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Original Article

Gene polymorphisms and occurrence of type 2 diabetes in a Gabonese population

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Abstract: Background: Type 2 diabetes (T2DM) is a metabolic disease characterized by chronic hyperglycemia. We investigated the relationship between the polymorphisms *rs5219* of KCNJ11, *rs7903146* of TCF7L2, and *rs13266634* of SLC30A8 in a Gabonese population with T2DM. Method: This case-control study was conducted at the Endocrinology Department of the University Hospital of Libreville. We enrolled 97 patients with T2DM and, from the general population, 87 control subjects who met the inclusion criteria. Genomic DNA was extracted with the Qiagen kit, and polymorphisms were analyzed using the RFLP method. Results: For KCNJ11, the wild type (EE) genotype frequency was 62.2% in controls versus 42.6% in cases, whereas the mutant type (KK) genotype frequency was 28.7% in cases versus 21.1% in controls (P=0.0243). For TCF7L2, the wild type (CC) genotype was found in 51.7% of controls and 37.1% of cases, and the mutant type (TT) genotype was found in 22.7% of cases versus 9.2% of controls (P=0.0253). For SLC30A8, the wild type (CC) genotype occurred in 26.0% of cases and 24.6% of controls (P=0.9326). After adjustment for age and body mass index, the recessive transmission models of *rs5219* (KCNJ11) and *rs7903146* (TCF7L2) were significantly associated with T2DM (P=0.021 and P=0.026, respectively). Conclusion: The *rs5219* variant of KCNJ11 and the *rs7903146* variant of TCF7L2 were associated with the occurrence of T2DM in this population.

Keywords: Polymorphism, *rs5219* KCNJ11, *rs7903146* TCF7L2, *rs13266634* SLC30A8, type 2 diabetes, Gabon

Introduction

Type 2 diabetes (T2DM) is a metabolic disease characterized by chronic hyperglycemia caused by impaired insulin secretion by pancreatic β-cells and insufficient responses of insulin-sensitive tissues to insulin [1]. T2DM is a major global health threat with substantial social and economic burden. In 2024, 589 million people aged 20-79 years were reported to have diabetes worldwide, representing a prevalence of 11.1%, compared with 537 million in 2021 [2, 3]. By 2050, this chronic disease is projected to be the second leading cause of death worldwide and one of the major global health emergencies of the 21st century, with a mortality rate of 9.3% [2]. The primary manifestations of complications associated with type 2 are several, such as kidney disease, retinopathy, neuropathy, peripheral artery disease and foot ulceration. Diabetes-related mortality is largely due to severe cardiovascular complications such as myocardial infarction and cerebrovascular accidents [2]. The increasing burden reflects the complexity of T2DM, which arises from interactions among genetic, environmental, and lifestyle factors [4]. Consequently, elucidating the genetic architecture of T2DM is of great interest for risk prediction and preventive interventions [5].

Genetics are linked to T2DM. Individuals with family history with first degree diabetics type 2 face 2 or 3 times greater risk to T2DM [5]. There is compelling evidence that genetic susceptibility to the disease is polygenic, and genome-wide association studies have identified over 400 loci associated with T2DM risk. Indeed, several T2DM genome wide association studies have shown the complex polygenic nature of T2DM in which most of these loci increase T2DM risk through reducing insulin action [6].

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Numerous susceptibility loci for T2DM have been identified, largely through genome-wide association studies, predominantly in populations of European ancestry [6]. Among the implicated genes, those involved in insulin secretion or signaling are particularly important, including KCNJ11 (Potassium inwardly-rectifying channel, subfamily J, member 11), TCF7L2 (Transcription factor 7-Like 2), and SLC30A8 (Solute carrier family 30 member 8). The adenosine triphosphate (ATP)-sensitive potassium channel (KATP) plays a key role in insulin secretion by glucose-stimulated pancreatic β-cells [7]. The KCNJ11 gene, located at 11p15.1, encodes the KATP subunit Kir6.2, which is highly expressed in the pancreas and is critical for insulin secretion [7, 8]. Several single nucleotide polymorphisms (SNPs) in KCNJ11 have been identified, including *rs5219*, which has been associated with diabetes. The *rs5219* polymorphism reflects a guanine-to-adenine substitution at codon 23, resulting in a glutamic acid (E) to lysine (K) change that can impair glucose-induced insulin secretion [7, 8]. This alteration reduces the potassium channel's sensitivity to ATP, leading to channel hyperactivity and inhibition of insulin secretion [7]. KCNJ11 thereby links the membrane potential of pancreatic β-cells to glucose metabolism [7].

Another gene with a strong effect on T2DM risk is TCF7L2, particularly the SNP *rs7903146*. TCF7L2 is located on chromosome 10q25.2-25.3 (also known as the TCF4 locus), spans 215.9 Kb, and contains 17 exons encoding a 596-amino acid protein [9, 10]. TCF7L2 encodes a transcription factor of the T cell factor family that is expressed in numerous tissues, including liver, adipose, and pancreatic tissue [11, 12]. It is a key transcriptional effector of the Wnt/β-catenin signaling pathway, which is involved in cell proliferation [13], and functionally interacts with the insulin signaling pathway through shared targets such as insulin receptor substrate IRS1, thereby activating insulin signaling [4, 9, 14]. TCF7L2 regulates not only proinsulin synthesis, but also the conversion of proinsulin to insulin [10].

Zinc has shown potential to improve glucose metabolism [15]; thus, alterations in zinc homeostasis can affect glucose control. SLC30A8, located on chromosome 8q24.11, encodes the zinc transporter ZnT8. This 369-amino acid protein has six transmembrane domains with histidine-rich regions between domains IV and V [16, 17]. It is predominantly expressed in pancreatic β-cells, which contain the majority of cellular zinc. ZnT8 transports zinc into the lumen of insulin-containing vesicles, in exchange for a proton via an ATPase pump; within these vesicles, Zn^{2+} is chelated by insulin hexamers to facilitate storage [18]. The most commonly studied SLC30A8 SNP is *rs13266634* (C/T), which reflects substitution of arginine (allele C) at position 325 with tryptophan (allele T) in the carboxy-terminal domain [18-20]. This variant has been proposed to alter the kinetics of zinc transport in insulin granules [19]. In Gabon, the prevalence of T2DM reported in 2024 was 7.5%, with annual increases similar to global trends [2]. Studying polymorphisms in genes associated with T2DM may therefore aid in identifying tools for the treatment or prevention of T2DM. This led us to investigate the relationships between *rs5219* in KCNJ11, *rs7903146* in TCF7L2, and *rs13266634* in SLC30A8 and T2DM in a Gabonese population.

Materials and methods

This case-control study was conducted from May 27, 2019, to November 15, 2022, at the Endocrinology Department of the University Hospital of Libreville, the Biochemistry Laboratory of the University of Health Sciences (Libreville), and the Molecular Biology Laboratory of the Research Institute of Health Sciences (Bobo-Dioulasso). The study adhered to the principles of the Declaration of Helsinki and was approved by the National Ethics Committee of Gabon (PROT N°015/2018/PR/CNE). All blood samples and sociodemographic data were collected after written informed consent was obtained. At CHUL, we enrolled 97 T2DM cases and 87 controls from the general population who met the inclusion criteria.

Study population

Case's inclusion criteria: Participants in this study were individuals recruited from the Endocrinology Department who were undergoing treatment for diabetes classified as type 2 according to the ADA 2019 criteria [21]. Additionally, they were fasting and at least 20 years old, having provided their consent.

Case's exclusion criteria: Participants were excluded from the study if they had type 1 diabe-

tes, as determined through an interview assessing age and insulin dependence. Additionally, pregnant women, those with gestational diabetes, and individuals with other confirmed types of diabetes were not included in this study.

Control's inclusion criteria: The control subjects of the study population were fasting patients who came to the biochemistry laboratory for routine check-ups (blood glucose, triglycerides, total cholesterol, HDLc, LDLc, and transaminases ALT and AST). Furthermore, the control subjects were aged 20 years or older with no family history of diabetes and consented.

Control's exclusion criteria: Exclusion criteria for control subjects were based on systolic blood pressure, diastolic blood pressure, and the analysis of blood glucose, CRP, triglycerides, total cholesterol, HDLc, LDLc, transaminases ALT/AST, and HIV test. Patients who had known inflammatory diseases and fasting blood glucose outside 74.5-110.9 mg/dL were excluded.

The weight of all patients was measured using a TEFAL scale, and height with a stadiometer. Waist circumference was measured with a tape measure. Body mass index (BMI) was calculated as: $BMI = \frac{Weight_{(kg)}}{(Height_{(m)})^2}$. Blood pressure (BP) was measured with a BEURER monitor after 5 minutes of rest on both arms, and the mean value was recorded.

Biochemical analysis

Blood glucose, triglycerides, total cholesterol, and creatinine were determined by standard enzymatic methods at the Biochemistry Laboratory of USS. HDL cholesterol was obtained after precipitation of other lipoprotein fractions with phosphotungstic acid and magnesium. LDL cholesterol was calculated using the Friedewald equation for triglyceride concentrations <353.9 mg/dL. The triglyceride-glucose index (TyG) was calculated as $TyG = \ln\left(\frac{\left[Triglyceride_{\frac{mg}{dL}}\right] \times \left[Glycemia_{\frac{mg}{dL}}\right]}{2}\right)$ with a threshold of 8.18 [22].

Molecular genotyping

Genotyping was performed at the IRSS Molecular Biology Laboratory. Genomic DNA was extracted with the Qiagen kit using the DNeasy Blood & Tissue protocol from 250 µL of whole blood and stored at -20°C until PCR. Polymorphisms were analyzed by RFLP. KCNJ11 was amplified with the primers: forward 5'-GACTCTGCAGTGAGGCCCTA-3' and reverse 5'-ACGTTGCAGTTGCCTTTCTT-3' [23]. TCF7L2 priemrs were forward 5'-TTAGAGAGCTAAGCACTTTTTAGGTA-3' and reverse 5'-AGAGATGAAATGTAGCAGTGAAGTG-3' [24]. SLC30A8 primers were forward 5'-GGACAGAAAGAGTTCCCATAGCG-3' and reverse 5'-ATAGCAGCATGTTTGAAGGTGGC-3' [18]. Primer concentrations were 5 µM, 3 µM, and 4 µM for KCNJ11, TCF7L2, and SLC30A8, respectively. The reaction mixture was prepared as described in **Table 1**.

For *rs5219* (KCNJ11), PCR cycling conditions were: initial denaturation at 94°C for 5 minutes; 35 cycles of 95°C for 30 seconds, 60°C for 30 seconds, and 72°C for 30 seconds; final extension at 72°C for 9 minutes; and hold at 4°C for 10 minutes [23]. For *rs7903146* (TCF7L2), conditions were: initial denaturation at 94°C for 5 minutes; 36 cycles of 94°C for 30 seconds, 51°C for 30 seconds, and 72°C for 30 seconds; final extension at 72°C for 10 minutes; and hold at 4°C for 10 minutes [24]. For *rs13266634* (SLC30A8), conditions were: initial denaturation at 94°C for 4 minutes; 36 cycles of 94°C for 35 seconds, 55°C for 40 seconds, and 72°C for 30 seconds; final extension at 72°C for 5 minutes; and hold at 4°C for 10 minutes [18].

Following amplification, PCR product integrity was checked by loading 1 µL of amplicon on a 2% agarose gel (**Figure 1**). Amplicons were then digested with restriction enzymes: Ban II for *rs5219* (KCNJ11), Rsa I for *rs7903146* (TCF7L2), and Hpa II for *rs13266634* (SLC30A8). For each gene, 10 µL of amplicon was mixed with 1 µL of enzyme, 5 µL of 10× buffer, and 34 µL of water (total volume 50 µL), and incubated for 4 hours at 37°C. Digestion products were resolved on 2% or 3% agarose gels in 1× TAE buffer with ethidium bromide and a molecular weight marker. Electrophoresis was run for 1.5 hours at 300 V/300 mA, and bands were visualized on a 360 nm UV transilluminator.

Statistical analysis

Analyses were performed using IBM SPSS Statistics, Version 25. Quantitative variables are presented as mean ± standard deviation; qualitative variables are presented as percentages with 95% confidence intervals (CI). Group comparisons for quantitative variables used ANOVA. The chi-square test was used for qualitative variables, along with odds ratios (OR) and

Table 1. Reaction mixture according to the PCR

Polymorphism	Reagents final concentration for PCR mixture					Total volume (µl)
	Forward primer	Reverse primer	Mastermix (1X)	DNA	H_2O DNA free	
rs5219 (KCNJ11)	1	1	4	2	12	20
rs7903146 (TCF7L2)	0.6	0.6	4	2	12.8	20
rs13266634 (SLC30A8)	1	1	5	2	16	25

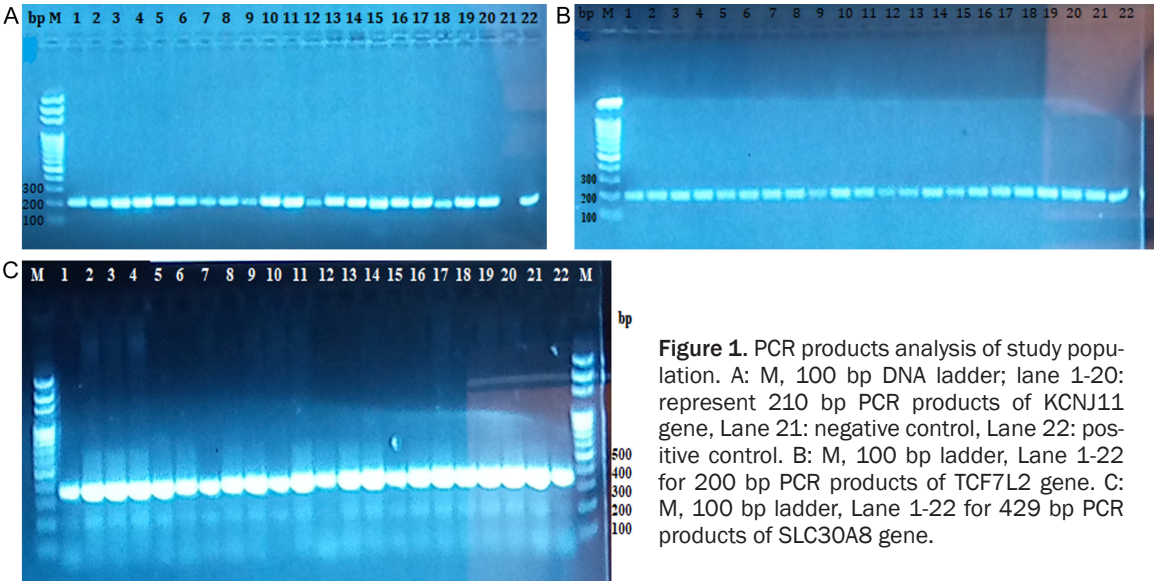

Figure 1. PCR products analysis of study population. A: M, 100 bp DNA ladder; lane 1-20: represent 210 bp PCR products of KCNJ11 gene, Lane 21: negative control, Lane 22: positive control. B: M, 100 bp ladder, Lane 1-22 for 200 bp PCR products of TCF7L2 gene. C: M, 100 bp ladder, Lane 1-22 for 429 bp PCR products of SLC30A8 gene.

95% CIs. Hardy-Weinberg equilibrium was assessed using the χ^2 goodness-of-fit test. Logistic regression models were fitted to assess associations between polymorphisms and T2DM occurrence, adjusted for age and BMI. The aim was to simulate three types of genotype transmission models: dominant, recessive, and codominant. This was done to assess the association between the different polymorphisms and the occurrence of type 2 diabetes. In the dominant model, having KK genotype was compared to having KE or EE genotypes of the KCNJ11 gene; having TT genotype was compared to having CT or TT genotypes for TCF7L2 gene; and having TT genotype was then compared to having CC or TT genotypes of the SLC30A8 gene. In the recessive models, the comparison was made between having EE genotype and to having the KE or KK genotypes of KCNJ11; having TT genotype and to having CT or CC genotypes of TCF7L2 gene, and having TT genotype against to having CT or CC genotypes of SLC30A8 gene. Finally, in the codominant model, having KE genotype was compared to having KK or EE genotypes; having CT genotype was compared to having CC or CT genotypes, and having CT genotypes were compared to having CC or TT genotypes, respectively, for KCNJ11, TCF7L2, and SLC30A8 genes. Furthermore, the association between mutant alleles and the risk of developing type 2 diabetes was assessed by calculating the odds ratio (OR) for each gene with a 95% confidence interval (CI). The OR is a statistical measure that allows estimation of the association by comparing different genotypes of the "patient" and "control" groups. A protective variant allele results in an OR between 0 and 1, and if the OR is greater than 1, the variant allele is predisposing. The association is considered statistically significant when the 95% confidence interval of the OR does not include the value 1. Two-sided *p*-values 0.05 were considered statistically significant.

Results

Sociodemographic and biological parameters of the study population

In total, 184 participants were enrolled (97 T2DM cases and 87 controls). Mean age was

Table 2. Socio-demographic and biological parameters of the study population

Variables	Total	Cases	Controls	p
Age (years)	48.4±13.8	56.3±10.3	39.6±11.8	0.0000
BMI (kg/m²)	27.3±5.7	28.2±6.3	26.2±4.9	0.0204
SBP (mmHg)	134.4±24.4	142.8±25.1	124.9±20.0	0.0000
DBS (mmHg)	84.3±18.5	89.2±19.0	78.8±16.3	0.0001
Abdominal perimeter (cm)	93.8±13.8	96.9±13.8	90.2±13.0	0.0008
Blood glucose (mg/dl)	118.2±65.4	147.3±76.4	85.4±18.2	0.0000
Triglycerides (mg/dl)	70.8±44.2	79.6±26.5	53.1±26.5	0.0002
Total cholesterol (mg/dl)	177.9±46.4	181.7±46.4	170.1±42.5	0.1673
HDL cholesterol (mg/dl)	46.4±15.5	50.3±15.5	42.5±19.3	0.0513
LDL cholesterol (mg/dl)	119.9±50.3	112.1±50.3	123.7±46.4	0.1527
Triglyceride index	8.0±0.7	8.4±0.7	7.6±0.4	0.0000

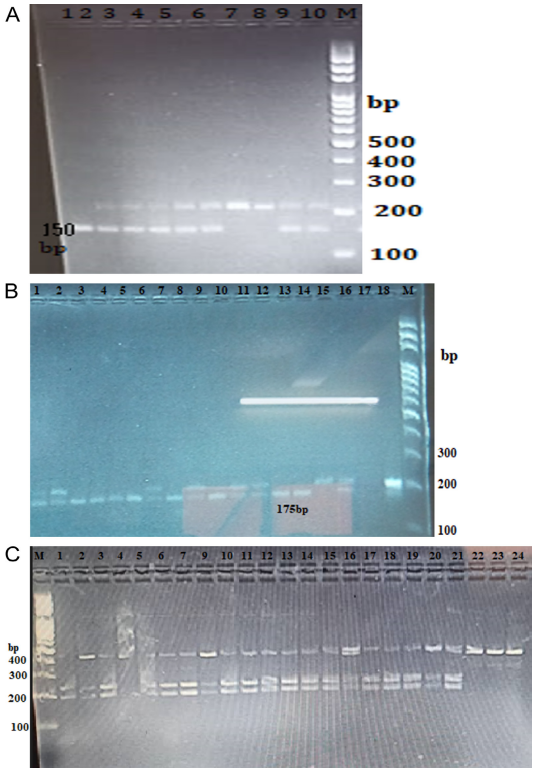

Figure 2. Digestion products for RFLP analysis of study population. A: Digestion products for KCNJ11-rs5219 by BanII enzyme with 2% agarose gel. Lane M: 100 bp ladder, Lane (1): homozygote EE (wild type), Lane (2-6, 9, 10): heterozygote EK (wild/mutant type), Lane (7, 8): homozygote KK (mutant type). B: Digestion products for TCF7L2-rs7903146 by RSAI enzyme with 3% of electrophoresis gel. Lane (1,2,7,9, 10,11,12,16, 18): heterozygote CT (wild/mutant type); Lane (3,4,5,6,8,13,14): homozygote CC (wild type); lane 15: homozygote TT (mutant type); lane 17: negative control. C: Digestion products for rs13266634- SLC30A8 gene by HpaII enzyme with 3% of electrophoresis gel. Lane M: 100 bp ladder; Lane (1): homozygote CC (wild type); Lane (2, 3, 5-21): heterozygote CT (wild type/mutant type); lane (4, 22-24): homozygote TT (mutant type).

48.4±13.8 years overall, 56.3±10.3 years in cases, and 39.6±11.8 years in controls (P< 0.001). Body mass index (BMI) averaged 27.3±5.7 kg/m^2 overall; it was 28.2±6.3 kg/m^2 in T2DM cases versus 26.2±4.9 kg/m^2 in controls (P=0.0204). Triglycerides averaged 70.8± 44.2 mg/dL in the total population; among T2DM cases the concentration was 79.6±26.5 mg/dL versus 53.1±26.5 mg/dL in controls (P=0.0002) (**Table 2**).

Distribution of genotypes and alleles of the KCNJ11 gene

Digestion of *rs5219* (KCNJ11) with Ban II yielded a wild-type EE band at 150 bp, a heterozygous EK pattern with bands at 150 and 210 bp, and a mutant-type KK band at 210 bp; fragments <50 bp were not visualized (**Figure 2A**). The EE genotype frequency was 62.2% in controls versus 42.6% in T2DM cases, whereas the KK genotype frequency was 28.7% in cases versus 21.1% in controls (P=0.0243). At the allele level, the E allele frequency was 56.9% in cases versus 76.6% in controls (P=0.0023) (**Table 3**).

Distribution of genotypes and alleles of the TCF7L2 gene

After digestion of *rs7903146* (TCF7L2) with Rsa I, three patterns were observed: wild type (CC) at 175 bp, heterozygous (CT) at 175 and 200 bp, and mutant type (TT) at 200 bp (**Figure 2B**). The CC genotype was present in 51.7% of controls and 37.1% of cases; the TT genotype was found in 22.7% of cases versus 9.2% of controls (P=0.0253). Among T2DM cases, the T allele predominated (42.8%), whereas the C

Table 3. Comparison of the distribution of genotypes and alleles of the KCNJ11, TCF7L2 and SLC30A8 genes in diabetics and controls

	Total	Cases	Controls	p
KCNJ11				
Genotypes				0.0243
EE	96 (52.2)	40 (42.6)	56 (62.2)	
EK	42 (22.8)	27 (28.7)	15 (16.7)	
KK	46 (25.0)	27 (28.7)	19 (21.1)	
Alleles				0.0023
E	234 (63.6)	107 (56.9)	127 (70.6)	
K	134 (36.4)	81 (43.1)	53 (29.4)	
TCF7L2				
Genotypes				0.0253
CC	81 (44.0)	36 (37.1)	45 (51.7)	
CT	73 (39.7)	39 (40.2)	34 (39.0)	
TT	30 (16.3)	22 (22.7)	8 (9.2)	
Alleles				0.0443
C	235 (63.9)	111 (57.2)	124 (71.3)	
T	133 (36.1)	83 (42.8)	50 (28.7)	
SCLC30A8				
Genotypes				0.9326
CC	34 (25.3)	19 (26.0)	15 (24.6)	
CT	69 (51.5)	38 (52.0)	31 (50.8)	
TT	31 (23.1)	16 (22.0)	15 (24.6)	
Alleles				0.4350
C	137 (51.1)	76 (52.1)	61 (50.4)	
T	131 (51.1)	70 (47.9)	61 (50.0)	

allele predominated in controls (71.3%; P= 0.0443), with an OR of 0.6 (95% CI, 0.2-1.0) (**Table 3**).

Distribution of genotypes and alleles of the SLC30A8 gene

For *rs13266634* (SLC30A8), digestion with Hpa II yielded the following patterns: wild type (CC) at 200 and 229 bp, heterozygous (CT) at 429, 200, and 229 bp, and mutant type (TT) at 429 bp (**Figure 2C**). The CC genotype frequency was 26.0% in cases and 24.6% in controls (P=0.9326). The C allele frequency was 52.1% in cases versus 50.0% in controls (P=0.4350) (**Table 3**).

Association by genetic transmission models

After adjustment for age and BMI, recessive models for *rs5219* (KCNJ11) and *rs7903146* (TCF7L2) were significantly associated with T2DM (P=0.021 and P=0.026, respectively) (**Table 4**).

Discussion

The genetic profiles of the *rs5219* polymorphism of the KCNJ11 gene were determined. The genotype distribution conformed to Hardy-Weinberg equilibrium, and analysis showed that the homozygous mutant (KK) and heterozygous (EK) genotypes were significantly more frequent in individuals with T2DM, whereas the wild-type (EE) genotype predominated in controls. Thus, the K allele and the KK and EK genotypes were associated with the occurrence of T2DM in this Gabonese population. Similar findings have been reported by several authors, including Al-Khalayfa et al. in a Jordanian population (2023) and Houshman et al. in a Kuwaiti population (2020) [25, 26]. Moreover, a 2022 meta-analysis by Yaxuan et al. encompassing 31 studies further supported the association between the E23K polymorphism of KCNJ11 and T2DM [27]. By contrast, a few studies reported no association [28]. Discrepancies may reflect the multifactorial nature of T2DM, in which genetic effects are modified by environmental and lifestyle factors, or differences in study design, ancestry, and sample size. The link between hyperglycemia in T2DM and the K allele can be explained by mutation-induced reduction in the ATP sensitivity of the K^+ channel, which decreases insulin secretion and thereby promotes elevated blood glucose levels.

The intronic polymorphism *rs7903146* (C/T) in intron 3 of TCF7L2 is among the strongest genetic risk factors for T2DM and has been widely implicated in the disease [29]. In our study, the CC genotype was more common in controls, whereas the CT and TT genotypes were significantly more frequent in T2DM cases. This pattern is consistent with a recessive

Table 4. Association between polymorphisms rs5219 (KCNJ11), rs7903146 (TCF7L2) and rs13266634 (SLC30A8), according to genetic transmission models

Genotypes/alleles	Cases n (%)	Controls n (%)	OR [95% CI]	p
KCNJ11 rs5219				
Recessive model			0.384 [0.171-0.865]	0.021
EE	38 (42.7)	51 (57.3)		
KE+KK	53 (63.1)	31 (36.9)		
Dominant model			1.933 [0.763-4.897]	0.165
KK	27 (62.8)	16 (37.2)		
KE+EE	64 (49.2)	66 (50.8)		
Co-dominant model			1.824 [0.730-4.556]	0.198
KE	26 (63.4)	15 (36.6)		
KK+EE	65 (49.2)	67 (50.8)		
TCF7L2 rs7903146				
Recessive model			3.460 [1.161-10.308]	0.026
TT	22 (73.3)	8 (26.7)		
CT+CC	75 (48.7)	79 (51.3)		
Dominant model			0.742 [0.344-1.601]	0.447
CC	36 (44.4)	45 (55.6)		
CT+TT	61 (59.2)	42 (40.8)		
Co-dominant model			0.684 [0.316-1.481]	0.336
CT	39 (53.4)	34 (46.6)		
CC+TT	58 (52.3)	53 (47.7)		
SLC30A8 rs13266634				
Recessive model			0.757 [0.244-2.350]	0.630
TT	16 (51.6)	15 (48.4)		
CT+CC	54 (59.3)	37 (40.7)		
Dominant model			0.625 [0.202-1.934]	0.414
CC	19 (63.3)	11 (36.7)		
CT+TT	51 (55.4)	41 (44.6)		
Co-dominant model			1.000 [0.488-2.050]	1.000
CT	35 (57.4)	26 (42.6)		
CC+TT	35 (57.4)	26 (42.6)		

inheritance model even after adjustment for age and BMI, indicating that the T allele is a risk factor for T2DM in this population. Comparable associations between *rs7903146* and T2DM have been reported in India [6], Morocco [30], and across Asian cohorts [31]. Mechanistically, TCF7L2 variation has been linked to impaired exocytosis of insulin granules and reduced glucose tolerance [30]. Nonetheless, genotype and allele distributions vary across populations. The prevalence of the TT genotype has been reported as low as 5.7% in Iraq and 7% in parts of Asia, whereas in Morocco (24.0%) it is similar to our finding. Other studies, such as Farag (Egypt, 2024), did not detect an association between the T allele of *rs7903146* and T2DM [32].

For SLC30A8, the *rs13266634* (C/T) variant - proposed to alter zinc transport kinetics in insulin granules [20] - showed no significant differences in genotype or allele frequencies between T2DM cases and controls in our data, indicating no association with T2DM in this Gabonese cohort. This observation aligns with results from Abu-Khadra et al. (Jordan, 2025) [33]. However, discordant findings have been reported elsewhere, including Iran (Yazdi et al., 2020), Jordan (Mashal et al., 2020), and India (Goyal et al., 2022) [18, 34, 35]. For example, Mashal et al. reported a CC genotype frequency of 52.8%, whereas Yazdi et al. reported 9.88%. Such variability likely reflects population-specific genetic backgrounds and environmental exposures, as well as differences in sampling

frames and analytic approaches. Our sample size (n=184) may limit statistical power relative to larger studies, a challenge noted in work from Central Africa. Nevertheless, to our knowledge, this is the first study to examine these genetic factors in relation to T2DM in Gabon.

The principal limitation of this study is the modest sample size. Larger studies, ideally with replication cohorts and sequencing, will be necessary to confirm the associations observed and to identify additional variants relevant to T2DM risk in this population.

Conclusion

Two polymorphisms were associated with the occurrence of T2DM in this population: *rs5219* in KCNJ11 and *rs7903146* in TCF7L2. By contrast, *rs13266634* in SLC30A8 was not associated with the disease. Future work should include larger samples and extend genotyping to additional loci involved in diabetes and glucose metabolism.

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Disclosure of conflict of interest

None.

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