

Original Article

Tabari Cohort Profile and Preliminary Results in Urban Areas and Mountainous Regions of Mazandaran, Iran

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Abstract

Background: The Tabari cohort study (TCS), part of the Prospective Epidemiological Research Studies in IrAN (PERSIAN), is a large longitudinal prospective cohort designed to better understand the risk factors associated with major non-communicable diseases (NCDs) across two urban and mountainous regions in north of Iran.

Methods: The enrollment phase of TCS started in June 2015 and ended in November 2017. During this phase, individuals aged 35–70 years from urban and mountainous regions of Sari township (Mazandaran province) were invited to the cohort center by health volunteers (urban regions) and Behvarz (mountainous areas) using census information. Data was collected based on the PERSIAN cohort study protocols. Hypertension was defined as systolic blood pressure ≥ 140 mm Hg or a diastolic blood pressure ≥ 90 mm Hg or history of diagnosis with hypertension or taking antihypertensive medications among participants free from cardiovascular diseases. Diabetes was defined as fasting blood sugar ≥ 126 mg/dL or a history of diagnosis or taking glucose-lowering medications among all participants.

Results: A total of 10,255 participants were enrolled in TCS, 59.5% of whom were female. Among the total population, 7,012 participants were urban residents (68.4%). The prevalence of daily smoking in the total population was 9.1%. Body mass index in 75.9% of participants was ≥ 25 kg/m². The prevalence of hypertension, diabetes, and thyroid disorders were 22.2%, 17.2%, and 10.5%, respectively.

Conclusion: The Tabari cohort is different from other cohorts in terms of levels of risk factors associated with NCDs. This study has certain important strengths including its population-based design and large sample size that provides a valid platform for conducting future investigations and trials. A biobank that has been designed to store blood, nail, hair and urine samples for future research is another strength of this study. Researchers who are interested in using the information can refer to the following web page: <http://persiancohort.com>.

Keywords: Cancer, Cardiovascular, Cohort, Mazandaran, PERSIAN, Risk factor, Tabari cohort

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Introduction

Cardiovascular diseases, cancers, diabetes, and chronic lung and liver diseases are considered major non-communicable diseases (NCDs). Although some of their shared risk factors including tobacco use, an unhealthy diet, physical inactivity, and alcohol use are modifiable, NCDs are still the number one causes of death worldwide and a great public health concern.^{1,2} Prevalence of major NCDs is increasing globally.³ Low and middle-income countries are more affected by this global threat due to socioeconomic improvements,² fast growth in urbanization and great changes in lifestyles.^{3,4} In Iran, like other developing countries that are experiencing the epidemiologic transition phase, the leading causes of death have been replaced by NCDs in recent decades.⁵⁻⁸ It is predicted that the burden of disease due to NCDs will increase dramatically (35%) by 2025 in Iran.⁹

Health status of individuals and societies can be affected by numerous factors including social, environmental, lifestyle, and genetic factors; designing population-based cohort studies greatly contributes to the identification of these health predictors, investigating various diseases and their interaction with environmental and lifestyle exposures.¹⁰⁻¹³ Regional and national studies estimating prevalence, incidence, mortality rate of major diseases and their trends and risk factors can be utilized by policymakers to prioritize health challenges in countries.¹⁴ Several population-based cohort studies with various aims and populations are currently ongoing in different parts of Iran including the Tehran Lipid and Glucose Study,¹⁵ the Golestan,⁷ Pars,⁸ and Isfahan Cohort Studies,¹⁶ the Shahroud Eye Cohort Study¹⁷ and the Amirkola Health and Ageing Project.¹⁸ Mazandran province in north of Iran has some unique features driving us to conduct a population-based cohort in this province. These include the highest levels of obesity,¹⁹ population density, exposure to agricultural pesticides, proximity to the Caspian sea as well as being a highly touristic region. Moreover, geographically, Mazandaran province is divided into coastal plains and mountainous areas, enabling us to conduct a population-based study in two groups of individuals with different backgrounds, lifestyles and exposures, providing a great opportunity to compare risk factors in these two populations.

Due to the above-mentioned points, the Tabari cohort study (TCS), named after Tabaristan, the former name of Mazandaran province, was designed as part of the Prospective Epidemiological Research Studies in IrAN (PERSIAN cohort study) to better understand the risk factors associated with NCDs among the urban and mountainous populations. The specific objectives of TCS are to determine the incidence and prevalence of major NCDs including cardiovascular diseases, common malignancies in the province (breast, stomach, colon, prostate and thyroid as the most common cancers in

Mazandaran),²⁰ diabetes mellitus and hypertension, and their risk factors as well as to create a biobank of blood, hair, urine and nail samples for future biochemical, molecular, and genetic studies.

Material and Methods

Study Design and Participant Selection

The rationale, objectives, and design of the PERSIAN cohort study have been explained in detail elsewhere.^{21,22} TCS has been designed and undertaken by the support of the Iranian Ministry of Health and Medical Education as well as Mazandaran University of Medical Sciences, Sari, Iran. Among cities of Mazandaran province, Sari was selected as the study site by the steering committee of TCS, due to its population diversity and the availability of adequate research facilities. Sari is a district located in the foothills of the Alborz mountain range including mountainous and plain areas. After a comprehensive assessment of various health centers in Sari, a neighborhood covered by Health Center number five and Kiasar city were selected as the urban and mountainous regions, respectively.

TCS is a closed cohort. The enrollment phase of the study was carried out between June 2015 and November 2017. Participants were males and females aged 35 to 70 years, selected from a population census. A list of the target populations in the urban and mountainous regions was generated from health records in health centers and all those eligible (being Iranian, resident of the defined regions and without physical/mental abnormalities hindering participation) were invited to refer to the cohort centers by healthcare volunteers in Sari and Behvarz workers in Kiasar. Behvarz are health house staff in rural areas who are in charge of vaccination programs, family planning, and reporting births.⁷ All personnel were trained regarding the study objectives, methods, and principles of communication/interview. They referred in person to all households and invited the residents to participate in the study at least two weeks prior to an interview date. Those who agreed to participate received reminder calls one week and one day before the scheduled date. Upon arrival at the cohort center, written informed consent was obtained from each participant after detailed explanations of the design and aims of the study.

Outcomes

We defined three outcomes of interest including: 1. death (confirmed cause of death); 2. Incidence of major NCDs including malignancies, cardiovascular diseases (myocardial infarction and other ischemic heart diseases, hypertension and heart failure), stroke and cerebrovascular accidents, diabetes mellitus, pulmonary diseases (asthma, pneumoconiosis, COPD, chronic bronchitis and pulmonary emphysema), chronic renal failure leading to dialysis, hepatic fibrosis and cirrhosis, Alzheimer's and Parkinson's disease, all classified based on International

Classification of Diseases (ICD-10); and 3. trends in risk factors or protective factors including anthropometric, physiologic, nutritional, lifestyle, environmental and occupational factors.

Data Collection and Variables Measured

Data was collected and recorded using an online software, designed by the PERSIAN cohort.²¹ Data was collected using a structured questionnaire and through face to face interview. The collected information included demographic characteristics, socioeconomic status, occupational history, fuel use, habitat characteristics, life-style factors, history of fertility and chronic diseases, medication use, family history of diseases, sleep habits, physical activity, personal habits (smoking and drinking), dietary habits, pesticide exposure, and mobile use. In addition, a general physical examination including anthropometric measurements, blood pressure measurements, and oral examinations were performed and biological samples including blood, urine, hair, and nail samples were collected in the fasted state. In the urban area, all samples were processed right after collection, in the cohort laboratory center. In the mountainous region, samples were transferred to the cohort laboratory center after preliminary preparation. A portion of collected blood was used for biochemistry tests and a complete blood count, while the rest was separated into whole blood, plasma, serum and buffy coat and then stored in -70°C freezers. Urine samples were stored in -30°C freezers. Hair and nail samples were wrapped in aluminum foil, placed in plastic bags and kept at room temperature. For the sake of biosafety, all freezers are equipped with sensors, which alarm in case of temperature fluctuations and electricity loss. Biobank rooms are also equipped with air conditioners, fire alarm and electric generator in case of power outage.

Backup software has been designed to keep the data safe. To respect confidentiality, all participants received a unique cohort ID, which issued for any data analysis. The principal investigator is the only one who can access the dataset.

Follow-up

The follow-up phase of TCS includes annual phone calls and periodic reassessments. All participants are contacted every year in order to investigate the occurrence of death or any major NCDs. In case any of our outcomes of interest are reported in the phone call, our follow-up team visits the relevant medical centers where participants were hospitalized or diagnostic/therapeutic procedures were done. All clinical, pathology and hospital records are collected. Our outcome review team, including a general practitioner, two internists, one cardiologist, and an endocrinologist, evaluate all the documents and examine the participants if needed, then the final diagnose is defined based on ICD-10 codes. In case of inconsistencies,

a third blind specialist evaluates all documents and his/her decision is considered as the final diagnosis.

Reassessment will be conducted every 5 years for 20% of the participants who will be selected randomly. They will be re-interviewed and all biological samples will be collected again. We currently plan to continue the follow-up phase for 15 years.

Quality Control

The quality of data was controlled by interviewers and field supervisors on a daily basis. Quality control activities in TCS, conducted monthly by the quality control supervisors are as follows: 1) completing surveys for randomly selected participants in order to evaluate participants' views and satisfaction with the cohort study (the checklist was provided by PERSIAN central team); 2) Random voice recordings of different parts of interviews used for the assessment of interviewer techniques; 3) Data clean-up and fixing of probable errors. In the laboratory, all instruments were checked daily. Instrument calibrations were performed monthly. It is worth mentioning that all procedures followed the PERSIAN Cohort study protocol and activities were supervised by the PERSIAN cohort central team in addition to local quality control supervisors.^{21,22}

Statistical Methods

Baseline data was transferred into STATA (StataCorp, USA) version 14 for data analysis. Data was described by percentage, frequency, mean and standard deviations. Qualitative variables were compared between groups using chi-square tests and quantitative variables were compared between groups using t test or analysis of variance. P values less than 0.05 were considered to be statistically significant. Participation rate in the enrollment phase was calculated from the portion of the individuals who entered the study and the total target population invited.

Variable Definitions

We defined hypertension as systolic blood pressure ≥ 140 mm Hg or a diastolic blood pressure ≥ 90 mm Hg or history of diagnosis with hypertension or taking antihypertensive medications among participants free from CVD. We defined diabetes as fasting blood sugar ≥ 126 mg/dL, or history of diagnosis with diabetes, or taking glucose-lowering medication among all participants. Body mass index (BMI) was calculated as weight in kilograms divided by height in squared meters (kg/m^2).

Results

During the enrollment phase, participation rate was 61.7% including 57.5% of urban residents (7012 of 12191) and 73.4% of those in the mountainous areas (3243 of 4417). A total of 10255 participants were enrolled in TCS, 59.5% of whom were female. Of the

total cohort population, 14.9% were illiterate, and 23.1% had university education.

Among all participants, 32.5% were younger than 45 years and 34.6% were older than 54. Regarding socioeconomic status, 5.8% of urban residents had level 1 status (the lowest level) versus 50.7% in the mountainous regions. Prevalence of daily smoking in the total population, urban and mountainous regions were similar: 9.1%, 9.1% and 8.9%, respectively. Prevalence of Hookah use and drinking in the total population were 5.7% and 7.9% respectively. Over 75% of individuals in the total population had a BMI ≥ 25 kg/m². In urban and mountainous regions 80.4% and 66.1% of participants had BMI ≥ 25 kg/m², and 36.3% and 27.6% had BMI ≥ 30 kg/m², respectively. Other characteristics of the baseline population are presented in Table 1. All anthropometric indices and lipid profiles were significantly different between men and women in the total population, and between urban and mountainous regions ($P < 0.05$). The prevalence of hypertension, diabetes and thyroid disorders were 22.2%, 17.2% and 10.5% respectively. Prevalence of major diseases in male and female participants are shown in Table 2.

Discussion

TCS is a prospective cohort in north of Iran. The study population was selected from two different geographical areas with different exposures. Participation rate in this cohort was 61.7%. Different participation rates have been reported in other cohorts including 94.9% in the Yazd Health Study,²³ 70% in the Golestan Cohort Study,⁷ 57.5% in the Tehran Lipid and Glucose Study¹⁵ and 76.4% in the Harbin Cohort Study.²⁴ Similar to the Golestan Cohort study,⁷ the response rate in rural regions was higher than urban areas. While cohort staff tried to provide flexible questionnaire and sampling schedules for those with limited free time, asking them to visit the cohort centers at their most convenient time, many individuals in the urban areas did not participate because of their busy lifestyles and also higher socioeconomic status.

Our primary analysis shows that the majority of participants in the mountainous regions have less than 5 years of education and have a lower socioeconomic status. On the other hand, alcohol consumption is more prevalent in urban areas as is a BMI ≥ 25 kg/m². Urban-rural health disparities have been reported previously.^{25,26} Health disparities are associated with demographic characteristics, socioeconomic factors, and lifestyles²⁷ and are highly influenced by culture. As previously mentioned, one of the main rationales for conducting Tabari cohort was the inclusion of different geographical regions as well as populations from rural and urban areas. Therefore, the differences being observed in this cohort will encourage the establishment of further studies focusing on diseases and risk factors associated with each population.

Similar to other cohorts, the baseline participation rate was higher among women. One of the main reasons is men's employment and their limited time for participation. Additionally, self-care is generally lower in men than women.

There were substantial differences in preliminary results of the current cohort study compared to Golestan and Pars cohort studies, despite similarities in their design, definitions, and implementation. In the Pars Cohort Study, the prevalence of smoking, alcohol use and obesity were reported as 14%, 2.1% and 18.2%, respectively. Moreover, the prevalence of hypertension and diabetes in the Pars cohort was 26.9% and 9.4%, respectively.⁸ In the Golestan cohort study, the prevalence of smoking was 10.5% (slightly higher) while the prevalence of drinking was lower than TCS (0.7% versus 7.9%).⁷ Prevalence of hypertension in TCS was much lower than the Golestan cohort study (22.2% versus 42.7%).²⁸ It should be mentioned that participants' age in the Golestan cohort and TCS are slightly different (40–75 in Golestan cohort versus 35–70 in TCS).

Our study has several strengths. One of them is its large sample size, making it possible to compare the relevant diseases and risk factors in different geographical areas. Carrying out the study in two different regions in terms of climate and altitude is another strength of this cohort, which will show the effects of various exposures and their impacts among urban and mountainous rural residents. The majority of participants in the mountainous regions are involved in farming and animal husbandry. Active collaboration of different medical specialists in the fields of internal medicine, cardiology, endocrinology, psychiatry, dentistry, public health, midwifery and gynecology with the cohort team is another strength of our study. A specialized clinic (Baghban Clinic) has been designated for all cohort participants to refer to at times of need, providing various consultation and treatment services. This strategy was adopted to minimize loss to follow-up as well as ease of access to many relevant follow up documents. Updated data collection on exposure and comprehensive follow-up is another characteristic of this cohort leading to minimum information and misclassification biases. This cohort is expected to potentially develop into an elderly cohort, yielding little information bias.

There are limitations as well. Determining the impact of risk factors on some rare outcomes may be difficult as is in many cohort studies. Another predictable limitation of the cohort is the probable loss to follow-up, reducing the power to predict the risk factors of interest. We have taken many steps to minimize loss to follow-up. In addition to the Baghban specialized clinic previously mentioned, we have provided incentives and special services by health volunteers and Behvarz and facilitated contact with family physicians.

With the data gathered in TCS, it is anticipated that

Table 1. Selected Variables in TCS, by Area Residence (Urban/Mountainous)* and Gender

Variables	Total**			Urban**			Mountainous***		
	Total (10255)	Men (4149)	Women (6106)	Total (7012)	Men (2946)	Women (4066)	Total (3243)	Men (1203)	Women (2040)
University/ 9-12 y	2374 (23.1)	1333 (32.1)	1041 (17)	2209 (31.5)	1230 (41.8)	979 (24.1)	165 (5.1)	103 (8.6)	62 (3)
6-8 y	2896 (28.2)	1328 (32)	1568 (25.7)	2413 (34.4)	1055 (35.8)	1358 (33.4)	483 (14.9)	273 (22.7)	210 (10.3)
1-5 y	1121 (10.9)	503 (12.1)	618 (10.1)	832 (11.9)	324 (11)	508 (12.5)	289 (8.9)	179 (14.9)	110 (5.4)
Illiterate	2332 (22.7)	674 (16.2)	1658 (27.2)	1223 (17.4)	282 (9.6)	941 (23.1)	1109 (34.2)	392 (32.6)	717 (35.1)
Age group, No. (%)	1532 (14.9)	311 (7.5)	1221 (20)	335 (4.8)	55 (1.9)	280 (6.9)	1197 (36.9)	256 (21.3)	941 (46.1)
<45	3331 (32.5)	1241 (29.9)	2090 (34.2)	2504 (35.7)	954 (32.4)	1550 (38.1)	827 (25.5)	287 (23.9)	540 (26.5)
45-54	3379 (32.9)	1305 (31.5)	2074 (34)	2488 (35.5)	1006 (34.1)	1482 (36.4)	891 (27.5)	299 (24.9)	592 (29)
>54	3545 (34.6)	1603 (38.6)	1942 (31.8)	2020 (28.8)	986 (33.5)	1034 (25.4)	1525 (47)	617 (51.3)	908 (44.5)
Socioeconomic level, No. (%)	2051 (20)	653 (15.7)	1398 (22.9)	408 (5.8)	117 (4)	291 (7.2)	1643 (50.7)	536 (44.6)	1107 (54.3)
1 (lowest level)	2052 (20)	797 (19.2)	1255 (20.6)	1149 (16.4)	424 (14.4)	725 (17.8)	903 (27.8)	373 (31)	530 (26)
2	2050 (20)	815 (19.6)	1235 (20.2)	1673 (23.9)	679 (23)	994 (24.4)	377 (11.6)	136 (11.3)	241 (11.8)
3	2051 (20)	915 (22.1)	1136 (18.6)	1807 (25.8)	796 (27)	1011 (24.9)	244 (7.5)	119 (9.9)	125 (6.1)
4	2051 (20)	969 (23.4)	1082 (17.7)	1975 (28.2)	930 (31.6)	1045 (25.7)	76 (2.3)	39 (3.2)	37 (1.8)
5 (highest level)	929 (9.1)	893 (21.5)	36 (0.6)	640 (9.1)	607 (20.6)	33 (0.8)	289 (8.9)	286 (23.8)	3 (0.1)
Daily smoking, No. (%)	806 (7.9)	727 (17.5)	79 (1.3)	763 (10.9)	684 (23.2)	79 (1.9)	43 (1.3)	43 (3.6)	0
Drinking, No. (%)	583 (5.7)	476 (11.5)	107 (1.8)	480 (6.8)	383 (13)	97 (2.4)	103 (3.2)	93 (7.7)	10 (0.5)
Hookah, No. (%)	46 (4)	27 (0.7)	19 (0.3)	20 (0.3)	12 (0.4)	8 (0.2)	26 (0.8)	15 (1.2)	11 (0.5)
BMI, No. (%)	2427 (23.7)	1373 (33.1)	1054 (17.3)	1355 (19.3)	792 (26.9)	563 (13.8)	1072 (33.1)	581 (48.3)	491 (24.1)
18-24.99	4343 (42.4)	1896 (45.7)	2447 (40.1)	3094 (44.1)	1452 (49.3)	1642 (40.4)	1249 (38.5)	444 (36.9)	805 (39.5)
25-29.99	3439 (33.5)	853 (20.6)	2586 (42.4)	2543 (36.3)	690 (23.4)	1853 (45.6)	896 (27.6)	163 (13.5)	733 (35.9)
≥30	221 (2.2)	29 (0.7)	192 (3.1)	119 (1.7)	24 (0.8)	95 (2.3)	102 (3.1)	5 (0.4)	97 (4.8)
Marital status, No. (%)	9420 (91.9)	4086 (98.5)	5334 (87.4)	6505 (92.8)	2895 (98.3)	3610 (88.8)	2915 (89.9)	1191 (99)	1724 (84.5)
Married	471 (4.6)	11 (0.3)	460 (7.5)	266 (3.8)	5 (0.2)	261 (6.4)	205 (6.3)	6 (0.5)	199 (9.8)
Widow	143 (1.4)	23 (0.6)	120 (2)	122 (1.7)	22 (0.7)	100 (2.5)	21 (0.6)	1 (0.1)	20 (1)
Divorced	189.4±38.9	184.2±39.4	192.9±38.2	191.1±39.9	187.1±40.7	193.9±39.1	185.8±36.5	177.1±35.3	190.9±36.2
Cholesterol	50.3±10.7	46.6±9.5	52.8±10.7	50.2±10.9	46.3±9.5	53.0±11.1	50.6±10.0	47.4±9.4	52.5±9.9
HDL	158.9±108.03	172.5±127.6	149.7±91.2	167.3±113.3	184.4±132.7	154.9±95.1	140.8±92.9	143.2±109.1	139.3±82.0
TG	0.91 ±0.07	0.92±0.06	0.9±0.07	0.91±0.07	0.93±0.06	0.89±0.07	0.91 ±0.07	0.9±0.07	0.91 ±0.07
WHR (Mean ± SD)									

* P value of comparing all variables between urban and mountainous population <0.001 (except for WHR P value = 0.385; HDL, P value=0.043; Daily Smoking, P value: 0.723); **P value for all variables <0.001, *** P-value for all variables <0.001 (except for WHR, P value=0.002; TC, P value=0.279)

Table 2. Prevalence of Self-reported NCDs in TCS Population by Gender

Disease	Men (4149), No. (%)	Women (6106), No. (%)	Total (10255), No. (%)	P Value
Hypertension	758 (18.3)	1523 (24.9)	2281 (22.2)	<0.001
Cardiovascular disease	359 (8.7)	550 (9.0)	909 (8.9)	0.535
Diabetes	646 (15.6)	1119 (18.3)	1765 (17.2)	<0.001
Myocardial infarction	100 (2.4)	67 (1.1)	167 (1.6)	<0.001
Stroke	49 (1.2)	59 (1.0)	108 (1.1)	0.296
Thyroid disorder	139 (3.4)	933 (15.3)	1072 (10.5)	<0.001
Chronic respiratory disease	84 (2.0)	202 (3.3)	286 (2.8)	<0.001
Chronic headache	201 (4.8)	1131 (18.5)	1332 (13)	<0.001
Depression	127 (3.1)	683 (11.2)	810 (7.9)	<0.001
Rheumatoid disease	73 (1.8)	306 (5.0)	379 (3.7)	<0.001
Kidney stone	897 (21.6)	778 (12.7)	1675 (16.3)	<0.001

collaborative projects will be established at national and international levels. This study has established a suitable infrastructure for various cross-sectional studies in the enrollment phase and also nested case-control, case-cohort, and interventional studies during the follow-up phase.

Data Archive and Collaboration

The Tabari cohort team is willing to collaborate with national and international research institutes and individuals. We kindly request all proposals be submitted to mmoosazadeh1351@gmail.com and mmoosazadeh1351@mazums.ac.ir. Interested researchers may receive required data after their proposal is reviewed and accepted by the Tabari Cohort steering committee.

Authors' Contributions

MM and MK conducted and managed the entire study. MM, MK, MS, HP, SE, RE, RA, AH, RN, AR, GJ, ZK, MS, MSA, MA, BG, MA, IM, HTF, AG, MZ and AG contributed in study design, manuscript drafting, data collection, analysis, and critical revision of the manuscript. MM and MK supervised the entire processes of the study. All authors approved the final version of manuscript.

Conflict of Interest Disclosures

The authors declare that there is no conflict of interest.

Ethics Statement

This cohort has been approved by the ethics committee of Mazandaran University of Medical Sciences, Sari, Iran (IR.MAZUMS.REC.94.1020).

Informed Consent

Written informed consent was obtained from all participants included in this study.

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