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The practice of consanguineous marriage and the risk of diabetes among offspring in the province of Tetouan (Morocco)

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Abstract
Purpose – The practice of consanguinity has been culturally preferred in most Arab countries, including Morocco. This behavior leads to an increase in genetic abnormalities, such as hypertension and diabetes. This paper examines the prevalence and determinants of first-cousin marriages and their impact on diabetes among offspring.
Design/methodology/approach – Data on 882 couples were collected through face-to-face interview via a pre-established questionnaire based on the variables selected within the objectives of this study. The authors used the multiple logistic regression modeling procedure in this study.
Findings – The results of the study indicate that the prevalence of first-cousin marriages were 15% among students' parents. From the multiple logistic regression modeling, the authors found a significant effect of paternal and maternal grandparents' first-cousins marriage on that of parents (aOR = 3.27 and aOR = 3.36, respectively). However, an 11-fold higher risk of first relative marriages among parents once the paternal and maternal grandparents were first-cousins and the father was illiterate (aOR = 11.01). Moreover, the authors reported a diabetes risk of more than 14 times when the effects of first-cousin maternal grandparents and parents and the hypertension among mother or her sibling were combined (aOR = 14.48) or when the effects of first-cousins maternal grandparents, first-cousin parents and mother's age at marriage between 21 and 29 years were combined (aOR = 14.56).
Originality/value – First-cousin marriage depends on the father's illiteracy and the consanguinity of grandparents' factors. The cumulative effect of first-cousin marriage among grandparents, parents and a family history of hypertension among mother or her sibling increase the risk of diabetes among these mothers.

Keywords Consanguinity, First-cousins, Diabetes, Hypertension
Paper type Research paper

Introduction
Consanguinity is a special case of marital relationship. It is defined as a union between two individuals related as second degree or closer cousins with a coefficient of consanguinity (F) equal to or greater than 0.0156 (Bittles, 2001). Consanguinity can include more distant unions that can go up to a coefficient of inbreeding $F = 0.0039$ (Hamamy *et al.*, 2011). Like in

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other Arab-Muslim countries, Morocco record high rates that vary between 23.7% and 24.37% in the north of the country (Ossmani, Ouardani, Habibeddine, Amzazi, & Talbi, 2018; Hajjaji, Khadmaoui, & El Bakkali, 2020). Marriage between first-cousins is the most popular form among all types of consanguineous marriage (Bener & Alali, 2006; Ben Halim *et al.*, 2016). In other areas like Pakistan, 28.13% to 34.1 % of couples were first relatives (Ahmad, Hameed, Jehangir, & Khttak, 2013; Tufail, Rehman, & Malik, 2017; Khan & Mazhar, 2018). It appears that the dominance of this so-called first degree marriage is a characteristic of marriages in Morocco according to several studies carried out in different regions (Talbi, Khadmaoui, Soulaymani, & Chafik, 2008; Latifi *et al.*, 2009; Hami, Soulaymani, & Mokhtari, 2009). Marriage may seem like an individual matter involving only future spouses. But in reality, this practice depends on several factors such as early marriage (Sidi-Yakhlef & Metri, 2013), level of education and parents' consanguinity (Bener, Hussain, & Teebi, 2007).

Consequently, this behavior will contribute to the impoverishment of the genetic variability, and will offer a possibility of manifestation of deleterious or harmful genes in the genotype of the population, and therefore a harmful effect on health profile (Fareed, Ahmad, Anwar, & Afzal, 2017). In addition, several studies confirm diabetes rate increase among the offspring of consanguineous couples (Bener *et al.*, 2007; Elhadd, Al-Amoudi, & Alzahrani, 2007; Bener & Mohammad, 2017). The occurrence of diabetes in the offspring of couples between first-cousins is higher compared to nonconsanguineous (Anaya *et al.*, 2006), or second cousin parents (Albishi, AlAmri, & Mahmoud, 2022). In Saudi population, type 2 diabetes is correlated with consanguinity particularly among the offspring of first-cousin marriages (Alzahrani *et al.*, 2021). The heritability of type 2 diabetes with a polygenic mode in Iranian population is higher than the global average, and the risk of developing this type of diabetes is higher in individuals with affected first-cousin parents than in individuals with affected second-cousin parents (Akbarzadeh *et al.*, 2022).

From a medical perspective, diabetes represents a series of metabolic conditions associated with hyperglycaemia caused by partial or total insulin insufficiency (Garg & Duggal, 2022). It can be associated with premature morbidity as microvascular complications, multiple visits to healthcare providers and mortality (Egan & Dinneen, 2019). In 2019, 16,300 deaths were caused by diabetes in population below 25 years globally (Cousin *et al.*, 2022). In Morocco 2.5 million adults suffer from diabetes, and in 2018, 51.5% of total medical expenses were generated by long-term illnesses, while diabetes represents 10.4% of these expenses (Benmaamar *et al.*, 2021).

The northern Moroccan province of Tetouan, a gateway to Europe, is located in a valley near the Strait of Gibraltar. The studied individuals in this area were Jebala, originated from the surrounding mountains. According to 2014 General Population and Housing Census of Morocco, this population stands at 550,374. The urban provincial agglomeration comprises 397,973 inhabitants, compared to 152,401 inhabitants in rural areas. This province is characterized by a total illiteracy rate of 27.5%. To our knowledge, only few studies have considered the cumulative effect of consanguinity through several generations, among socio-demographic characteristics on diabetes in offspring. In this context, we suggest modeling the cumulative effect of consanguinity of maternal and paternal grandparents across that of parents among socio-demographic characteristics that differ on diabetes among offspring in Tetouan.

Materials and methods

Study design

This is an observational, cross-sectional study design carried out in 2017 on a sample of 1500 couples from parents' and grandparents' generation of 500 students who voluntarily participated in this study, randomly selected from those enrolled at Abdelmalek Essaadi

University in Tetouan. Given the ethical considerations, the study was approved by the participants' university administration, and the research team applied all possible ethical measures to ensure the protection of the participants. The students were latter informed that they could withdraw from the study at any time without being subject to penalty, and anonymity and confidentiality were maintained throughout the study. The instruments included demographic, pathological and obstetrical characteristics. "Beyond first cousins" were defined by combining the first cousins once removed, second cousins and nonconsanguineous categories and data are analyzed considering "first cousin marriages" as a separate category along with 'Beyond first cousins' for better interpretation. The dependent variable was diabetic pathology in mothers or their siblings (Yes/No) for the first logistic model, and parents' marital status (first cousins/beyond first cousins) for the second model. In the first model, the independent variables degree of maternal grandparents' consanguinity, degree of parents' consanguinity, mother protogenesic interval, hypertension among mother or her siblings and mother's age at marriage were selected on the basis of the literature (Bener & Mohammad, 2017; Salameh *et al.*, 2022; Lin *et al.*, 2022). On the other hand, the independent variables, degree of paternal grandparents' consanguinity, degree of maternal grandparents' consanguinity, provenance of the maternal grandfather (Urban/rural: where individuals were born and spent their childhood), education level of the student's father (Illiterate, primary, secondary and superior) and mother's provenance were considered in the second model (Talbi, Khadmaoui, Soulaymani, & Chafik, 2006; Bener *et al.*, 2007; Metgud, Naik, & Mallapur, 2012; Mahboub, Alsaqabi, Allwimi, Aleissa, & Al-Mubarak, 2020).

During the development of the protocol and analysis of the results in this study, three types of bias were considered to limit their effects and their consequences on our conclusions. In selection bias, we carried out a random sampling of the subjects to avoid any distorted vision of the source population (Infante-Rivard & Cusson, 2018), while in classification bias, the subjects of our sample were checked before their classification according to exposure (supposed risks factors) or the studied risk (parents' consanguinity and diabetes in the mother or her sibling) to avoid any distorted image of reality (Greenland, 1980). On the other hand, the phenomenon of confusion was taken into account in the multivariate logistic analysis (Jean *et al.*, 2009).

Initially, after obtaining the oral consent of interviewed students, the data were collected through face-to-face interview via a pre-established questionnaire based on the variables selected within the objectives of this study. After excluding those refusing to continue the interview (276 out of 1500) and the incomplete questionnaires (342 out of 1500), we collected an amount of demographic and socio-cultural information for a total of 882 couples from parents' and grandparents' generations.

Modeling and analytic strategy

Data are expressed in percentage for categorical variables in descriptive analysis. In a bivariate analysis, the comparison between the qualitative variables was made using the χ^2 test, and Fisher's exact probability was determined in the case of dichotomous variables and for samples of less than five cases. A "p" value ≤ 0.05 was considered statistically significant. The choice of our explanatory variables is based on knowledge of diabetes among offspring of consanguineous marriages and the possible factors influencing it. Thus, the variables, which could have a relationship with diabetes among the student's mother or her sibling, were introduced in the logistic regression. An in-depth review of the data in the literature was essential beforehand. The choice of variables is therefore based on their clinical relevance and knowledge of proven or supposed confounding factors (Hosmer *et al.*, 2013). The explanatory variables, which were sufficiently strongly linked to dependent variables, were then preserved in the model. All variables whose significance level is less than 0.20 during the univariate analysis were included in the initial multiple logistic regression model. The threshold of 0.20 makes it possible to take into account variables that are supposed to be factors of possible confusion or interaction terms. Variables forced ($p > 0.20$) or known to be associated with two dichotomous responses were also included in the analysis. Furthermore, to determine the best model when carrying out mathematical modeling using logistic regression, we focused on a strategy involving three stages: (1) variable specification, (2) interaction assessment and (3) confounding assessment followed by consideration of precision. The fit of the model was tested by the Hosmer–Lemeshow fit test. The odds ratios (OR) and 95% confidence intervals (CI) were calculated to determine whether an exposure factor is significantly associated with the dichotomous variable. Full models include simultaneous multivariate analysis of risk factors for parents' consanguinity or diabetes among mothers or their siblings (adjusted ORs). Other additional post-estimation analyses were performed by the "Lincom" command (Linear combinations of parameters) for the calculation of the adjusted OR and the 95% CI of combined effects between factors from the previous multivariate logistic models. The purpose of this strategy was to obtain a valid estimate of an exposure–consanguinity relationship that accounts for confounding and effect modification (Aminot & Damon, 2002; Kleinbaum, Klein, & Regression, 2005; El Sanharawi & Naudet, 2013).

The statistical software package Stata 14 and R software (https://www.r-project.org/) were used in this analysis, particularly heavy use of the Stata commands logit, or, and lincom. On the other hand, R software (https://www.r-project.org/) was used for the graphical representations by the "ggplot2 packages" (Wickham, 2016), "tidyverse package" (Wickham, 2017) and "ggstatsplot package" (Patil, 2021). All tests were two-tailed, and values of $p < 0.05$ were considered statistically significant.

Results

The results of this study showed that 15% of students' parents were first-cousins and 85% beyond first-cousins. With regard to paternal grandparents, our results showed that 6.5% of paternal grandparents were first-cousins and 93.5% beyond first-cousins. In addition, 8% of maternal grandparents were first-cousins and 92% beyond first-cousins (Figure 1). Considering hypertension among students' mothers or their siblings, 31.9% of students

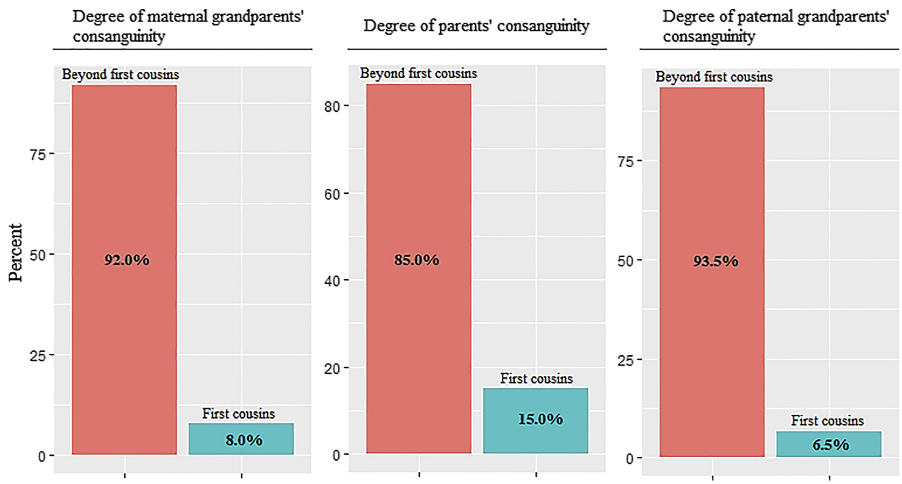

Figure 1. Distribution of the percentage of consanguinity among parents, paternal grandparents and maternal grandparents

had at least one family member with hypertension (a mother or her sibling) compared to 68.1% as normal. In addition, 26.6% of students had at least a mother or one of her siblings with diabetes.

According to Figure 2, diabetes was significantly lower among mothers or their siblings descended from beyond first-cousins maternal grandparents (74% versus 26%, $p < 0.05$), while a significantly higher rate of hypertension among diabetic mothers or their siblings (36% versus 22%, $p < 0.05$). In addition, a high rate of diabetes has been observed among students' mothers with a protogenesic interval between 18 and 24 months (34% versus 26 and 20%) and a low rate of diabetes was recorded when mother's age at marriage was <21 years (22% versus 25 and 37%).

The multivariate analysis of first-cousin maternal grandparents, protogenesic interval between 18 and 24 months, hypertensive mother or her sibling and mother's age at marriage between 21 and 29 years of the student's mother with diabetes in mothers or her siblings, controlling for other variables, indicated the risks of 4.91, 3.02, 2.19 and 2.21 times that mothers and their siblings had diabetes (aOR 4.91 (95%CI 1.06–22.68), aOR 3.02 (95%CI 1.23–7.42), aOR 2.19 (95% CI 1.04–4.89) and aOR 2.21 (95% CI 1.08–4.97), respectively) (see Table 1).

Logistic regression was performed, by adjusting additionally, for first-cousin maternal grandparents with first-cousin parents, hypertensive mother or her sibling, mother's age at marriage between 21 and 29 years or protogenesic interval of 18–24 months. The risk of

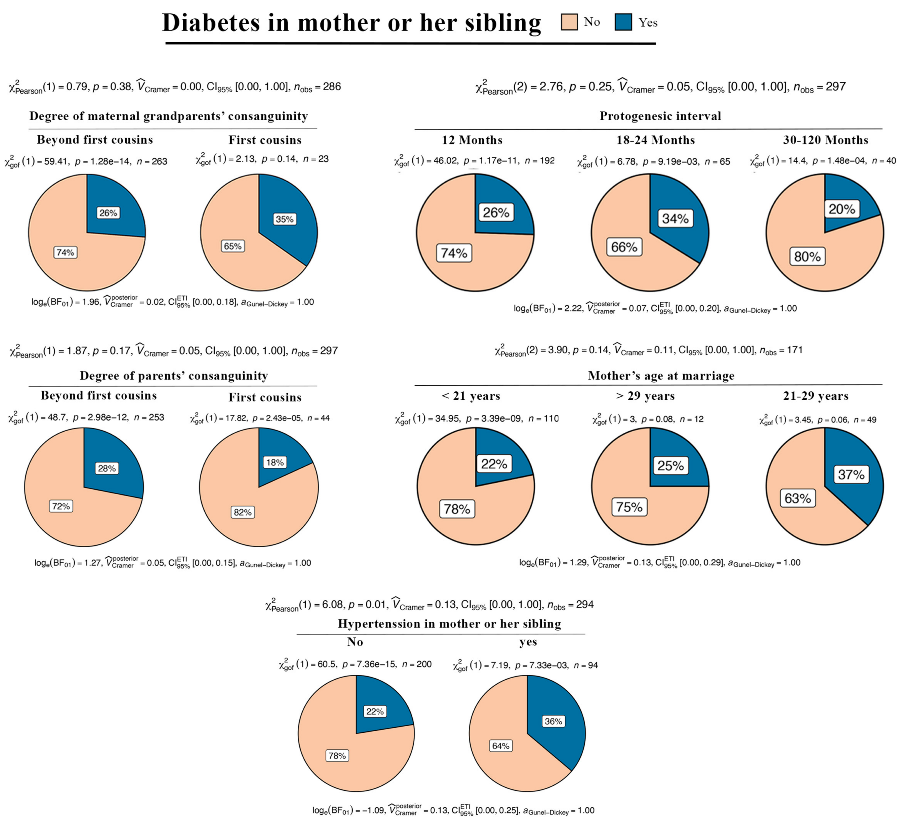

Figure 2.
Distribution of diabetes among mothers or their siblings according to degree of consanguinity and other characteristics

Diabetes in mothers or her siblings $^{\phi}$ ($n = 79$) Covariates	Crude analysis ^{c}OR (95% CI) $^{p\text{-value}}$	Adjusted analysis ^{a}OR (95% CI) $^{p\text{-value}}$
Degree of maternal grandparents' consanguinity		
Beyond first cousins	Reference	Reference
First cousins	1.49 (0.60−3.69)	4.91 (1.06−22.68)
Degree of parents' consanguinity		
Beyond first cousins	Reference	Reference
First cousins	0.56 (0.25−1.28)	1.33 (0.46−3.86)
Protogenesic interval		
12 months	Reference	Reference
18–24 months	1.49 (0.81−2.74)	3.02 (1.23−7.42) **
30–120 months	0.72 (0.31−1.68)	1.16 (0.33−4.09)
Hypertension among mother or her siblings		
No	Reference	Reference
Yes	1.95 (1.14−3.33)	2.19 (1.04−4.89) *
Mother's age at marriage		
<21 years	Reference	Reference
21–29 years	2.08 (0.99−4.34)	2.21 (1.08−4.97) *
30–40 years	1.19 (0.29−4.76)	1.04 (0.24−4.58)
Degree of maternal grandparents' consanguinity [a]		6.58 (0.89−48.34)
Degree of maternal grandparents' consanguinity [b]		10.81 (1.64−71.24) *
Degree of maternal grandparents' consanguinity [c]		10.87 (1.74−67.81) *
Degree of maternal grandparents' consanguinity [d]		14.87 (2.09−105.51) **
Degree of maternal grandparents' consanguinity [a,b]		14.48 (1.44−145.28) *
Degree of maternal grandparents' consanguinity [a,c]		14.56 (1.52−139.01) *
Degree of maternal grandparents' consanguinity [a,d]		19.91 (1.82−217.87) *

Note(s): [a] maternal grandparents first cousins adjusted for parents first cousins; [b] maternal grandparents first cousins adjusted for hypertension in the mother and her siblings; [c] maternal grandparents first cousins adjusted for mother's age at marriage between 21 and 29 years; [d] maternal grandparents first cousins adjusted for protogenesic interval 18–24 months; ^{c}OR: crude odds ratio; ^{a}OR: adjusted odds ratio; CI: confidence interval, *$p < 0.05$, **$p < 0.01$; ϕ: dependent variable

Table 1. Risk factors analysis for diabetic vs. no-diabetic mothers or their siblings

diabetes in mothers or their siblings was still increasing when first-cousin maternal grandparents were adjusted for hypertensive mother or her sibling aOR 10.81 (95%CI 1.64−71.24), mother's age at marriage between 21 and 29 years, aOR 10.87 (95%CI 1.74−67.81), protogenesic interval of 18–24 months, aOR 14.87 (95%CI 2.09−105.51), first-cousin parents and hypertensive mother or her sibling, aOR 14.48 (95%CI 1.44−145.28), first-cousin parents and mother's age at marriage between 21 and 29 years, aOR 14.56 (95%CI 1.52−139.01) and first-cousin parents and protogenesic interval of 18–24 months, aOR 19.91 (95%CI 1.82−217.87), respectively.

To accurately identify independent risk factors significantly associated with first-cousin parents, a bivariate analysis and multivariate regression logistic model analysis were performed. Our results showed that first-cousin maternal grandparents, and first-cousin paternal grandparents indicated the risks of 3.27 and 3.36 times that parents were first-cousins (aOR 3.27 (95%CI 1.010−10.59), aOR 3.36 (95%CI 1.042−10.87), respectively). In contrast, secondary educational level of the father showed statistically lower odds (aOR 0.21 (95% CI 0.055−0.76)) for having consanguineous marriage (first-cousins) when compared to illiterate educational level. However, adjusting additionally for first-cousin maternal and paternal grandparents with educational level of the student's father, the risk that parents were first-cousins was increased when first-cousin paternal grandparents adjusted for first-cousin maternal grandparents and illiterate educational level of the father, aOR 11.01 (95% CI

2.77–43.77), first-cousin maternal grandparents adjusted for primary educational level of the father, aOR 3.36 (95%CI 1.04–10.87), first-cousin paternal grandparents adjusted for primary educational level of the father, aOR 3.27 (95%CI 1.010–10.59) (see Table 2).

Discussion

The results of this study showed that 15% of students' parents were first-cousins, 8% of paternal grandparents were first-cousins and 6.5% of maternal grandparents were first-cousins. It seems that the dominance of the so-called first–degree marriages is a characteristic of Arab-Muslim marriages according to studies carried out in Morocco (Talbi *et al.*, 2008), Algeria (Sidi-Yakhlef & Metri, 2013), Tunisia (M'rad & Chalbi, 2004), Qatar (Bener & Hussain, 2006) Saudi Arabia (El Mouzan, Al Salloum, Al Herbish, Qurachi, & Al Omar, 2008) and among Shiite groups in Lebanon (El-Kheshen & Saadat, 2013). First-cousin unions in the parents' generation increased by 2.30 times over the paternal grandparents' generation and 1.88 times over the maternal grandparents' generation, respectively. In contrast, in the population of Doukkala in Morocco, unions between first-cousins decreased from 45% in the generation of paternal grandparents and from 41% in maternal grandparents to 24% in the generation of the couple studied (Talbi *et al.*, 2008).

The multivariate logistic regression analysis, which includes the possible variables influencing diabetes after controlling for other variables, showed that the risk of having diabetes in student's mother or her sibling was 4.91 times higher when maternal grandparents were first-cousins compared to beyond first-cousin maternal grandparents. The association between consanguinity and diabetes among offspring has been highlighted

Degree of parents' consanguinity $^{\phi}$ (n = 45) Covariates	Crude analysis ^{c}OR (95% CI) $^{p\text{-value}}$	Adjusted analysis ^{a}OR (95% CI) $^{p\text{-value}}$
Degree of paternal grandparents' consanguinity		
Beyond first cousins	Reference	Reference
First cousins	4.65 (1.75–12.34)	3.27 (1.010–10.59)
Degree of maternal grandparents' consanguinity		
Beyond first cousins	Reference	Reference
First cousins	3.40 (1.34– 8.61)	3.36 (1.042–10.87)
Provenance of the maternal grandfather		
Urban	Reference	Reference
Rural	1.51 (0.60–3.80)	1.86 (0.56–6.21)
Level of education of the student's father		
Illiterate	Reference	Reference
Primary	1.037 (0.46–2.30)	0.77 (0.33–1.81)
Secondary	0.27 (0.08–0.94)	0.21 (0.055–0.76)
Superior	0.35 (.071–1.73)	0.34 (0.062–1.87)
Mother's provenance		
Urban	Reference	Reference
Rural	1.35 (0.67–2.71)	0.80 (0.33–1.95)
Degree of paternal grandparents' consanguinity[a]		11.01 (2.77–43.77) **
Degree of maternal grandparents' consanguinity [b]		3.36 (1.04–10.87) *
Degree of paternal grandparents' consanguinity [c]		3.27 (1.010–10.59) *

Note(s): [a]: paternal grandparents first cousins adjusted for maternal grandparents first cousins and illiterate educational level of the father; [b]: maternal grandparents first cousins adjusted for primary educational level of the father; [c]: paternal grandparents first cousins adjusted for primary educational level of the father, ^{c}OR: crude odds ratio, ^{a}OR: adjusted odds ratio, CI: confidence interval, *$p < 0.05$, **$p < 0.01$; ϕ: dependent variable

Table 2.
Determinants of first cousin vs. beyond first cousin marriages

by several authors (Bener *et al.*, 2007; Elhadd *et al.*, 2007; Bener & Mohammad, 2017). In the northwestern part of Colombia, the occurrence of diabetes in the offspring of first-cousin couples is higher compared to nonconsanguineous individuals (Anaya *et al.*, 2006). The risk of diabetes due to consanguinity in this study was closer to that found in a study conducted in Algeria, by Dali-Sahi, where consanguinity increases three times the chance of exposure to type 2 diabetes (Dali-Sahi, Benmansour, Aouar, & Karam, 2012). According to our results, a mother or her sibling with hypertension increases the risk of having diabetes in the mother or her sibling by 2.19 times. More recent studies have confirmed this link between hypertension and diabetes (Nibouche & Biad, 2016; Salameh *et al.*, 2022). According to Chung and Won, hypertension in diabetic patients is approximately twice as common as those without diabetes (Chung & Won, 2011). In a systematic review and meta-analysis carried out in Ethiopia, hypertension increases the risk of having diabetes (Tesfaye *et al.*, 2019). In Sudan, Bushara *et al.* showed that the prevalence of hypertension in Rural and Urban areas is high among patients with diabetes mellitus (Bushara *et al.*, 2015, 2016).

This risk of diabetes in mothers or their siblings becomes 10.81 times higher when first-cousin maternal grandparents were adjusted for hypertension in mother or her sibling. This can be explained, on the one hand, by the fact that consanguinity can increase the risk of diabetes and hypertension when high susceptibility genes are transmitted in an autosomal recessive way (Hamamy *et al.*, 2011). Consanguinity leads to an increase in homozygosity through the expression of certain deleterious recessive genes which in their turn leads to an increase in genetic abnormalities, such as the circulatory system abnormalities, and multifactorial disorders such as hypertension and diabetes (Mosayebi & Movahedian, 2007; Shawky & Sadik, 2011; Halim *et al.*, 2013; Bener & Mohammad, 2017; Hawari *et al.*, 2022). On the other hand, hypertension is also responsible for the occurrence of a part of diabetes in the offspring (Nibouche & Biad, 2016; AlMutair, AlSabty, AlNuaim, Al Hamdan, & Moukaddem, 2021; Lin *et al.*, 2022). Some types of diabetes, such as type 2 diabetes, are associated with an increased risk of pulmonary arterial hypertension (Nundlall, Playford, Davis, & Davis, 2021). The co-existence of hypertension with type 2 diabetes increases the diabetic complications among patients (Sabuncu *et al.*, 2021). A total of 80% of diabetics die from coronary vascular disease, especially from hypertension (Abdissa & Kene, 2020).

However, when first-cousin maternal grandparents were adjusted for first-cousin parents and hypertensive mother or her sibling, or when first-cousin maternal grandparents were adjusted for first-cousin parents and age at marriage of the student's mother between 21 and 29 years old, the risk of diabetes rises and becomes more than 14 times higher compared to the reference group (nonhypertensive mothers or their siblings, parents and grandparents beyond first-cousins). This relationship between the degree of consanguinity of individuals and the risk of the occurrence of a congenital anomaly has been confirmed by several studies (Jaouad *et al.*, 2009; Tadmouri *et al.*, 2009; Borhany *et al.*, 2010; Obeidat *et al.*, 2010; Halim *et al.*, 2013; Becker *et al.*, 2015; Oniya, Neves, Ahmed, & Konje, 2019). The excessive risk of developing these recessive conditions linked to consanguinity is proportional to the average inbreeding coefficient (Bittles & Black, 2010; Bener & Mohammad, 2017). Indeed, this confirms the combined effect of the consanguinity of parents and maternal grandparents on the occurrence of diabetes in the student's mother or her sibling. In Saudi Arabia, parental consanguinity was associated with type 1 diabetes; however, children of first-cousin parents showed a higher risk of developing type 1 diabetes than the children of second-cousin parents (Albishi *et al.*, 2022). Consanguinity itself is not responsible for the appearance of unfavorable traits. However, deleterious autosomal recessive alleles are sometimes hidden within the family in a heterozygous state for many generations, and consanguineous unions between mutation carriers will bring them to the surface (Halim *et al.*, 2013). The expression of these genes accelerates with the accumulation of consanguinity over several generations (Bittles,

2011) and with the proximity of the relations between spouses (Bener & Hussain, 2006; Becker *et al.*, 2015). Studied samples from the population of Saudi Arabia using the GlobalFiler kit highlighted an excess homozygosity in autosomal STRs. This study suggests that the excess of homozygosity observed is caused by the elevated rate of consanguinity (Alsafiah & Goodwin, 2022).

To determine the variables affecting the marital choice between first-cousins in the students' parents' generation, demographic and sociocultural characteristics of the population were studied. According to the results of the multivariate analysis, three variables 1) degree of consanguinity of the paternal grandparents, 2) degree of consanguinity of the maternal grandparents and 3) the level of the student's father's education seem to have an impact on the matrimonial choice between first-cousins.

The results showed an increase in first-cousin marriage 3.27 times higher in couples when the paternal grandparents were also first-cousins compared to beyond first-cousins, and 3.36 times higher in couples when the maternal grandparents were also first-cousins compared to beyond first-cousins. This testifies the anchoring of this practice in the matrimonial system from generation to generation. Children, therefore, imitate their parents when choosing their future spouses (Bener & Hussain, 2006; Bener *et al.*, 2007; Shawky & Sadik, 2011). In Saudi Arabia, individuals with higher attitude toward consanguineous marriage were people who have frequent family history of consanguineous marriage and people with parental consanguinity (Mahboub *et al.*, 2019, 2020). In other cases, parents even recommend their sons and daughters to choose their spouses within the family circle (Sidi-Yakhlef & Metri, 2013; Jabeen & Malik, 2014). This shows the impact of the socio-cultural environment on the genes flows of human populations (M'rad & Chalbi, 2004). For several populations, marriages between cousins guarantee a stable marital life and reduce divorces (Talbi *et al.*, 2006; Tadmouri *et al.*, 2009; Bhopal, Petherick, Wright, & Small, 2014; Saadat, 2015). This stability is justified by socio-cultural factors such as the ease of marriage arrangements, continuity of culture and way of life, degree of social compatibility and the ease of integrating the new environment (Bittles, 2001; Talbi *et al.*, 2006; Sandridge, Takeddin, Al-Kaabi, & Frances, 2010; Hamamy *et al.*, 2011).

The risk of marriage between first relatives' parents becomes 11 times higher when both paternal and maternal grandparents were first-cousins and the father was illiterate. In this study, the father's level of education was an important factor when choosing the future spouse. In fact, this variable has been cited by several authors as an explanatory variable for this marital behavior (Benhamadi, 1996; Bittles, 2001; Attazagharti *et al.*, 2006; Bener & Hussain, 2006; Talbi *et al.*, 2006; Bener *et al.*, 2007; Chalbi, 2009; Metgud *et al.*, 2012). According to M'rad and Chalbi, when it comes to marriage, individuals tend to conform to a collective pattern, regardless of their awareness of the consequences (M'rad & Chalbi, 2004). These results highlighted the importance of education (illiteracy) in the perpetuation and transmission of traditions and collective values across generations (Talbi *et al.*, 2006). In Turkey, the risk of consanguinity is 3.8 times higher for a woman who is illiterate or does not complete primary school (Çiçeklioğlu, Ergin, Demirelöz, Ceber, & Nazlı, 2013). In Jordan, a higher level of education and an increasing rate of urbanization emerged as predictors of declining consanguinity in the population (Islam, 2018) because there is an association between high educational level and awareness of the consequence of consanguineous marriage (Mahboub *et al.*, 2019).

This study however has several limitations. Since the data were collected from students enrolled at Abdelmalek Essaadi University of Tetouan, this could be a selection bias excluding other Moroccan regions, and thus our findings do not represent the overall Moroccan population. Furthermore, the interviewees were not able to determine the exact type of diabetes, and clinical data were missing because records of diabetic cases were not available. This led us to assemble different types of this disease in one single category (diabetic/non diabetic). Also, 276 students refused to continue the interview and 342 questionnaires were incomplete. These missing cases reduce the statistical power for which the sample size was calculated at the start of this study (1500 couples).

Conclusion

In this work, a prevalence of 15.0% of students' parents were first-cousins against 8.0% and 6.5% respectively, for maternal and paternal grandparents. However, consanguineous marriage between first-cousins depends on two main factors: the husband's level of education (illiteracy) and the matrimonial choice of parents and in-laws (first relatives). Inheriting this behavior increases homozygosity in offspring leading to an increased risk of autosomal recessive diseases such as diabetes. The cumulative effect of marriage between first relatives among maternal grandparents' and parents' generation, and the existence of hypertension among mother or her sibling increase to a greater extent the risk of diabetes among these mothers.

We believe that these findings hold promise for further genetic studies of diabetes among Moroccan population. The data obtained can be used to frame health care policies and support genetic counseling strategies to raise public awareness of the increased risk of diabetes among offspring of first-cousin marriages.

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