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Research Article

The ATREA Survey: Study Design and Main Results

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Abstract

Background: The ATERA Survey is a prospective epidemiological study aiming to determine the prevalence of dyslipidemia and other conventional risk factors for CHD; the relationship between environmental and lifestyle factors with dyslipidemia, the perception and the knowledge of cardiovascular risk factors by the population.

Methods: In this observational cross-sectional study we adopted a two stage stratified sampling method to obtain representative sample of the general Tunisian population. The study included a sample of the population coming from seven Tunisian regions (great Tunis, North East, North West, central East, central West, South East and southwest) and aged between 25 and 75 years old. The ATERA Survey was on in a random sampling including 10 576 men and women. The screening was assessed using an initial and an endpoint surveys covering socioeconomic, nutritional and anthropometric measures in addition to biological assessments.

Results: The total studied population was 10 576 participants divided into 4642 (43.9%) men and 5934 (56.1%) women. The results of our study show that in Tunisia, a high prevalence of cardiovascular risk factors was observed especially for dyslipidemia (n = 5125; 48.5%) followed by hypertension (n = 4678; 44.2%) then Diabetes (n = 2428; 23.0%). High prevalence of hypertension was discovered fortuitously (n = 2464; 23.3%). In addition, a high prevalence of overweight (n = 4259; 40.3%) was found, with 69.3% of subjects having a BMI> 25 kg/m^2 (n = 7333). A high percentage (48.5%) of dyslipidemia was an incidental discovery by the ATERA Survey, in both genders.

Conclusion: The results of the ATERA survey show a serious situation since we are witnessing an explosion of cardiovascular risk factors and particularly dyslipidemia.

Keywords: Dyslipidemia; Cholesterol; Triglyceridemia; Diabetes; Glycated Hemoglobin; Hypertension; Obesity; Nutrition; Intervention; Digital Tools; Behavioural Changement

Introduction

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality (Mensah et al, 2019) [1,2]. The rate of CVD death was ~ 3 times higher in lower- and middle-income countries than in high-income countries (Jagannathan et al., 2019) [3]. The most preventable form of CVD is atherosclerotic cardiovascular disease (ASCVD) which is one of the common non-communicable diseases (NCD) with high disability-adjusted life year (DALY) in the Middle East and North Africa (MENA) (Arnett et al. 2019 ; Azizi et al, 2019; WHO 2020) [4-6]. ASCVD is the largest contributor to the prevalence of important risk factors and varying greatly according to geographical region, sex and ethnic background (Wong, 2014) [7].

Assessing the prevalence of risk factors and predictors of this condition is of paramount importance for the prevention and control of the disease and its complications. Knowledge of the lipid profile of a population is important for the adoption of preventive and therapeutic measures to combat atherosclerosis (Ference et al. 2017) [8].

However, the majority of studies involved the European and Asian populations. In Tunisia, there is an increasing spread of chronic diseases, due to environmental and behavioral changes such as the adoption of new eating habits, sedentary housing, the stress of urbanization and working conditions (Ben Romdhane et al, 2015) [9,10]. These changes have led increased incidence of cardiovascular disease and other chronic diseases exacerbated by longer life expectancy. There are very few studies on the cardiovascular risk factors epidemiology in Tunisia. Most of them covered a small number of individuals or only one region except for THES study that included 9000 individuals (Maatoug et al, 2010; Belfki et al., 2012) [11,12].

The main objective of this study is to determine the prevalence of dylipidemia and other risk factors for coronary artery disease (smoking, diabetes, hypertension, obesity, etc.) at the national level.

ATERA survey Design

ATERA survey was designed as a prospective observational (cross-sectional) study of a randomly selected sample from general population. The study included a representative sample of the Tunisian population. The ATERA Survey was carried out from January 2016 to April 2019.

Sampling

The target population was recruited by random sampling drown by the national institute of statistics. The number of households selected for recruitment 5919. The sampling used a two stage cluster (district, household), according to national tunisian population census of 2014 (Chart 1). Characteristics of households were collected at the beginning of the survey and a screening of individuals living within the household identified the eligible population. A detailed questionnaire reviewed the social conditions of the household.

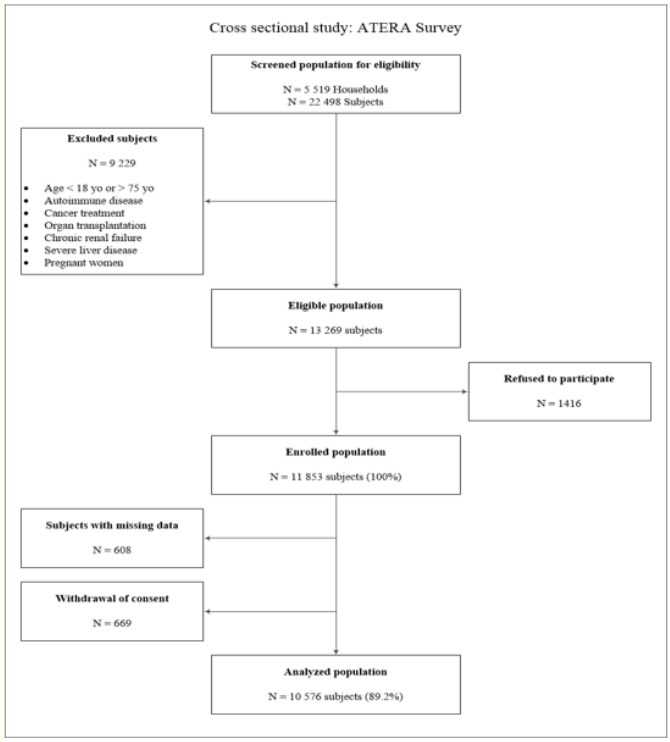

Chart 1: Patient Study Flow.

Selection criteria

Subjects aged more than 25 years and below 75 years old at the inclusion date were selected. Individuals who are under prescribed treatment for cancer, who have received an organ transplant, who are known to have autoimmune disease, who have severe liver disease, who have chronic renal failure, pregnant women, will be excluded before and during the project.

Interview with each eligible participant was conducted after consenting, it was notified all the demographic, behavioral history, family history, cardiovascular risk factors and medical history.

Study population

An overall number of 11 853 subjects was enrolled in the survey. The study retained 10576 individuals with complete data collection (response rate of 89.2%), including Men 4642 (43.9%) and 5934 women (56.1%). All the participants signed an informed consent before enrollment.

Survey tools and questionnaires: three successive steps were performed to capture data in our study population.

- A socio-demographic questionnaire and health record assessment: answered to surveys covering socioeconomic, nutritional and anthropometric measures in addition. During the assessment visit, Physical examination/anthropometry data
- Nutritional questionnaire with diet survey was filled up by the interviewer. The questionnaire was developed by the ATERA team and validated by the National Institute of Nutrition (Tunisia).
- Biological assessments (fasting glucose, Glycated hemoglobin, Creatinine, Uric acid, ASAT, ALAT, Cholesterol, HDL-C, Triglycerides, Complete Blood Count).

Training of trainers specific to the staff involved in the study to master the questionnaires and to follow the guides specific to the doctor, nutritionist, phlebotomist and supervisor.

Centrifugation of samples in remote regions of Tunis before sending them to the biochemistry laboratory of the Rabta hospital to be analyzed on the architect C8200 (Abbott) and in the hematology laboratory for the blood count on Sysmex XT 4006.

Data collection: Data capture was performed by the DACIMA Clinical Suite according to FDA 21 CFR part 11 requirements (Food and Drug Administration 21 Code of Federal Regulations part 11), the HIPAA specifications (Health Insurance Portability and Accountability Act), and the ICH standards (International Conference on Harmonisation). Ethical considerations and regulatory approvals: The Ethic authorization was attributed under the number 15/2015 from the National Council of Statistics of Tunisia, and the IRB of Rabta Hospital (Tunisia) with the approval of the Ministry of Health and Ministry of Interior Affaires.

Endpoint measures: the survey screened the epidemiological profile of the population, the cardio-vascular risk factors (i.e. diabetes, hypertension, dyslipidemia, overweight and obesity, etc.), the medical examination, the labs profile (metabolic biological data, hematological and kidney labs) and the detailed nutritional habits.

Data auditing and cleaning: two independent trained datamanagers reviewed the subjects' data for accuracy. All the eligible subjects were audited in order to search for discrepancies, missing values and eligibility criteria compliance. The data capture system was designed to set controls on the data while it was captured, and to set verification process on all the subjects' files. Tabular reports were generated by the data capture system to identify outliers and data issues. Corrections were made by resuming source documents (i.e. labs values) or by re-contacting the subject to check the accuracy of the information. In case of persistence of data discrepancy, the whole subject file was excluded from the dataset. Data auditing and cleaning were performed according the Good Clinical Data Management Practices [13].

Data auditing and cleaning: an independent trained data manager reviewed the subjects' data for accuracy. All the eligible subjects were involved in the final statistical analysis.

Statistical analysis consideration: the categorical variables were described by the frequencies and the percentages of the valid values. Continuous variables were described by the mean and standard-deviation. No imputation of missing values was done. Confidence intervals were computed based on 95% on confidence. Statistical tests were performed at a level of significance of 5%. Frequencies were compared using Chi-Square test or its correction of continuity in case of theoretic values less than 5. Means were compared by the One-Way Anova test, or by Kruskal-Wallis test when the continuous variables distribution wasn't found normal. Kolomogorov-Smirnov test was used for normality distribution testing.

Results

The total studied population was 10576 participants divided into 4642 (43.9%) men and 5934 (56.1%) women. The results of

our study show that in Tunisia, a high prevalence of cardiovascular risk factors was observed especially for dyslipidemia (48.5%) (Chart 2) followed by hypertension (44.2%) (Chart 3) then Diabetes (23.0%) (Chart 4). High prevalence of hypertension was discovered fortuitously (52.7%). Besides, the prevalence of prediabetes is very high (21.8%) and increases with age to reach 21.5 to 28.5% from 55 years of age.

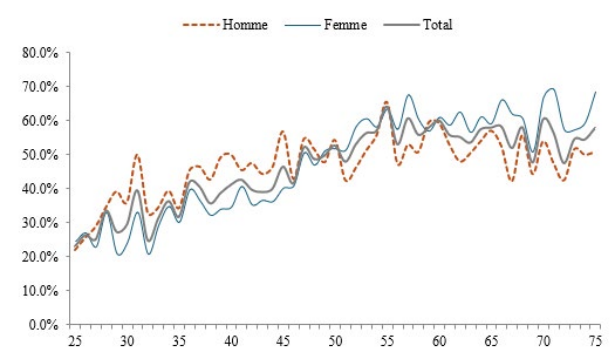

Chart 2: Dyslipidemia prevalence distributed by age.

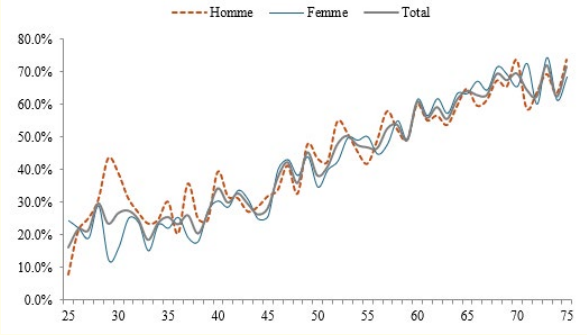

Chart 3: Hypertension prevalence distributed by age.

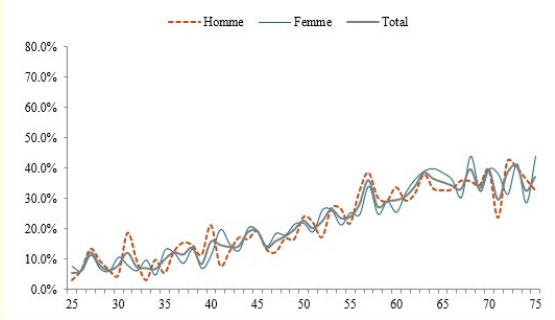

Chart 4: Diabetes prevalence distributed by age.

In addition, a high prevalence of overweight (40.3%) was found (Chart 5), with 70.9% of subjects having a BMI> 25 kg/m^2. A high percentage (48.6%) of dyslipidemia was an incidental discovery by the ATERA Survey, especially in men. Four point five percent of subjects have simultaneous disturbances of CT; TG and HDL (6.4% in men and 3.0% in women) (table 1).

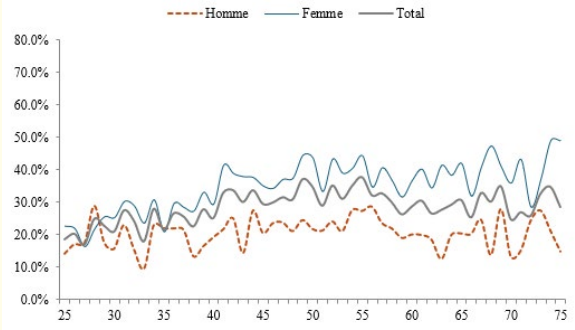

Chart 5: Obesity prevalence distributed by age.

Item	Total		Men		Women		Urban		Rural	
	N	%	N	%	N	%	N	%	N	%
Age (years)										
25-34	1377	13,0%	550	11,8%	827	13,9%	1032	13,3%	345	12,3%
35-44	1976	18,7%	766	16,5%	1210	20,4%	1433	18,5%	543	19,3%
45-54	2598	24,6%	1057	22,8%	1541	26,0%	1862	24,0%	736	26,2%
55-64	2750	26,0%	1265	27,3%	1485	25,0%	2070	26,7%	680	24,2%
> 65	1875	17,7%	1004	21,6%	871	14,7%	1366	17,6%	509	18,1%

Educational level										
Illitrate	2371	22,4%	599	12,9%	1772	29,9%	1385	17,8%	986	35,1%
Elementary	4174	39,5%	1911	41,2%	2263	38,1%	3004	38,7%	1170	41,6%
Secondary	2959	28,0%	1609	34,7%	1350	22,8%	2401	30,9%	558	19,8%
University	1072	10,1%	523	11,3%	549	9,3%	973	12,5%	99	3,5%
Social security										
None	1038	9,8%	456	9,8%	582	9,8%	776	10,0%	262	9,3%
Free treament card	738	7,0%	299	6,4%	439	7,4%	424	5,5%	314	11,2%
Minimum rate treatment card	1435	13,6%	602	13,0%	833	14,0%	721	9,3%	714	25,4%
National social security Fund	6770	64,0%	3032	65,3%	3738	63,0%	5331	68,7%	1439	51,2%
Other national security fund	359	3,4%	153	3,3%	206	3,5%	305	3,9%	54	1,9%
Full payement	236	2,2%	100	2,2%	136	2,3%	206	2,7%	30	1,1%
NCDs										
Dyslipidaemia	5125	48.5	2256	48.6	2869	48.3	3937	50.7	1188	42.2*
Diabetes	2428	23	1107	23.8	1321	22.3*	1903	24.5	525	18.7*
Hypertension	4678	44.2	2166	46.7	2512	42.3*	3459	44.6	1219	43.3
Obesity	3074	29,1%	959	20,7%	2115	35,6%	2413	31,1%	661	23,5%

Table 1: Characteristics of the study population.

*: $p < 0.05$.

Discussion

Ben Romdhane H and al found in 2005 a national prevalence of Type 2 Diabetes of 15.1%, among population aged between 35 and 70 years [14]. In the other side, the TAHINA project conducted in 2005, showed hypertension prevalent of 30.6% and obesity prevalent of 26.8% among population aged between 35 and 74 years [15]. Our current survey shows a enormous increase of the NCDs rates. This could highlight the need to implement new primary prevention models among Tunisian population.

Strengthening Tunisian prevention strategies with sophisticated and digital means constitutes a pillar of digital health in favor of anchoring imperative behavioral change to improve the current prevalence of cardiovascular risk factors.

Study Limitations

Though the sample size was high and might be extrapolated to the general population, the survey didn't include the youngest subjects, aged from 18 to 25 years, as the occurrence of NCDs seem to involve more and more the young population.

Fundings

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The survey protocol is registered at Clinical trials: NCT03799185.

Project collaborators

- Ministry of Health of Tunisia
- National Institute of Health of Tunisia
- National institute of Nutrition
- Department of Biochemistry, Research of laboratory LR99ES11, la Rabta Hospital, Tunis El Manar University, Tunis
- National Institute of Statistics
- National statistics council

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