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Original Article

# Enrolment Phase Results of the Tabari Cohort Study: Comparing Family History, Lipids and Anthropometric Profiles Among Diabetic Patients

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ABSTRACT

***Objectives:*** Different factors are responsible for the silent epidemic of diabetes mellitus in developing and developed countries. This study aimed to determine the role of demographic factors, lipid profile, family history (the estimation of genetic association) and anthropometric factors on diabetes onset.
***Methods:*** Data from the enrolment phase of the Tabari Cohort study was applied for this study and included 10,255 participants aged between 35-70 years. Anthropometric variables were measured by trained staff using standard tools. Blood specimens were collected for lipid profile and blood glucose measurements. Data analyses were performed using SPSS version 24, with univariate and multivariate logistic regression.
***Results:*** The prevalence of diabetes mellitus was estimated to be 17.2% in the cohort population, 15.6% in men, and 18.3% in women. The adjusted odds ratios (95% confidence intervals) for age groups 40-49, 50-59 and over 60 were 2.58 (2.20-3.69), 5.80 (4.51-7.48) and 8.72 (6.67-11.39), respectively. In addition, the odds ratios (95% confidence intervals) for 2 (or more), and 1 affected family member were 4.12 (3.55-4.90) and 2.34 (2.07-2.65), respectively. Triglyceride concentrations more than 500, and abnormal high-density lipoprotein levels increased the odds of diabetes mellitus by 3.29- and 1.18- fold, respectively.
***Conclusion:*** The current study showed that old age and a family history were strong predictors for diabetes mellitus.



## Introduction

Diabetes mellitus is a common metabolic disorder worldwide and is defined as a lack of insulin production or resistance to insulin, and therefore diabetes mellitus is an insulin dysfunction disorder [1,2]. Diabetes mellitus has significantly increased over recent decades. In 2013, approximately 382 million people suffered from diabetes mellitus worldwide which increased to 422 million patients in 2014. It has been predicted that there will be a 55% increase in the prevalence of diabetes by 2035. It should be noted that the highest burden of the disease worldwide is attributed to low- and middle-income countries. Prevalence of diabetes mellitus in Iran in 2013 was 9.9%, with predictions that this will increase to 10.1% in

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2035. Although during this period, the total population size of Iranian adults will increase to 30.5%, the proportion of diabetic patients has been proposed to increase by 91% (from 4,400,000 to 8,400,000) [3-6]. Results from a cohort study in Kerala, India showed the incidence of diabetes during a 10-year period as 24.5 per 1,000 person-year (cumulative incidence was 21.9% and annual increase was 2.9%) [7].

Worldwide prevalence of diabetes mellitus has increased in parallel with population growth, aging, urbanization, high prevalence of obesity and low physical activity [5,8]. Controversies in the results reported from different parts of the world have been due to different factors such as race, age, familial history of diabetes mellitus, birth weight, socioeconomic status, rapid urbanization and industrialization, emigration, change in lifestyle, low physical activity and tobacco use [5,9,10].

Considering the limited research, as well as the increasing trend of diabetes mellitus, investigating the related factors of this disorder is of great importance. Therefore, the present study was carried out to determine the role of demographic factors, lipid profile, family history (the estimation of genetic association) and anthropometric factors on the development of diabetes mellitus.

## Materials and Methods

Data collected during the enrolment phase of the Tabari Cohort study was used in the current study. This cohort is a part of the national cohort entitled: Prospective Epidemiological Research Studies in Iran (PERSIAN) [11,12] and has been described in detail [13]. During this enrolment phase of the cohort, 10,255 participants (7,012 urban residents and 3,243 rural residents) of the Sari (capital city of Mazandaran province, North of Iran) population aged 35-70 years were recruited. Informed consent was obtained from all participants who understood that participation was voluntary and they were free to exit the study at any time. All data collected were confidential.

Information required from the Tabari cohort was collected through questionnaires and blood sampling. The questionnaire was a standard checklist explained in the methodological and cohort profile studies of the cohort [11-13].

Anthropometric indices including weight, height, waist circumference and hip circumference were measured by trained staff according to standard protocols. The height was measured using a SECA 226 stadiometer (SECA, Hamburg, Germany). Participants were requested to take off their shoes and lean against the wall. Their head should be upright along with the body axis. The weight was measured using a mechanical SECA 755 column scale (SECA, Hamburg, Germany) [14].

Prior to blood sampling, all participants were requested to be fasted for at least 12 hours. Fasting blood glucose, total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides (TG) were measured by an autoanalyzer, BT 1500 (Biotechnical, Italy) using a Pars Azmoon kit (Pars Azmoon, Iran). CBC were measured using an alpha cell counter (Nihon Kohden, Tokyo, Japan). A FBS concentration that was higher than 126, a history of diabetes mellitus, or anti diabetic drug use were considered as confirmation of diabetes mellitus. To record the socioeconomic factor of participants levels 1 to 5 were assigned where Level 1 was the lowest and Level 5 was the highest socioeconomic situation.

Waist circumference that was equal or more than 88 cm for women and 102 cm for men was considered abnormal. In addition, a WHR of more than 0.9 cm in men and 0.85 cm in women was considered abnormal [15,16].

Data were described by frequency, mean, standard deviation, maximum and minimum. During univariate analysis, factors were compared between patients with and without diabetes mellitus using Chi square test. Independent t test was applied to compare age of onset between genders. Adjustment of potential confounders was performed using multivariate logistic regression models based on the Enter method. Data analysis was performed using SPSS software version 24.0 (IBM Corp., Armonk, NY, USA). A $p$ value less than 0.05 was considered statistically significant.

## Results

The target population (Tabari cohort) consisted of 10,255 participants, of whom 59.5% were women, and 31.6% were living in mountainous areas. Prevalence of diabetes mellitus in the total cohort population (aged 35-70), men, and women were 17.2%, 15.6% and 18.3% respectively ($p < 0.001$). Prevalence of diabetes among residents of urban and mountainous regions was 17.2% and 17.3%, respectively ($p = 0.829$).

Among different age groups, the lowest prevalence of diabetes was observed in participants under 40 years (4.1%), whilst those older than 60 had the highest rate (29.2%). Prevalence of diabetes among the 1$^{st}$ and 2$^{nd}$ socioeconomic levels was 18.7% and 19.2% respectively, which was higher than the rates of those observed in higher socioeconomic levels. In addition, the prevalence of diabetes among smokers was lower than non-smokers (12.1% versus 17.7% respectively, $p < 0.001$). Participants with low HDL had a higher rate of diabetes than those with high HDL (19.6% versus 16% respectively, $p < 0.001$). The corresponding figures for those with a cholesterol concentration higher than 240 (20.5%) was more than those with a cholesterol level between 200-239 (16.9%) and lower than 200 (16.8%). Participants with more than 1 diabetic in their family

Table 1. Univariate and multivariate estimates of the effect of different factors on the prevalence of diabetes mellitus.

| Variables | | Total | Univariate (chi-square) | | Multivariate (logistic regression) | | |
|---|---|---|---|---|---|---|---|
| | | | With diabetes (%) | p | OR | CI 95% | p |
| Gender | Male | 4,149 | 15.6 | < 0.001 | - | - | - |
| | Female | 6,106 | 18.3 | | 0.82 | 0.71 - 0.97 | 0.017 |
| Age group (y) | < 40 | 1,908 | 4.1 | < 0.001 | - | - | - |
| | 40 - 49 | 3,135 | 12.1 | | 2.85 | 2.20 - 3.69 | < 0.001 |
| | 50 - 59 | 3,230 | 22.5 | | 5.80 | 4.51 - 7.48 | < 0.001 |
| | ≥ 60 | 1,982 | 29.2 | | 8.72 | 6.67-11.39 | < 0.001 |
| Type of area of residence | Urban | 7,012 | 17.2 | 0.829 | - | - | - |
| | Rural | 3,243 | 17.3 | | 0.78 | 0.67 - 0.92 | 0.003 |
| Social economic level (1 = lowest) | 1 | 2,051 | 18.7 | 0.002 | - | - | - |
| | 2 | 2,052 | 19.2 | | 1.06 | 0.88 - 1.27 | 0.522 |
| | 3 | 2,050 | 17.1 | | 1.05 | 0.85 - 1.28 | 0.661 |
| | 4 | 2,051 | 15.0 | | 1.03 | 0.82 - 1.29 | 0.803 |
| | 5 | 2,051 | 16.1 | | 0.99 | 0.78 - 1.26 | 0.956 |
| Educational level (no. y in school) | University/college | 2,374 | 12.2 | < 0.001 | - | - | - |
| | 9 - 12 | 2,896 | 14.5 | | 1.20 | 1.01 - 1.44 | 0.040 |
| | 6 - 8 | 1,121 | 17.3 | | 1.31 | 1.04 - 1.65 | 0.021 |
| | 1 - 5 | 2,332 | 19.7 | | 1.42 | 1.15 - 1.76 | 0.001 |
| | 0 | 1,532 | 26.2 | | 1.63 | 1.27 - 2.11 | < 0.001 |
| Smoker | No | 9,326 | 17.7 | < 0.001 | - | - | - |
| | Yes | 929 | 12.1 | | 0.83 | 0.66 - 1.05 | 0.119 |
| HDL (mg/dL) | > 40 (male), > 50 (female) | 6,800 | 16.0 | < 0.001 | - | - | - |
| | ≤ 40 (male), ≤ 50 (female) | 3,455 | 19.6 | | 1.18 | 1.04 - 1.34 | 0.012 |
| Waist circumference (cm) | < 102 (male), < 88 (female) | 5,229 | 12.0 | < 0.001 | - | - | - |
| | ≥ 102 (male), ≥ 88 (female) | 5,026 | 22.7 | | 1.23 | 1.04 - 1.45 | 0.018 |
| WHR | ≤ 0.9 (male), ≤ 0.85 (female) | 3,245 | 7.3 | < 0.001 | - | - | - |
| | > 0.9 (male), > 0.85 (female) | 7,010 | 21.8 | | 2.06 | 1.74 - 2.44 | < 0.001 |
| LDL (mg/dL) | < 100 | 351 | 18.5 | < 0.001 | - | - | - |
| | 100 - 129 | 1,487 | 17.6 | | 0.82 | 0.59 - 1.13 | 0.232 |
| | 130 - 159 | 2,722 | 15.1 | | 0.58 | 0.42 - 0.79 | < 0.001 |
| | 160 - 189 | 2,690 | 15.8 | | 0.45 | 0.32 - 0.62 | < 0.001 |
| | ≥190 | 3,005 | 20.1 | | 0.46 | 0.31 - 0.68 | < 0.001 |
| Total cholesterol (mg/dL) | < 200 | 6,546 | 16.8 | 0.014 | - | - | - |
| | 200 - 239 | 2,716 | 16.9 | | 1.04 | 0.86 - 1.26 | 0.672 |
| | ≥ 240 | 993 | 20.5 | | 0.99 | 0.76 - 1.31 | 1.000 |
| TG (mg/dL) | < 150 | 5,988 | 13.8 | < 0.001 | - | - | - |
| | 150 - 199 | 1,979 | 19.6 | | 1.42 | 1.21 - 1.67 | < 0.001 |
| | 200 - 499 | 2,184 | 23.5 | | 1.88 | 1.57 - 2.26 | < 0.001 |
| | ≥ 500 | 104 | 33.7 | | 3.29 | 2.02 - 5.38 | < 0.001 |
| BMI ($kg/m^2$) | < 25 | 2,473 | 10.2 | < 0.001 | - | - | - |
| | 25 - 29.9 | 4,343 | 16.5 | | 1.17 | 0.98 - 1.40 | 0.079 |
| | ≥ 30 | 3,439 | 23.1 | | 1.48 | 1.20 - 1.83 | < 0.001 |
| No. of family members with a degree and diabetes | 0 | 6,071 | 11.6 | < 0.001 | - | - | - |
| | 1 | 3,111 | 22.1 | | 2.34 | 2.07 - 2.65 | < 0.001 |
| | ≥ 2 | 1,072 | 34.6 | | 4.17 | 3.55 - 4.90 | < 0.001 |

BMI = body mass index; HDL = high-density lipoprotein; LDL = low-density lipoproteins; TG = triglycerides.

had a higher prevalence of diabetes than those with no familial history of diabetes mellitus (34.6% versus 11.6% respectively, $p < 0.001$). Detailed information is illustrated in Table 1.

Among the variables entered into the logistic regression model (Table 1), the odds of developing diabetes mellitus among women compared with that among men, was 0.82 (0.71-0.97). The odds of diabetes among those aged 60 and over was 8.72-fold greater than that among participants under 40 years. The corresponding observations for those aged 50-59 and 40-49 years compared with participants under 40 years were 5.80 (4.51-7.48) and 2.85 (2.20-3.69) respectively. The odds ratio for rural residents compared with urban residents was 0.78 (0.67-0.92). Compared with those with an academic education, the odds of diabetes among those with 9-12, 6-8 and 1-5 years of school training, as well as illiterate participants was 1.20 (1.01-1.44), 1.31 (1.04-1.65), 1.42 (1.15-1.76) and 1.63 (1.27-2.11) respectively. Participants with low HDL compared with those with high HDL, had 1.18-fold (1.04-1.34) higher odds of developing diabetes. The odds ratios for high waist circumference and body mass index (BMI) more than 30 ($kg/m^2$) were 2.06 (1.74-2.44) and 1.48 (1.20-1.83) respectively. The odds ratios for low-density lipoproteins (LDL) between 130-159 mg/dL, LDL between 160-189 mg/dL and LDL higher than 190 mg/dL were 0.58 (0.42-0.79), 0.45 (0.32-0.62) and 0.46 (0.31-0.68) respectively as compared with a LDL concentration of less than 100 mg/dL.

The odds ratios for TG between 200-499 mg/dL and TG more than 500 mg/dL were 1.42 (1.21-1.67), 3.29 (2.02-5.38) respectively as compared with TG less than 150 mg/dL. Compared with those without a family history of diabetes, having 1, or more than 1 family member with diabetes increased the odds of diabetes to 2.34 (2.07-2.65) and 4.12 (3.55-4.90) respectively.

## Discussion

In this study, the prevalence of diabetes mellitus and its risk factors in the Tabari cohort was investigated. It was observed that women and residents from rural areas (mountainous) had 18% and 22% lower odds respectively, of developing diabetes than men and residents from urban areas. It was also observed that participants aged 60 and older, illiterate people, those with an abnormal waist circumference, abnormal waist to hip ratio and a BMI of 30 ($kg/m^2$) and above had 8.72-fold, 63%, 23%, 2.06-fold and 48% respectively, a higher chance of developing diabetes mellitus than those under 40 years, participants with an academic education, a normal waist circumference, a normal waist to hip ratio and a normal BMI. Moreover, participants with abnormal HDL had an 18% higher odds of developing diabetes mellitus, whilst those with LDL > 190 mg/dL, LDL between 160-189 mg/dL and 130-159 mg/dL had a 54%, 55% and 42% lower risk of developing diabetes respectively, compared with those with LDL less than 100 mg/dL. In addition, a TG concentration of more than 500 mg/dL, between 200-499 mg/dL and between 150-199 mg/dL increased the risk of diabetes approximately 3.29%, 1.88% and 1.42%, respectively. Finally, presence of family members with a history of diabetes increased the odds of diabetes 2.34-fold (1 family member) and 4.17-fold (more than one family members). It should be noted that socioeconomic level, smoking status and overweight were not associated with diabetes mellitus.

A multitude consortium including 17 cohorts and clinical trials, reported that 25% of 135,156 participants (3-88 years) had diabetes mellitus, which was higher than that estimated in the present study [17]. Comparing the results of the Tabari cohort with those reported on the cohorts carried out in other northern provinces in Iran, the crude prevalence of diabetes in this area was higher than that reported in the Golestan cohort (6.9%) [18], and lower than that reported for the Guilan cohort (24.1%, 20.2% and 27.3% for all population, men and women, respectively) [19]. Another study conducted in Golestan province reported the prevalence of diabetes amongst the total population, men, and women as 8.3%, 6.8%, and 9.7%, respectively [20]. Gilles et al [21] showed that out of 119,666 residents of countries with different socioeconomic status, 11% had diabetes mellitus. They also reported that the prevalence of this disease in high-income, upper to middle-income, lower to middle-income, and low-income countries was 6.6%, 11.1, 8.7%, and 12.3%, respectively.

A systematic review showed that 6.8% (95% CI: 6.1-7.6) of 1,100,746 residents who came from rural areas of countries with different economic levels were diabetic which was the same between genders [22]. Prevalence of diabetes in low to middle income countries during 1985-1989 and 2005-2011, was 1.8% and 7.5%, respectively, and in high income countries during 1985-1989, and during the most recent period, was 8.2% and 14.3%, respectively, indicating a higher incidence of diabetes mellitus in rural areas of low to middle income communities [22]. Deov et al [23] showed that of 26,620 Russians (20-79 years), 5.4% had diabetes (4.7% in men and 6.1% in women). They also reported that the prevalence of diabetes in residents in rural areas was higher than urban areas. However, another study showed 6.1% of Chinese people living in urban areas had diabetes whilst only 1.9% of rural residents had diabetes [24]. Hosseini Nejhad et al [25] observed that age, gender, marital status and socioeconomic status were determinant factors for diabetes while the type of area residence, and educational level were not associated with diabetes. In the current study, although women had a higher prevalence of diabetes, controlling the effect of confounding factors such as age, and familial history, the difference was converted. Moreover, in univariate analysis, the prevalence of diabetes was the same in urban and rural (mountainous) regions. Multivariate logistic regression models showed a higher chance of diabetes among residents residing in urban areas.

Talaei et al [26] showed that several factors were associated with the risk of diabetes mellitus and waist to hip ratio among men, and BMI among women were the best continuous predictors of diabetes. The best cut off of BMI for men and women to predict diabetes mellitus was 26 and 30 kg/m$^2$ respectively, where there was an increased risk of diabetes approximately 3 and 2 times, respectively. They also observed that all central obesity indices in men, and WHR in women were significantly associated with diabetes independent of BMI. Moreover, BMI was associated with diabetes just in men.

In the study conducted by O'Connor and Wellenius [27], the prevalence of diabetes mellitus among rural residents was higher than urban residents. The difference was attributed to factors including poverty, obesity and smoking. Controlling for the effect of these confounders, increased the effect of urban residency (Prevalence OR = 0.94, $p$ = 0.032). Harati et al [28] showed that age, a family history of diabetes, a high concentration of triglycerides, and obesity were independent predictors for diabetes mellitus.

Similar to many other studies, in the Tabari cohort, people with a low level of education, signs of obesity, an abnormal waist circumference and WHR, low HDL, high LDL and a positive familial history, had greater chances of developing diabetes mellitus. Smoking was indicated as currently smoking or not, and did not include previously smoked. The Tabari cohort had a low prevalence of currently smoking. Since this population were 35-70 years old, they may have ceased smoking but non-communicable diseases developed consequently. Therefore, considering the smoking history in the analyses may have been beneficial.

One of the strengths of the current study was the estimation of genetic association indicating the increase in the risk of disease with an increase in the number of family members with diabetes mellitus. Moreover, the effect of most of the risk factors was confirmed in this study. Ignoring the effect of smoking history and duration of exposure with tobacco was one of the limitations of the present study.

In conclusion, this study revealed that age, familial history, gender, area of residence, educational level, lipid profile and anthropometric indices are predictors of diabetes mellitus among the Iranian population aged over 35 years. Among these factors, age and family history (the estimation of genetic association) were the strongest predictors.

## Conflicts of Interest

The authors have no conflicts of interest to declare.

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