

TEKHARF 2013 taraması ve diyabet prevalansında hızlı artış

Turkish Adult Risk Factor survey 2013: rapid rise in the prevalence of diabetes

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ÖZET

Amaç: TEKHARF Çalışması'nın 2013 takip taramasında saptanan 1) cinsiyete özgü ve belirli yaş kesimindeki genel mortalite ve koroner mortalitesinin analizi ve 2) ülke çapında tip-2 diyabet prevalansının son 12 yıldaki değişiminin açıklanması.

Çalışma planı: Ölüm konusunda birinci derece akraba ve/veya sağlık ocağı personelinin bilgi alındı. Yaşayanlarda bilgi edinmekten başka, kardiyovasküler sistem fizik muayenesi ve dinlenme EKG kaydı yapıldı. Diyabet varlığı Amerikan Diyabet Birliği ölçütlerine dayandırıldı. **Bulgular:** İzlenecek 1370 kişilik örneklemden 768'i incelendi, 452 kişi hakkında bilgi edinildi ve 29 erkek ile 18 kadının öldüğü belirlendi. Ölenlerden 22'si koroner kalp hastalığı (KKH) kökenli sayıldı. Tüm kohortun 23 yıllık takibinde 45-74 yaş kesiminde genel mortalite bin kişi-yılında erkekte 16.8, kadınlarda 9.9 oranındaydı. KKH kökenli ölümler erkeklerde bin kişi-yılında 7.5, kadınlarda 3.74 düzeyinde (Avrupa ülkelerine göre yüksek seviyede) bulundu. Diyabet genel prevalansı 1998'i izleyen 12 yıl içerisinde, yaklaşık 2600 kişide yaşı kontrol edilmesi durumunda %80 oranında yükseldi. Yıllık %5 artışa denk düşen bu gelişme ileri derece kaygı vericidir.

Sonuç: Yetişkinlerimizde genel mortalite ve koroner mortalitesi yüksek düzeylerini sürdürmektedir. Daha düşündürücü saptama, nüfus artışı ve yaştan arındırılan tip-2 diyabet sıklığının kabul edilmeyecek hızda yükselmesi olup yeni önlemlere ihtiyaç göstermesidir.

ABSTRACT

Objectives: To analyze (1) the sex-specific and age-bracket defined all-cause and coronary mortality in the 23-years' follow-up of the Turkish Adult Risk Factor Study, and (2) to determine the nation-wide prevalence of Type-2 diabetes and its recent trend.

Study design: Information on the mode of death was obtained from first-degree relatives and/or health personnel of local health office. Information collected from survivors was based on history, physical examination of the cardiovascular system and Minnesota coding of resting electrocardiograms. Diabetes was defined by criteria of the American Diabetes Association without the use of glycated hemoglobin.

Results: Of the 1370 participants to be surveyed, 768 were examined, in 452 subjects information was gathered, and 29 men, 18 women were ascertained to have died. Cumulative assessment of the entire cohort in the age bracket of 45-74 years disclosed coronary mortality to be 7.5/1000 person-years in men and 3.74 in women, persisting to be high among the European countries. The recent decline observed in overall mortality seemed to halt as well. Of greatest concern was the finding in the past 12 years that the rate of rise in the age-controlled prevalence of Type-2 diabetes was as high as 5% annually.

Conclusion: Overall and coronary mortality in Turkish adults continue to be high, while an elicited annual increase of 5% in the age-controlled prevalence of diabetes is virtually alarming and requires new public health policies.

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Data about all-cause, and coronary mortality provided by TEKHARF^[1] cohort study which represents our middle-aged and elderly population are still required, as was the case in the past. The development of coronary heart disease (CHD), and diabetes has been suggestively attributed to a common ground, while it is known that American Heart Association regards diabetes as an equivalent to CHD. Furthermore, diabetes has a very high rate of mortality among our adult population ^[2], and its incidence rises rapidly in our community. On the other hand, the monitorization, and examination of the individuals during annual screenings should be considered as an important task which is helpful for more improved planning of future surveys.

In this article the following assessments concerning TEKHARF survey which was realized mostly in the Marmara, and Central Anatolian regions in early autumn are reviewed: 1) Disclosure of all-cause, and coronary mortality rates recorded in our adult population during the last screening period, 2) Determination of all-cause, and coronary mortality rates in the age range of 45-74 years, and especially 3) evaluation of current prevalence of type 2 diabetes, and increase in its prevalence during the last 12-15 years. Besides, limited number of new participants enrolled in the cohort, and sampling size ready for future screening will be declared.

PATIENTS AND METHOD

Communities and individuals surveyed

In this TEKHARF survey, Marmara, and Central Anatolian Regions were firstly screened at the end of the summer of 2011, were surveyed again. ^[3] In lieu of the districts of Vefa-Kocamustafapaşa, Kurtuluş, Beşiktaş, and Levent which were screened at even-numbered years for logistic reasons during the previous survey period, communities of Kaynaşlı, Zonguldak, Kütahya, and Güre (Uşak) were surveyed. A total of 1370 individuals to be surveyed consisted of 50% of the available nationwide TEKHARF cohort. Besides, 57 new participants were included from the city of Kütahya, and the Marmara region.

Total individual follow-up periods of those ascertained as dead (to estimate mortality rate), and participants examined, and subjects for whom reliable information was gathered about their health state constituted overall duration of the follow-up. Since presence of silent myocardial ischemia is relevant for coronary events, as used in previous surveys ^[3] only follow-up periods of those examined, and deceased

were taken into consideration.

Method of gathering information

Medical history, examination and electrocardiograms were used to gather direct information in the survey. Current medical health status of individuals who could not be examined was mostly obtained via phone calls or through their relatives and neighbors. The date of information obtained was recorded and individuals were included in a follow-up period of ≤ 12 months.

Definitions

Information was gathered about place, type, cause, and approximate time of death as much as possible. Sudden death was defined as the death event which occurred within 24 hours of the onset of symptoms which was generally associated with cardiac causes in the absence of any other relevant information.

New coronary event: For definitions of fatal coronary event, definite, and suspect CHD the previously reported definitions were accepted ^[4] Fatal coronary event was defined as a death event which developed in an individual who had not previously experienced heart failure within the last two weeks caused by an event suggestive of myocardial infarction or suddenly developed death event. Non-fatal coronary events were defined as non-fatal coronary events which understandably developed after the last follow-up visit including a) new episode(s) of myocardial infarction (as revealed by anamnesis and/or electrocardiogram(s)) , b) typical angina pectoris occurring in men, post menopausal women or individuals older than 50 years of age, c) myocardial ischemia (Minnesota codes for ECG: 4.1-2, 5.1-2 or 7.1) ^[5] or d) current or past history of coronary artery bypass or intracoronary intervention for a newly developed disease

Type 2-diabetes was defined as history of antidiabetic drug use, and presence of higher fasting (≥ 126 mg/dl) or post-prandial (≥ 200 mg/dl) blood glucose levels

Autoimmune interaction was defined as the detection of evidence of both a dysfunctional state in which sensing of damaged epitopes of some proteins in the blood in the presence of increased chronic systemic inflammation, as foreign substances, and subsequent aggregation via a chronic, occult, and insidious process triggered by our protective plasma proteins (HDL, and apolipoproteins) or involvement of some serum proteins in immune complex demonstrated by gaps in immunoassay measurements. ^[6,7]

The ratio between adult population of Turkey and our sample

Based on the assumption that total population of our country aged ≥ 43 years was 24.5 million, the number of the participants in the TEKHARF study who were available for follow-up in the years 2012, and 2013 represented 1/9060 of the total population within this age bracket

RESULTS

A. Final survey data

A total of 768 (men, 371, and women, 397) individuals out of 1,370 previous participants to be screened this year were examined, and 47 death events were ascertained. A hundred and sixty-one (21 %) individuals who were not examined during the 2011 survey could be examined this time. Information alone could be obtained from 452 participants, and 103 individuals were lost to follow-up. Mean age of the examined participants was 60.1 ± 10.3 years (95% confidence interval of birthdates: 1933; 1973), without any gender difference ($p=0.3$). Total follow-up period was 2,460 person-years. Individuals ascertained as dead and those examined made up 60% of the total number of individuals to be followed up. . Forty-seven death events corresponded to 19.1 individuals per 1000 person-years. A total of 57 participants (mean age, 60.4 ± 8.8) from the Marmara, and Aegean regions were included in the cohort for the first time.

A total of 47 (29 men and 18 women) participants died including 30 participants of the original cohort. Death events were associated with autoimmune activation ($n=9$), CHD ($n=13$), cerebrovascular events ($n=2$), cancer ($n=9$), traffic accidents ($n=3$), renal failure ($n=2$), diabetes, postoperative complications, fracture-related problems, pulmonary embolism, Parkinson's disease, (each $n=1$), and undetermined causes ($n=4$). During this period, annual mortality rates related to autoimmune activation, and all coronary events were 0.8 and 8.0 (men 11.2 and women, 5.0) per 1000 individuals surveyed.

Newly developed coronary events

During this year's survey, a previously undetected CHD newly developed in 41 participants (5.2 % of those examined). This corresponds to an incidence of 20 per 1000 person-years, equally distributed between gender, and consistent with an annual incidence of CHD (400,000 patients/year) in Turkey. Most of these newly diagnosed cases were associated with the emergence of angina pectoris and /or ischemic left bundle block on ECG, acute myocardial infarction or stent implantation, and coronary bypass interventions.

B. Analysis of 23-years' follow-up

Overall mortality and age at death

The distribution of 789 death events which occurred in all TEKHARF cohorts are shown in Table 1 by mortality rate and temporally. Across all survey periods, mortality rate among a relatively young cohort with a median age of 47 years was 11.2 death events per 1000 person-years. The mortality rate in the original cohort was 11.4 per 1000 person-years, while it was slightly lower (11.2 per 1000 person-years) as a whole.

All-cause and coronary mortality in the age bracket 45-74 years

All-cause and coronary mortalities in this age bracket of 45-74 years according to sex and duration of the follow-up period are shown in Table 3. Death events in this age range was 13.2 (16.8 for males, and 9.9 for females) per 1000 person-years.

Mortality rates were 7.5 and 3.74 per 1000 person-years in males and females since the survey was first initiated. Coronary mortality rates per 1000 person-years regressed in 2000s relative to 1990s (from 8.1 to 7.2 in men, and from approximately 1 /4 to 3.3 in women)

C. Changes in the prevalence of diabetes since the year 1998

Changes in the prevalence of diabetes among TEKHARF participants were estimated based on comparative evaluation of data obtained from three survey periods.

Table 1. Distribution of all death events according to cohorts, and TEKHARF study periods

	Annual death events (n)	Follow-up period	Annual (per 1000)
Original cohort			
1990-97/98	204	21,900	9.3
97/98-02/03	137	13,300	10.3
2002/03-12/13	299	21,080	14.2
	640	56,280	11.4
1997/98 cohort	22	31,40	7.0
97/98-02/03	77	5,320	14.5 11.7
2002/03-12/13	99	8,460	
2002/03 cohort	40	4,040	9.9
2007/08 cohort	10	1,470	6.8
All cohorts	789	70,250	11.2

Table 2. Death events occurred, and coronary mortality rates in the 45-74 age range of the TEKHARF survey cohort during 22,5 years of follow-up

	Total			Men			Women		
	Follow-up period (years)	Death events	Annual (per 1000)	Follow-up period (years)	Death events	Annual (per 1000)	Follow-up period (years)	Death events	Annual (per 1000)
All-cause mortality									
Turkey 1990-2000	11514	191	16.6	5705	116	20.3	5809	75	12.9
Turkey 2000-2010	18912	204	10.8	9140	130	14.2	9772	74	7.6
Turkey 2011-2013	5611	82 477	14.6	2754	49	17.8	2857	33	11.6
Turkey 1990-2013	36037		13.2	17599	295	16.8	18438	182	9.9
Coronary mortality									
Turkey 1990-2000	11514	73	6.3	5705	46	8.1	5809	27	4.65
Turkey 2000-2010	18912	96	5.1	9140	64	7.0	9772	32	3.3
Turkey 2011-2013	5611	32	5.7	2754	22	8.0	2857	10	3.5
Turkey 1990-2013	Rakamlar			eksis					

Based on the 1997/98 survey data, prevalence of diabetes during 2000-6, and 2007-12 periods were analyzed according to age groups. As seen in Table 3, and Figure 1, overall prevalence of diabetes estimated based on follow-up of nearly 2600 participants within a period of 12 years increased at a rate of 80% which corresponds to annual increase of 5%, after controlling the effect of age on estimates.

Newly recruited participants

In order to comply with changes in regional distribution of Turkey's population, 57 new participants (33 females) from urban areas of the Marmara region, and Kutahya were included in the TEKHARF study. The newly recruited participants were residents of Kutahya (n=12), Bursa (n=14), Canakkale (n=12), Üsküdar (n=12), and Kozyatağı (n=7).

Median age of this new cohort was comparable to those already existing participants.

Annual percentage of participants lost to follow-up, and the number of those available for future surveys

Cohorts included in the four previous surveys were followed up for a median of 18.8 years. During this period a total of 1907 individuals were lost to follow-up. When all these individuals were taken into consideration, annual rate of loss to follow-up was 2.32 percent. This means that every year 70 participants out of a cohort of 3000 individuals are expected to be lost to follow-up, excluding deaths.

Table 4 presents the distribution of the cohort consisting of 2,644 participants with complete medical information who underwent required examinations, and available for future follow-up according to their participation period, and geographic regions

Table 3. Distribution of type-2 diabetes prevalence according to age groups, and three study periods

	1998-2000			2002-2006			2007-2012		
	n	%	Total	n	%	Total	n	%	Total
<40	9	1.3	678	6	2.9	207	0	0	14
40-49	25	3.3	759	55	6.0	920	49	9.0	545
50-59	71	12.9	549	100	13.1	763	138	16.9	816
60-69	67	15.0	448	108	19.4	558	146	26.1	559
70-79	23	11.3	203	58	18.1	321	85	25.8	329
≥80	4	7.7	52	7	12.5	56	16	16.7	96
Total	199	7.4	2689	334	11.8	2825	434	18.4	2359

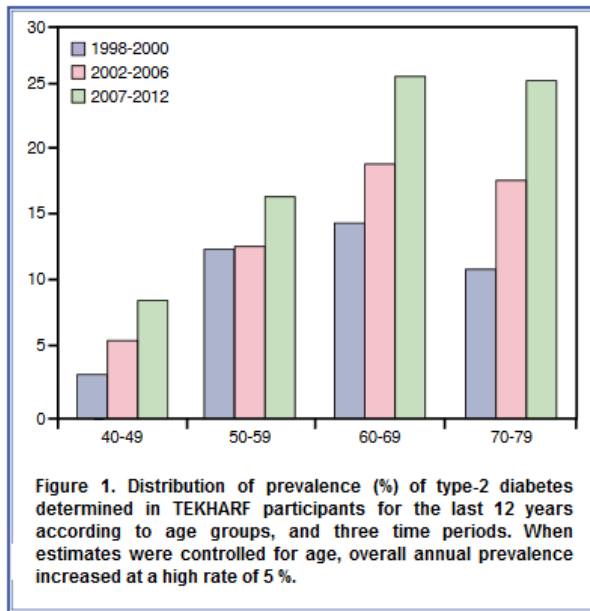


Table 4. Cohorts suitable for future follow-up, and their distribution among geographic regions

Cohorts	Total	2015 survey	2014 survey
Original	1515	816	699
1997/98 cohort	421	189	232
2002/03 cohort	294	124	170
2007/08 cohort	326	135	191
2012/13 cohort	88	57	31
All regions	2644	1321	1323
Marmara	755	637	118
Central Anatolia	470	470	
Aegean & Afyon	370	131	239
Black Sea	259	83	176
Mediterranean	316		316
Eastern Anatolia	200		200
South Eastern Anatolia	274		274

DISCUSSION

In this analysis of the TEK HARF Study encompassing the Marmara, and Central Anatolian regions, 3.4% of the participants to be followed up died, and 56 % of them were examined. As a striking finding, autoimmune activation appeared to have an important impact on mortality rates via various major causes of death

During a period of 23 years, rates of all-cause (13.2), and coronary (5.6) mortality rates per 1000 person-years in the age-bracket of 45-74 years differed only slightly. Besides, we have also observed that the incidence of type-2 diabetes in our adult cohort increased-after excluding factors effective on population growth, and age of the

participants- at an alarming rate of 5 percent.

All-cause and coronary mortality

During the screening period, median annual mortality rate among participants (mostly in the age bracket of 30-70 years) was found to be 11.2 per 1000 person-years, and significant improvements were not displayed. When all-cause mortality in age bracket 45-74 years was considered, mortality rate per 1000 person-years was estimated as 16.8 in men, and 9.9 in women which reflected the stabilization in mortality rates for the last three years. Data related to the year 2000 for the age bracket of 45-74 years in European countries, and associated trend was declared previously.^[8,9] Since median mortality rate in the age bracket of 45-74 years in 30 European countries was estimated as 13.2 in men, and 7.3 in women per 1000 person-years^[8], the corresponding rates in our country is still 30% higher. Regression in mortality rates halted in the age bracket we analyzed, deserving serious consideration

We observed similar standstill in coronary mortality rates (5.5 in men, and 3.5 in women per 1000 person-years) In 30 European countries median coronary mortality rates per 1000 person-years were 2.3 in men, and 0.72 in women. Accordingly, coronary mortality in Turkey continues to remain at high levels These standstills in mortality rates strongly suggest the role of underlying inflammation, defects in the protection for serum proteins, and autoimmune activation^[6,7] in this phenomenon

Alarming increase in the prevalence of diabetes

From our provided data, 4.6 million citizens can be estimated to have diabetes, without any gender difference. After excluding the effects of aging on the rate of population increase, an annual increase of 5% in the prevalence of type-2 diabetes is alarming. According to TURDEP II survey^[10] participants in which underwent also glucose loading tests, prevalence of diabetes in the population aged > 20 years was estimated to be 16.5%, and the total number of diabetics between 6 and 7 million.

In a current meta-analysis, 2008 prevalence of diabetes, standardized and adjusted for a world population aged 25 years or over, was determined as 9.5% (a total of 346 million) being 6.5% higher than that of the previous quarter century (3%)^[11]

Oceania, Southern Asia, Latin America, Northern Africa, and Middle East (incl. Turkey) were declared as the regions with the highest prevalence of diabetes.

It is very likely that the actual prevalence rate of diabetes in Turkey is probably 1.4 million higher than our above-mentioned estimate, were measurements of glycated hemoglobin included. This figure is much higher than our earlier estimates [2]

The autoimmune activation mechanism proposed by the TEKHARF Study in various publications should be taken into account in that it increases the incidence of diabetes, and CHD, and has fatal outcomes by exacerbating heart failure, renal, and other chronic diseases. [7]. Our findings require serious and urgent revision of relevant policies in effect. Among preventive measurements to be taken, modification by focusing on abdominal obesity rather than on strict, monotonous and indiscriminate anti-smoking campaign which fails to conform to real-life findings is needed.

Regional distribution of the cohort

One can say that the final composition of the cohort shown in Table 4 very closely represents the the characteristics of the relevant regions. TEKHARF cohort also very well represents Turkish adults in their middle, and advanced ages.

In conclusion, TEKHARF Study revealed precautionary data that regression in all-cause, and coronary mortality rates came to a standstill in our adult population. Moreover the major concern is detection of an annual 5 % increase in type-2 diabetes, after excluding age related factors. In our opinion, dogmatic approaches, and politics that do not take the outcomes of the survey studies which reveal characteristics of cardiac, and metabolic health state of our population into consideration will obviously result in frustration.

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Anahtar sözcükler: Diyabet; koroner hastalık/mortalite; mortalite/trend; Türkiye/epidemioloji.

Key words: Diabetes mellitus; coronary disease/mortality; mortality/trends; Turkey/epidemiology.