Iranian J Publ Health, Vol. 41, No.9, Sep 2012, pp.86-92

Report Article

Coronary Artery Disease Risk Factors in an Urban and Peri-urban Setting, Kerman, Southeastern Iran (KERCADR Study): Methodology and Preliminary Report

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(Received 16 Jan 2012; accepted 19 Aug 2012)

Abstract

Background: This article was to present the sampling and measurements methods and the main preliminary findings of the KERCADR cohort study (first round) in an urban and peri-urban setting, Kerman, southeastern Iran2009-11.

Method: 5900 (3238 female) people aged between 15 to 75 years were recruited in the household survey by non-proportional to size one-stage cluster sampling. Trained internal specialists, general practitioners, clinical psychologists and dentists have assessed the study subjects by person-assisted questionnaires regarding different NCD risk factors including cigarette and opium smoking, physical activity, nutrition habits, anxiety, depression, obesity, hypertension and oral health. Blood samples were also collected for determining FBS, HbA1c, cholesterol and triglyceride. Weighted standardized prevalence estimates were calculated by STATA 10 survey analysis package.

Results: The participation rate was more than 95% in all subgroups. Cigarette smoking (18.4% vs. 1.2%), opium use (17.8% vs. 3.0%) and triglyceridemia (16.1% vs. 12.0%) were significantly higher among men than women. In contrast, women were presented with higher level of sever anxiety (29.1% vs. 16.7%), obesity (16.8% vs. 9.2%), low-physical activity (45.1% vs. 39.2%) and uncontrolled diabetes (60.2% vs. 31.0%). More than 68% of all subjects have presented with moderate to severe gingival index scores.

Conclusion: The first round of the KERCADR cohort with sufficient sample size and response rate provided precise estimates for the main clinical and para-clinical NCD risk factors. These evidences need to be translated into public health interventions and monitored in the next rounds of the cohort.

Keywords: Household survey, CAD risk factors, Cohort, Iran

How did the study come about?

Kerman is the capital city of Kerman Province located in south east of Iran about 1000km far from the capital city, Tehran (Fig. 1). It's populated by 540,000 inhabitants (estimated for 2010) (1). People are mostly busy with white-collar works at governmental sections, agriculture and marketing.

The lifestyle patterns are typically aggregated in families. In 2005, as part of the national survey on non-communicable disease risk-factors (NCDRFs) in Kerman province, 1614 inhabitants aged 15 to 64 years were recruited. The familial aggregation of NCDRFs such as physical inactivity, obesity, high blood pressure, hyper cholestrolemia and high blood glucose with a risk ratio of 1.5 to 3.5 have been reported in a study published in 2007(2).

Fig.1: Kerman province and city

According to the national NCDRFs 2005-6 report(3), the prevalence of different risk factors among people living in Kerman were as follow: overweight 42%, obesity 12%, systolic and diastolic blood pressure more than 140/90 mmHg, 12.1%, every day cigarette smoking reported at the level of 18.6% in men.

When we look at the risk factors as one combined factor, about 41.9% (CI95%, 33.7-50.5%) of the inhabitants in Kerman have a raised risk factor which put it at the 12th rank among the provinces (out of the 31) in Iran(3). This high risk profile of the Kerman community is translated into 37 incidence case (per day) of myocardial infarction in Kerman. All of these highlight the susceptibility of Kerman population for cardiac events(4).

When we look at the impact indicators, i.e. the standardized crude mortality rate of all cardiac diseases, Kerman with 320 deaths (per 100,000) gets the 14th rank among the all provinces. In addition to cardiac risk-factors and diseases, the province's rank moved up to the 3rd position in the country, considering the standardized crude mortality rate of addiction and drug-abuse related disorders(5). Several studies has explored that mental health and disorders including addiction, depression affected a considerable proportion of inhabitants in Kerman which is a public health need among the all health priorities for this part of the country(5).

As mentioned above, the national NCD risk factor surveillance has been conducted in Iran since 2005. It has been designed to provide national estimates on major NCD risk factors by repeated survey among the Iranian populations aged from 25 to 65 years old. In line with the national NCD risk factor strategic plan, KERCADR has been designed and implemented to monitor the CAD risk factors at individual level (repeated measured among individuals rather than community) with a prospective cohort study6. In addition to basic routine NCD risk factors that are captured in the national NCD surveillance, KERCADR includes mental health (opium dependency, depression, and anxiety), oral health and HbA1c.

The present article aims to present the details of the sampling, measurement and analysis techniques applied in KERCADR to provide the most valid and reliable estimates on NCD risk factors and monitored the trend at the individual levels in an urban setting in south-east of Iran. We also present the preliminary results of the main CAD risk measured in the first round of KERCADR study and compared men and women accordingly.

What does the KERCADR cover?

The primary objectives of the study are:

1. To identify behavioral and biological risk factors for non-communicable diseases by a comprehensive assessment of self and familial past medical history, demographics, occupational and educational status.
2. To identify behavioral and biological risk factors for mental health disorders by a comprehensive assessment of self and familial past medical history, demographics and occupational and educational status.
3. To establish bio-bank for serum to be used for further cross-sectional and nested case-control studies

Who is in the sample?

The first round of the study has been initiated in Kerman in 2009 to recruit 5900 subjects aged between 15 to 75 years old.

The details of the recruited sample and the key findings are illustrated in Table 1. To maximize the sample size to be efficient for all the NCD and their risk factors, we have calculated the sample size for a prevalence of 50%, and consider the precision as the level of 5%. The initial calculation for the sample size was 384.16 cases. We did not apply the Finite Population Correction. However, we have corrected the sample size based on eight strata (15-24, 25-34, 35-54, 55-74 by sex), the design effect of 1.5 and the response rate 78% where lead to 5900 as the final sample size (Fig. 2).

The project has been funded by Kerman University of Medical sciences with the grant number 88/110.

The sampling method was a one stage cluster sampling. In the first stage, 250 postal codes (called seeds) were selected randomly among an updated roster of residential addresses in provincial post office. The data collection team firstly mapped the seeds and then contact them one by one. After briefing the household's member, all the eligible members (15-75 years old) have been listed in the Kish household coversheet and recruited to the study.

Step 1: Initial calculation:

$$n = \frac{3.8416 * (0.5 * (1 - 0.5))}{0.05 * 0.1} = 384.16$$

Step 2: Multiply by the design effect and number of age-sex estimates:

$$n = 384.16 * 1.5 * 8 = 4609.92$$

Step 4: Adjust for expected non-response to get your final sample size:

$$n = 4609.9 / 0.78 = \boxed{5910.154}$$

FINAL SAMPLE SIZE

Fig. 2: the sample size calculation formula

The written informed consent was signed by all of the participants after ensuring their well-understanding of the harm and benefits of the participation in the survey. It should be noted that the study protocol and procedures were reviewed and approved by the Research Review Board of the Kerman University of Medical Sciences (Ethic code 88-110KA).

In the case of any household being absent for twice, the other neighborhood households from the right direction of the seed were approached systematically and with the same method, eligible people were asked to participate in the study. The recruitment was continued to reach 24 subjects in each cluster. All recruited people were given an appointment card having the date, time and the place of attending collaborating clinic for blood sampling and face-to-face interview. They were asked to be fasted for 12-14 hours before the appointment time in the morning and bring their medicines with themselves.

In Fig. 3, the age distribution of the recruited sample is compared with the target population in Kerman (National consensus of population size for 2006). Base on the sampling methods (non-proportionate to size), the younger age groups were under-sampled and the older groups have been over-sampled. Although this will bring more precision to age-stratum specific estimates, the total combined estimates have to be always standardized based on the real age distribution of the target population.

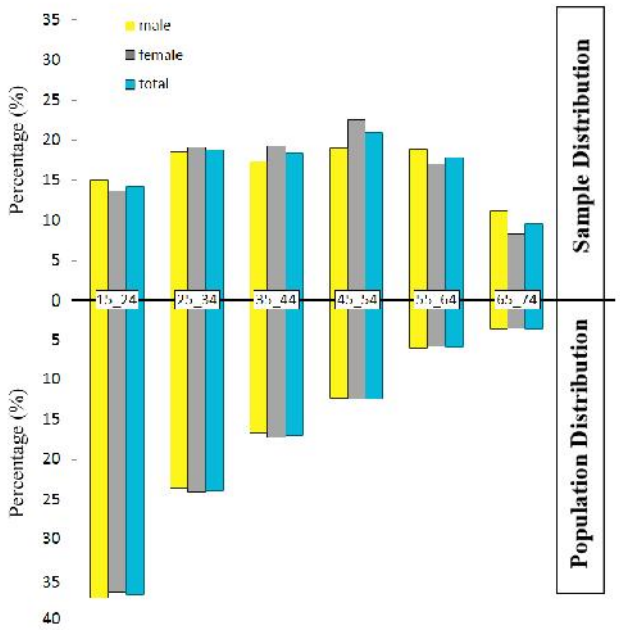

Fig. 3: The age distribution in the sample and target population, (N=5900) Kerman, Iran, 2009-11

The standardized estimates (based on age and sex subgroups) for the key measures of clinical and para-clinical findings were presented separately for men and women in Table 1. The standardized estimates are lower than the crude estimates. For sake of simplicity, we did not present crude estimates (as they have been confounded estimates). The reason for this confounding is the over-sampling of the older age-groups in the survey and the direct standardization has removed this sort of confounding.

For further analysis, we have considered household as the primary sampling unit (cluster). Proportions of categorical and ordinal variables reported by sex group and then compared using Chi square test. The means and 95% confidence interval (CI) of numerical variables were reported by sex group and compared using Post-Survey Estimation Student T-test. Association between disorders and risk factors were calculated using Poisson regression model. All statistical analyses were conducted under survey data analysis by STATA v.11. *P*-Value less than 0.05 considered as significant level.

How often they will be followed?

It is going to be repeated comparable surveys every four to five years having the components of the behavioral and biological measurements.

What has been measured?

- Behavioral risk factors: the nutritional habits were recorded as well as the food frequency questionnaire for all study subjects. Current and past smoking status also recorded. Physical activity at home and work places, daily movements and level of physical activities at recreation session was measured by Global Physical Activity Questionnaire (GPAQ) and Metabolic Equivalents was used to express the intensity of physical activities(6).
- Smoking and addiction status: Smoking status was measured in different ways. People were categorized as the current smoker if they mentioned that they have been smoking cigarette at the time of first assessment round of the survey. For addiction, a general practitioner asked the participants to disclose whether they have ever used any type of drug and still continue. Those with the positive drug history, the type of drug was also asked and recorded.
- Physical examination and biological risk factors: anthropometric measurements as height (a tape stadiometer with a minimum measurement of 0.1 cm in a standing position, without shoes, while the shoulders were in a normal resting state) and weight (light clothing without shoes measures by Seca 707 weighing Balance with the range of 0.1 to 150 kg, with an accuracy of up to 100 gr), Waist circumference (measured at the umbilical level and hip circumference was measured at the maximal level over light clothing, using a non-stretchable measuring tape, without any pressure to the body surface; both were

recorded to the nearest 0.1 cm), blood pressure (standard mercury manometer– Model RISHTER, Germany) and pulse rate, fasting blood glucose (KIMIA Kit, Code 890410, Iran) (HbA1C - NYCOCARD Kit, Code 1042184, Austria) - for known diabetic cases and those with high fasting blood glucose after two subsequent measurements), Triglyceride (KIMIA Kit, Code 890201, Iran), Total cholesterol (KIMIA Kit, Code 890303, Iran) (HDL – PARS Kit, Code 89022, Iran) - and LDL was calculated based on Frieldwald formula [LDL = Total chol. – (HDL + TG/5)].

Table 1: Standardized estimates for the clinical and para-clinical findings in KERCADR study round one, (N=5900), Kerman, Iran, 2009-11

	Male (N=2662)			Female (N=3238)			*P*-value
	Frequency	Percentage	CI 95%	Frequency	Percentage	CI 95%	
Clinical Findings							
Current daily cigarette smokers	602	18.40%	17.5-19.3%	55	1.20%	1.0-1.4%	<0.0001
Current opium use (occasionally or dependency)	674	17.80%	17.0-18.7%	176	3.00%	2.7-3.3%	<0.0001
Severe Anxiety (BAI score>25)	439	16.70%	15.6-17.8%	1041	29.10%	28-30.2%	<0.0001
Severe Depression (BDI Score>46)	6	0.20%	0.1-0.3%	16	0.60%	0.4-0.8%	<0.0001
Hypertension(BP≥140/90 mmHg or taking drugs)	558	10.70%	10.1-11.3%	775	10.70%	10.4-11.1%	0.9
Obese (BMI>=30)	269	9.20%	8.5-10.0%	779	16.80%	16.1-17.6%	<0.0001
Low physical activity (<600 MET per week)	1091	39.20%	37.9-40.6%	1518	45.10%	43.8-46.4%	<0.0001
Grade of Gingival index							
Moderate (1<GI Score≤2)	1551	69.70%	68.4-71.0%	1902	65.40%	64.1-66.6%	0.05
Severe (GI Score>2)	62	2.90%	2.4-3.5%	81	2.70%	2.4-3.1%	
DMFT(mean)		12.2	11.9-12.5		12.8	12.5-13.0	0.003
Para-Clinical Findings							
Diabetes (FBS≥126 mg/dL or taking drug or Insulin)	355	6.90%	6.4-7.4%	496	8.50%	8.1-9%	0.02
Uncontrolled Diabetes (HbA1c ≥7%)	174	31. 0%	25.3-37.3%	288	60.2%	52.0-68.4%	0.0001
Cholestrolemia (>200 mg/dL)	951	27.80%	26.8-28.9%	1401	30.10%	29.2-31.0%	0.1
Triglyceridemia (>200 mg/dL)	520	16.10%	15.2-17.1%	599	12.00%	11.4-12.6%	0.0002

* Estimates adjusted for Missing Response and also standardized based on the Kerman population size in 2006; MET: Metabolic Equivalents, BMI: Body Mass Index, BP: Blood Pressure, FBS: Fasting Blood Sugar

- Medical history: Hypertension and Diabetes history as well as other cardiovascular and vascular diseases, the name of medicines also were recorded by a general practitioner. Accordingly, all types of medical interventions and any of the mentioned disease in the immediate family were also recorded. Blood pressure (BP) was measured in sitting position after at

least 10 minutes at rest. If abnormal, BP was measured once again at the end of the session (at least 30 minutes after the first measurement) in the same conditions.

- Mental health: depression was measured by a valid-translation of the 21-question BECK-BDI questionnaire. Anxiety score was measured by a valid-translation of the 21-question BECK Anxiety questionnaire, both conducted by a face to face interview.
- Oral Health: Gingival Index, Dentition Status and Community Periodontal Index of Treatment Needs questionnaires were used for measuring the Gingival and DMFT indices and treatment needs respectively. These were completed by a dentist by inspection.
- Demographic measurements: age, sex, education, familial status, location and period of residency in Kerman.

What are the main strengths of the study?

The participation rate in all the suburban divisions was more than 95%. All the non-response households have been tracked twice and if the household did not find at the end, one neighborhood household was replaced. All the non-response in a family was track-able by Kish form. This approach makes it possible to count the number of non-response cases at the family which will be used for weighted analysis based on the none-responses.

All the biomedical assessment were performed free of charge for participants and the results with a recommendation note based on the results returned back to the study participants by local mail delivery system and further consultancy and required services also provided accordingly. This approach has improved the participation rate and the acceptability of the study among the local communities and families. And we believe this will continue for the next rounds of the cohort.

For each participant, two subsamples of the serum have been frozen and stored at -80oC for further investigation as complementary case-cohort and nested case-control studies.

Data entered into an Epi-data 3.1 database in maximum three days of the interview. Since it has been done with a specific control with several cross-check points, any type of inconsistency has been reported to the data collection team for further investigation and to be corrected even by re-calling the study subjects.

Laboratory QC and QA

Laboratory exams for FBS, Chol, TG and HDL have been done by Selectra E machine. The machine automatically has repeated the test based on the following cut points (Table 2):

Table 2: The cutoffs for automated exam repetitions

Lab. Exams	Cutoffs for automated exam repetition
FBS	>400
Chol	>500
TG	>750
HDL	<2 OR >440

Westgard rules have been used for the quality control. Shewhart chart has been developed for all the laboratory examinations and according to the standard deviation from the mean (SD), necessary decisions have made. If the three rules have been rejected, the test should be repeated. In the next step, the laboratory technician will review the results and according to the following cutoffs (Table 3), the tests will be repeated.

In all cases, the results will be reported if in two serial exams, the results will be in the range of ±5.

For, HbA1c, NYCOCARD kit is being used. HbA1c results is comparing with the FBS as for FBS equal to 126, we expected to have HbA1c around 6.5 and for every unit increase in HbA1c, FBS should be increase about 30. For example, for a person with HbA1c of 8%, FBS expected to be around 170. If the expected result varies more than ±0.5 from the observed result, HbA1c will be repeated. The results will be reported if in two

serial exams, the results will be in the range of ±0.5.

Table 3: The cutoffs for automated exam repetitions

Lab. Exams	Cutoffs for automated exam repetition
FBS	>115
Chol	>250
TG	>200
HDL	Male : <30 Female : <35

To control the quality of Selectra E machine, in a daily basis, the machine will be calibrated based on the standard controls from Roche Germany (Procured from KIMIA Pajoohan). The LOT number for the standard controls are varies (as the duration of the study is about 2 years) but has been registered.

For the external quality control, four specimens from the central Academic Laboratory in Kerman and two specimens from national reference laboratory have been sent to the laboratory to be tested and return back the results. If the results were not in the acceptable range, they will receive the feedbacks. Regarding the above tests, the quality has been approved up to now.

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.

Principal and co-investigators

The principal investigators for the study are listed as Authors. The others who have contributed a lot to the project are as: Medical Physicians: Hesami Kh, Yazdanpenah Sh, Tajadini H, Ahmadi Gohari N., Mir Rashidi F, and Dentists: Foad Rahim and Omrani Z; Interviewers: Ebrahimian Z., Kalantari M., Shahabi Sh., Shahabi F., Nazarieh S., Administration: Shadkam M. Montezarolghaem R, Namjoo H., Sadeghi Z., Khajooei S., Bakhshi N.; Clinical Laboratory: Doost Mohammadi M, Sheikholeslami Y., Khajeh Hasani H.; Community/Social Mobilizer: Nikvarz A., Nikvarz N., Iran-nejad H., Iran-nejad S., Molaei F., Panbeh Foroosh A., Zakavati M., Jamali M., Sadeghi Nejad S., Taghzadeh S., Jamshidi A., Mosazadeh P., Ramazani Nejad F., Yazdan panah M., Shojaei A., Khadem Nakhaei., Naser Asadi H., Servants: Soltani M., Mohammadi Z., Ghanbari N., Bagheri M., Mortazapour M., Iranmanesh M.,

Acknowledgements

We thank the men and women who have participated in the KERCADR (Kerman Coronary Artery Diseases Risk Factors) study, the specialists and the nurses and doctors who conducted the clinic interviews at the first round. We should send our best gratitude to Dr Maliheh Shadkam Farrokhi (God bless her soul) who has done a lot for the project and unfortunately passed away in the middle of the first round. The authors declare that there is no conflict of interest.

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