individuals regularly received their medical care from the clinics by the Da Qing Diabetes Study Group. In 1986, there were 519, 577, and 630 individuals in three groups: Normal glucose tolerance (NGT), impaired glucose tolerance (IGT), and patients with T2DM, respectively. Design details of the Da Qing Diabetes Study and the follow-up studies have been described previously.[2,11-17] During the period from July 9th, 2016 to September 1st, 2016, we collected 383 subjects from the Da Qing Diabetes Study, including 164 individuals in the NGT group, 130 individuals in the IGT group, and 89 individuals in the T2DM group.

Skin diseases or symptoms screening and diagnostic criteria

We screened and recorded the occurrence of skin diseases in 383 study subjects from the clinics (previously selected clinics in the Da Qing Diabetes Study). The patients with skin disorders were diagnosed by two experienced dermatologists from the Department of Dermatology, China-Japan Friendship Hospital. In addition, confirmation of the skin diseases was carried out by laboratory tests, determined by clinical features that confirmed diagnosis, or the use of medication to treat skin disorders in the medical record.

Diagnostic criteria of DM, IGT, and NGT

Diagnostic criteria of DM were determined by the guidelines set by the World Health Organization (WHO).[18,19] According to the 1985 WHO criteria, DM was diagnosed when fasting plasma glucose (FPG) was ≥7.8 mmol/L or 2-h plasma glucose (2-h PG) value >11.0 mmol/L; when FPG was <7.8 mmol/L, whereas subjects were classified as having IGT if 2-h PG was between 7.8 and 11.0 mmol/L and having NGT if 2-h PG was <7.8 mmol/L. In the Da Qing Diabetes Study, DM was defined from the results of 75 g oral glucose tolerance tests done every 2 years during the trial (1986–1992) at follow-up examinations, self-reported physician-diagnosed DM, and evidence of increased blood or plasma glucose concentrations, or the use of glucose-lowering medication in medical records. Subjects who were not already known to have DM underwent an oral glucose tolerance test which was interpreted by use of 1985 WHO criteria.[15]

Measurement standards of blood pressure (BP) and body mass index (BMI)

BP measurements were determined by the United States Joint National Committee and Chinese guidelines.[18,20,21] Hypertension was defined as an average systolic blood pressure (SBP) ≥140 mmHg or an average diastolic blood pressure (DBP) ≥90 mmHg. Stage 1 hypertension was defined as an average SBP range in 140 to 159 mmHg or an average DBP range in ≥90 to 99 mmHg; stage 2 hypertension was defined as an average SBP range in ≥160 to 179 mmHg or an average DBP range in ≥100 to 109 mmHg; stage 3 and above level hypertension was defined as an average SBP ≥180 mmHg or an average DBP ≥110 mmHg. BMI was defined as weight in kilograms (kg) divided by the square of height in meters (m^2). Based on the recommendations on obesity in China, underweight was defined as BMI <18.5 kg/m^2, normal was defined as 18.5

$kg/m^2 \leq BMI \leq 23.9\ kg/m^2$, overweight was defined as $24.0\ kg/m^2 \leq BMI \leq 27.9\ kg/m^2$, and obesity was defined as $BMI \geq 28.0\ kg/m^2$.[22]

Statistical analysis

Continuous variables data are shown as mean ± standard deviation (SD) and categorical variables data are shown as number (*N*) and percentage (%). The categorical variables were compared using the Chi-square test. For the Chi-square test in $R \times C$ contingency tables, there are two standards that need to be satisfied: (a) The categorical variables in the $R \times C$ contingency tables are all unordered variables. (b) In general, the expected count (*T*) of any grid in the $R \times C$ contingency tables should not be <1, and the number of grids with $1 \leq T < 5$ should not exceed 20% of the total number of grids. In this study, all contingency variables are unordered variables. If the dataset unsatisfied the standard (b), Fisher exact test was used to calculate the *P* value. Statistical package for social science (SPSS), version 22.0 (IBM Corp., Armonk, NY, USA) was used for all analysis. A two-sided *P* value < 0.05 was considered statistically significant in all analyses.

Results

Characteristics of study subjects

There were 383 valid subjects that were included in this study. The ratio of male to female was 161:222. In 2016, the age of study subjects ranged from 53.0 to 89.0 years, the mean age and SD are 69.8 and 6.7, respectively. There were 145 (37.9%), 226 (59.0%), 219 (57.2%) individuals with hypertension, overweight, and pathoglycemia (IGT and T2DM), respectively, in 1986. The corresponding numbers and ratios increase to 242 (242/373, 64.9%), 238 (238/371, 64.2%), and 315 (315/383, 82.2%) in 2016, respectively [Supplementary Table 1, http://links.lww.com/CM9/A509]. We found that the percentages of cardiovascular risk factors (eg, hypertension, overweight, and pathoglycemia) were increased during the 30-year period, which can explain previous results indicating an increased risk of death in the Da Qing Diabetes Study, likely due to a higher prevalence of cardiovascular diseases.[12,16]

Prevalence of skin diseases in the Da Qing Diabetes Study

The prevalence of skin diseases by categories in this cohort was: 157 (41.0%) individuals with "disturbances of pigmentation", 44 (11.5%) individuals with "allergic dermatosis", 54 (14.1%) individuals with "diseases of the skin appendages", 5 (1.3%) individuals with "metabolic dermatoses", 105 (27.4%) individuals with "skin tumors," 5 (1.3%) individuals with "papulosquamous dermatoses", 97 (25.3%) individuals with "neurological and psychogenic dermatoses", 344 (89.8%) individuals with "infectious skin diseases", and 99 (25.8%) individuals with other dermatoses. Furthermore, there were 25 (6.5%) individuals with other non-dermatoses. The overall prevalence of skin diseases was 93.5%; the detailed prevalence of skin diseases was shown in Supplementary Table 2, http://links.lww.com/CM9/A509. In addition, there were 75.7% of individuals who had two or more kinds of skin diseases [Supplementary Figure 1, http://links.lww.com/CM9/A509].

Prevalence of skin diseases or symptoms in patients with T2DM

In addition to the 89 patients with T2DM that were diagnosed in 1986, there were 175 patients who developed T2DM from the NGT and IGT groups during the 30 years. We explored the skin comorbidities in these 264 patients with T2DM. In total, there were 47 kinds of skin diseases or symptoms that were comorbid with T2DM. Importantly, there were eight kinds of comorbid skin diseases or symptoms with a prevalence of >10%. The top 15 comorbid skin diseases are shown in Figure 1, and the details of each comorbid skin disease or symptom are shown in Supplementary Table 3, http://links.lww.com/CM9/A509.

Differences in skin diseases prevalence among NGT, IGT, and T2DM groups

The total prevalence of skin diseases in NGT, IGT, and T2DM groups was 93.3% (153/164), 91.5% (119/130), and 96.6% (86/89), respectively. Regarding the differences in total prevalence of these three groups, there was no statistically significant difference. Next, stratified analysis was performed by categorical skin diseases to reveal the prevalence differences among these three groups. The results showed that there was a prevalence difference between the categories "disturbances of pigmentation" and "neurological and psychogenic dermatoses" with significant *P* values [Table 1].

Prevalence of skin diseases and BP development process

There were 233 normotensive individuals in the year 1986, and 134 individuals developed hypertension after 30 years. We hypothesized if the change in BP could influence the prevalence of skin diseases among these subjects. In the normal blood glucose (BG) group (NGT) and pathoglycemia group (IGT/T2DM), we compared the prevalence of skin diseases between the normotensive group (individuals with normal BP from 1986 to 2016) and the hypertension group (individuals with normal BP in 1986 and developed to hypertension during the period from 1986 to 2016). As a result, there was no statistically significant prevalence difference in all categorical skin diseases [Table 2].

Association between the prevalence of skin diseases and duration of T2DM

From the year 1986 to 2016, there were 58 T2DM patients that were diagnosed from the NGT group, and 117 T2DM patients were diagnosed from the IGT group. The average duration of these newly diagnosed T2DM patients (developed from NGT and IGT groups) was 16.37 years (SD = 9.58). There were 89 T2DM patients that were still categorized as DM patients with an average duration of 30 years. We hypothesized whether the duration of T2DM

had an effect on the prevalence of skin diseases. Therefore, we compared the prevalence of skin diseases between these two groups by categorical skin diseases. The results showed that the duration of T2DM has associated with the prevalence of two categories "disturbances of pigmentation" and "neurological and psychogenic dermatoses" [Table 3].

In addition, we backtracked the duration of all these 264 patients with T2DM, and we divided the duration of T2DM into four groups: ≥30 years (diagnosed in the year 1986), 20 to 29 years (diagnosed in the years 1987–1996), 10 to 19 years (diagnosed in the years 1997–2006), and 0 to 9 years (diagnosed in the years 2007–2016) [Supplementary Table 4, http://links.lww.com/CM9/A509]. The association between the prevalence of skin diseases and the duration of T2DM was then analyzed. Our results showed that the prevalence of the "disturbances of pigmentation" had a statistically significant association with the duration of T2DM [Supplementary Table 5, http://links.lww.com/CM9/A509].

Logistic regression analysis about affected factors of skin diseases prevalence

We attempted to find the possible factors that affect the categorical skin diseases showing the prevalence of >20% in the Da Qing Diabetes Study. Five factors including group (NGT and T2DM), gender, age, BMI, and BP (normotensive and hypertension) were included in the logistic regression analysis. For groups, we only included the NGT and T2DM groups because these two groups were more comparable in this analysis. Logistic regression analysis results showed that only group and sex possessed significant *P* values in the model [Table 4]. Then, stratified analysis was performed for associations between sex and prevalence of "disturbances of pigmentation" in NGT and T2DM groups. Results showed that the prevalence of "disturbances of pigmentation" was higher in males than females in both NGT ($P < 0.01$) and T2DM ($P < 0.01$) groups. In addition, the prevalence difference of "disturbances of pigmentation" was also significant in the NGT and T2DM groups ($P < 0.01$) [Supplementary Table 6, http://links.lww.com/CM9/A509].

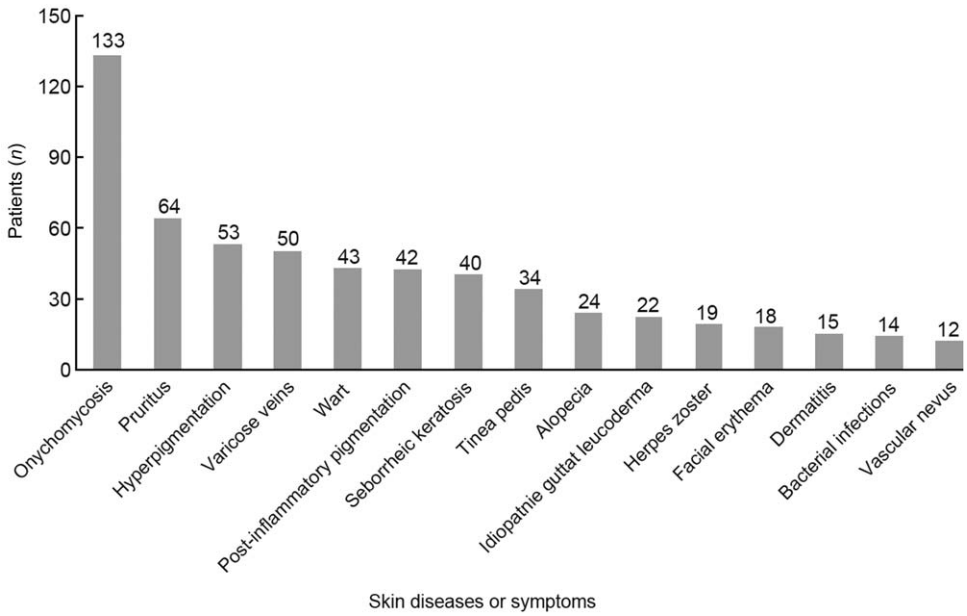

Figure 1: The top 15 kinds of comorbid skin diseases or symptoms in patients with T2DM. T2DM: Type 2 diabetes mellitus.

Table 1: The prevalence of skin diseases in NGT, IGT, and T2DM groups, *n* (%).

Categories	NGT (*n* = 164)		IGT (*n* = 130)		T2DM (*n* = 89)		χ^2	*P*
	Normal	Patients	Normal	Patients	Normal	Patients		
Disturbances of pigmentation	116 (70.7)	48 (29.3)	87 (66.9)	43 (33.1)	39 (43.8)	50 (56.2)	19.14	<0.01
Allergic dermatoses	144 (87.8)	20 (12.2)	115 (88.5)	15 (11.5)	80 (89.9)	9 (10.1)	0.25	0.88
Diseases of the skin appendages	136 (82.9)	28 (17.1)	118 (90.8)	12 (9.2)	76 (85.4)	13 (14.6)	3.80	0.15
Skin tumors	126 (76.8)	38 (23.2)	95 (73.1)	35 (26.9)	71 (79.8)	18 (20.2)	1.36	0.51
Neurological and psychogenic dermatoses	119 (72.6)	45 (27.4)	110 (84.6)	20 (15.4)	59 (66.3)	30 (33.7)	10.58	<0.01
Infectious skin diseases	64 (39.0)	100 (61.0)	49 (37.7)	81 (62.3)	31 (34.8)	58 (65.2)	0.43	0.81
Total*	11 (6.7)	153 (93.3)	11 (8.5)	119 (91.5)	3 (3.4)	86 (96.6)	2.26	0.32

*The total subjects: if someone had any one kind of skin disease, he or she was regarded as a patient with skin disease. IGT: Impaired glucose tolerance; NGT: Normal glucose tolerance; T2DM: Type 2 diabetes mellitus.

Table 2: Comparison of the prevalence of skin diseases between normotensive and hypertension groups, *n* (%).

Categories	Groups	BP	Normal	Patients	χ^2	*P*
Disturbances of pigmentation	NGT	Normotensive	42 (75.0)	14 (25.0)	0.51	0.47
		Hypertension	40 (69.0)	18 (31.0)		
	IGT/T2DM	Normotensive	29 (65.9)	15 (34.1)	1.13	0.29
		Hypertension	42 (56.0)	33 (44.0)		
Allergic dermatoses	NGT	Normotensive	48 (85.7)	8 (14.3)	0.12	0.73
		Hypertension	51 (87.9)	7 (12.1)		
	IGT/T2DM	Normotensive	39 (88.6)	5 (11.4)	0.01	0.91
		Hypertension	67 (89.3)	8 (10.7)		
Diseases of the skin appendages	NGT	Normotensive	48 (85.7)	8 (14.3)	1.78	0.18
		Hypertension	44 (75.9)	14 (24.1)		
	IGT/T2DM	Normotensive	37 (84.1)	7 (15.9)	1.78	0.18
		Hypertension	69 (92.0)	6 (8.0)		
Skin tumors	NGT	Normotensive	45 (80.4)	11 (19.6)	1.44	0.23
		Hypertension	41 (70.7)	17 (29.3)		
	IGT/T2DM	Normotensive	37 (84.1)	7 (15.9)	3.73	0.05
		Hypertension	51 (68.0)	24 (32.0)		
Neurological and psychogenic dermatoses	NGT	Normotensive	41 (73.2)	15 (26.8)	0.25	0.62
		Hypertension	40 (69.0)	18 (31.0)		
	IGT/T2DM	Normotensive	40 (90.9)	4 (9.1)	1.54	0.22
		Hypertension	62 (82.7)	13 (17.3)		
Infectious skin diseases	NGT	Normotensive	24 (42.9)	32 (57.1)	0.53	0.47
		Hypertension	21 (32.6)	37 (63.8)		
	IGT/T2DM	Normotensive	19 (43.2)	25 (56.8)	1.50	0.22
		Hypertension	24 (32.0)	51 (68.0)		

BP: Blood pressure; IGT: Impaired glucose tolerance; NGT: Normal glucose tolerance; T2DM: Type 2 diabetes mellitus.

Table 3: Association between the prevalence of skin diseases and the duration of T2DM who developed from NGT/IGT and T2DM groups.

Categories	T2DM patients (*n*)	Development from groups	Average duration (years), mean (SE)	Skin diseases, *n* (%)		χ^2	*P*
				Normal	Patients		
Disturbances of pigmentation	175	NGT/IGT	16.37 (9.58)	115 (65.7)	60 (34.3)	11.64	<0.01
	89	T2DM	30.00 (0.00)	39 (43.8)	50 (56.2)		
Allergic dermatoses	175	NGT/IGT	16.37 (9.58)	155 (88.6)	20 (11.4)	0.11	0.75
	89	T2DM	30.00 (0.00)	80 (89.9)	9 (10.1)		
Diseases of the skin appendages	175	NGT/IGT	16.37 (9.58)	159 (90.9)	16 (9.1)	1.80	0.18
	89	T2DM	30.00 (0.00)	76 (85.4)	13 (14.6)		
Skin tumors	175	NGT/IGT	16.37 (9.58)	131 (74.9)	44 (25.1)	0.79	0.37
	89	T2DM	30.00 (0.00)	71 (79.8)	18 (20.2)		
Neurological and psychogenic dermatoses	175	NGT/IGT	16.37 (9.58)	138 (78.9)	37 (21.1)	4.92	0.03
	89	T2DM	30.00 (0.00)	59 (66.3)	30 (33.7)		
Infectious skin diseases	175	NGT/IGT	16.37 (9.58)	66 (37.7)	109 (62.3)	0.21	0.65
	89	T2DM	30.00 (0.00)	31 (34.8)	58 (65.2)		

IGT: Impaired glucose tolerance; NGT: Normal glucose tolerance; SE: Standard error; T2DM: Type 2 diabetes mellitus.

Discussion

As healthcare innovation continues at a quick pace allowing for longer life expectancies, this causes different diseases to become more prominent, leading to the increasing prevalence of skin diseases. In 2013, one in four Americans reported receiving treatment for at least one skin disease, and nearly 50% of Americans over the age of 65 have a skin disorder, with an average of 2.2 kinds of skin diseases per person.[3] The overall prevalence of skin diseases was 9.92% with slightly higher rates in males than females in Kavre District, Nepal.[23] In our study, the higher overall prevalence of skin diseases was shown, and there are three-quarters of subjects with two and more kinds of skin diseases.

There have been several previous reports that outline comorbid skin diseases with DM. For instance, in a large number of patients with insulin-dependent DM (IDDM). The most frequent skin lesions observed in IDDM patients were vitiligo and psoriasis, followed by xerosis, warts, eczema, and candida infections. With non-insulin-dependent DM, the most frequent skin lesions were infectious

Table 4: Logistic regression analysis about the affected factors of dermatoses prevalence.

Factors	OR	95% CI	*P*
Disturbances of pigmentation			
Group	5.289	2.701–10.358	<0.01
Sex	0.153	0.080–0.293	<0.01
Age16	0.996	0.953–1.041	0.85
Bp16	0.967	0.884–1.057	0.46
BMI16	0.921	0.483–1.757	0.80
Constant	20.062		0.14
Skin tumors			
Group	0.757	0.385–1.490	0.42
Sex	0.933	0.497–1.749	0.83
Age16	1.010	0.963–1.059	0.69
Bp16	0.956	0.869–1.052	0.36
BMI16	1.591	0.791–3.198	0.19
Constant	0.389		0.66
Neurological and psychogenic dermatoses			
Group	1.168	0.642–2.125	0.61
Sex	1.082	0.610–1.919	0.79
Age16	1.013	0.970–1.058	0.55
Bp16	1.039	0.954–1.131	0.38
BMI16	1.191	0.643–2.207	0.58
Constant	0.046		0.12
Infectious skin diseases			
Group	1.332	0.751–2.361	0.33
Sex	0.892	0.522–1.525	0.68
Age16	0.994	0.954–1.034	0.75
Bp16	1.048	0.967–1.135	0.25
BMI16	1.033	0.586–1.821	0.91
Constant	0.860		0.93

95% CI: 95% Confidence interval; Age16: Age in the year 2016; Bp16: Blood pressure in the year 2016; BMI16: Body mass index in the year 2016; OR: Odds ratio.

dermatoses and diabetic dermatoses, psoriasis, pruritus, xerosis, lichen, and cutaneous complications of DM treatment, and some other skin lesions were also observed.[24] There are 47 kinds of skin diseases or symptoms that were comorbid with T2DM patients in this study. The most frequent skin lesions were infectious dermatoses (onychomycosis, tinea pedis, bacterial infections, wart, etc), disturbances of pigmentation (hyperpigmentation, vitiligo, freckle, post-inflammatory pigmentation, etc), and there are eight kinds of skin diseases or symptoms with prevalence >10%.

Skin lesions or diseases are frequently observed in patients with DM which may be due to complex interactions among biochemical, vascular, immune, and metabolic changes.[25] DM may affect the skin through several proposed mechanisms, in which hyperglycemia and advanced glycation end products being the most well-described. The prevalence of skin disorders in patients with DM are highly correlated with glycemic control. Skin disorders are highly associated with DM patients that display inadequate glycemic control, while DM patients with adequate glycemic control may reduce the prevalence and severity of skin disorders.[26,27] Reports demonstrate that insulin regulates skin proliferation and differentiation, while insulin-like growth factor 1 had different contrasting effects to insulin, indicating the direct involvement of insulin in transformation.[28,29] Weingarten *et al*[30] identified that insulin has a role in the regulation of cytoskeletal assembly in keratinocytes, and there is a link between insulin-regulated keratin assembly and skin tumorigenesis.

High glucose levels impair the normal function of keratinocytes *in vitro*, decreasing their proliferation and differentiation.[31] In a South Korea national cohort study, individuals with DM had a greater risk of skin and soft tissue infections compared to a control group of non-diabetic individuals.[32] A previous study focused on the relationship between refractory itchy skin diseases and BG, which revealed that fasting BG levels of patients with refractory itchy skin diseases are significantly higher than healthy controls.[33] In our study, stratified analysis revealed that there are significant differences of prevalence in the categories "disturbances of pigmentation" and "diseases of the skin appendages" among NGT, IGT, and T2DM groups. The difference in the prevalence of "disturbances of pigmentation" is significant in NGT and T2DM groups. In addition, it is interesting to note that the prevalence of "disturbances of pigmentation" was higher in males than females in both NGT and T2DM groups.

Hypertension is another factor that is associated with some kinds of skin diseases. For example, hypertension is independently associated with increased age at the onset of psoriasis[34] and is more prevalent in systemic lupus erythematosus (SLE) patients compared with people without SLE.[35] Our logistic regression analysis results showed that hypertension was not a significant factor, we speculate that the heterogeneity of the comorbid skin diseases may have an influence. Interestingly, the hypertension ratio of our study subjects raised from 37.9% to 64.9% since the year 1986 to 2016, this phenomenon attracted us to explore the association between BP development process and the prevalence of skin diseases. For the BP development process analysis in the normal BG group and pathoglycemia group, there was no statistically significant difference of skin diseases in prevalence shown in normal and abnormal BP groups.

A clinical trial showed that the duration of DM altered the response to intensive glucose control in difficult-to-control older individuals with T2DM, intensive therapy may reduce cardiovascular events in subjects with duration ≤15 years and may increase risks in those individuals with a longer duration.[36] There is also evidence that shows the prevalence of skin diseases in DM associated with the duration of T2DM. According to the reported literature, the prevalence of lower limb vascular lesions in DM patients with a duration of 5 years, 6 to 9 years, and >10 years were 22.6%, 23.0%, 66.7%, respectively. Additionally, the prevalence of DM being comorbid nerve dysfunction is 30% to 67% and is associated with the length of the DM duration, with up to 90% of patients with >10 years duration.[37] A comprehensive systematic review of literature from an Indian perspective shows that the duration of T2DM >2 years is one of the risk factors

for depression among diabetic patients.[38] Our result showed that the duration of T2DM is associated with the prevalence of "disturbances of pigmentation" and "neurological and psychogenic dermatoses" among three different groups. In addition, the "disturbances of pigmentation" also has a statistically significant association with the duration of T2DM from analysis of all DM patients as a whole.

There were four categorical skin diseases (disturbances of pigmentation, skin tumors, neurological and psychogenic dermatoses, and infectious skin diseases) with a prevalence of >20% in the Da Qing Diabetes Study. We explored the effect of five factors including group, gender, age, BMI, and BP on the prevalence of skin diseases. However, only group and sex factors were significant in a logistic regression model. Stratified analysis was performed for associations between sex and prevalence of "disturbances of pigmentation" in NGT and T2DM groups. It is interesting to note that the prevalence of "disturbances of pigmentation" was higher in males than females in both NGT and T2DM groups. In addition, the difference in the prevalence of "disturbances of pigmentation" was also significant in NGT and T2DM groups.

It is necessary to detail that there are some limitations in our study. The study sample size is relatively small and the addition of more study subjects will be encouraged to explore the prevalence of skin diseases in patients with T2DM. Additionally, we only have limited data points about the skin conditions in 2016; it would have been beneficial if dynamic data (such as the BG and BP) were available regarding the prevalence of skin diseases annually. Lastly, the existence of heterogeneity of comorbid diseases is a limitation. We had classified the skin diseases into several categories during our statistical analysis, but more approaches are needed to deal with the heterogeneity problem.

In conclusion, there is a high prevalence of skin diseases in the Da Qing Diabetes Study. The duration of T2DM is associated with the prevalence of "disturbances of pigmentation" and "neurological and psychogenic dermatoses." The prevalence of "disturbances of pigmentation" was higher in males than females in both NGT and T2DM groups. In the future, primary care physicians should be aware of the association between cutaneous manifestations and T2DM. A careful dermatological examination is required for patients with T2DM to provide them with adequate skin management.

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Conflicts of interest

None.

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