The Khuzestan Comprehensive Health Study (KCHS): Methodology and Profile of Participants

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Abstract

Background: Non-communicable diseases (NCDs) are the leading cause of death worldwide, with a disproportionately rising burden among low- and middle-income populations. While preventable risk factors highly contribute to this burden, population-based studies assessing these factors and the health status of these populations, are scarce.

Methods: The Khuzestan Comprehensive Health Study (KCHS)—a cross sectional study—was conducted between 2016-2019, including 30,506 Iranians aged 20 to 65 years, from 27 counties of Khuzestan province, southwest of Iran. KCHS aimed to provide a comprehensive health overview by investigating the prevalence and risk factors of NCDs and psychological disorders, along with viral hepatitis as a common communicable disease. Upon registration, 15 mL of blood and anthropometric measurements were obtained from participants. Afterwards, several interviewer-administered questionnaires were completed to gather data on demographics, socioeconomic status, sleep quality, physical activity, lifestyle habits, nutrition, and medical history.

Results: The mean ± SD age of participants was 41.7 ± 11.9 years. The majority were female (64.3%), of the Arab ethnicity (49%), married (83%), and urban residents (73.1%). About 70% had an educational level below high school diploma. Overall, 10.8%, 5.2%, and 2.8% of participants had used cigarettes, hookah, and drugs at least once in their lifetime, respectively. While body mass index and serum cholesterol levels were higher in females, blood pressure was higher in males (P<0.001).

Conclusion: KCHS assessed many aspects of health in the Khuzestan province. In addition to develop a biobank along with a comprehensive dataset, KCHS will serve as a valuable infrastructure for future research.

Keywords: Epidemiology, Iran, Khuzestan, Non-communicable diseases, Risk factors

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Introduction

Over two-thirds of deaths worldwide are attributable to non-communicable diseases (NCDs),1 rising disproportionately among marginalized as well as low- and middle-income populations.2 The rising burden of NCDs is mainly driven by rapid urbanization and increased life expectancy.3 Still, preventable risk factors mainly contribute to this burden and present targets for control measures.3 Despite recent lifestyle changes, limited population-based studies are available to assess the health status of people in low- and middle-income regions, including the Middle East.4

Fifteen million premature deaths occur annually due to NCDs, over 85% of which occur in low- and middle-income countries.5 NCD deaths are mainly caused by cardiovascular diseases, neoplasms, chronic respiratory diseases, and diabetes, imposing detrimental economic and health burdens on communities.1,2 In addition to

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traditional risk factors, such as smoking, dietary and lifestyle habits, nontraditional factors like pollution and climate change have emerged in recent decades, predisposing many countries to numerous health hazards.

Southwestern Iran is a unique region, given its natural conditions and geological, climatic, and soil characteristics. Recently, it has been exposed to dust storms, extremely high temperatures, air pollution, and soil contamination, all of which could threaten the health of its residents. Furthermore, the southern border of Iran, mainly Khuzestan province was heavily affected by the Iran-Iraq war (1980-1988). Many cities were partially or completely destroyed and much of the infrastructure in the area was destroyed during that time, also debilitating the physical and psychosocial health of its residents. Despite the above-mentioned facts, no cross-sectional study has yet assessed the health status of the people of Khuzestan province. Also, given the impact of war on mental health, a psychological assessment is particularly important for those residing in the region, but has not yet been completed. Therefore, the Khuzestan Comprehensive Health Study (KCHS) was conducted with the aim to provide a comprehensive overview of health in Khuzestan, including the prevalence and risk assessment of non-communicable and psychological diseases, as well as viral hepatitis as a common communicable disease in Iran. In this manuscript, the methodology used in KCHS is described in detail and the profile of the participants is presented.

Materials and Methods

Study Design

KCHS was a cross-sectional study conducted between October 2016 and November 2019 in 30,500 Iranian adults from 27 counties of Khuzestan province. This large population-based study was funded by the National Institute for Medical Research Development (NIMAD) and the Iranian Blood Transfusion Organization (IBTO), and executed by the Digestive Diseases Research Institute (DDRI), Jundishapur and Dezful Universities of Medical Sciences, as well as Abadan and Behbahan Faculties of Medicine. The KCHS protocol was approved by the ethics committee of NIMAD (IR.NIMAD.REC.1394.002).

Study Site

The Khuzestan province is located in southwestern Iran, sharing a border with Iraq to the west and lying north of the Persian Gulf (Figure 1). The province covers an area of about 64,000 km² and is home to a population of nearly 4,936,000 individuals of different ethnicities, including Arabs, Lurs, and Fars. Khuzestan has one of the hottest climates in Iran with an average daily high temperature of 35°C, and reaching as high as 49°C in the summers. This province is notable for its oil resources and is a central oil-producing region.

Study Population

The study population included all men and women in the age range of 20 to 65 years, residing in urban and rural areas of the Khuzestan, for a minimum duration of 12 months prior to the study recruitment. Exclusion criteria were unwillingness to participate and any mental, psychological, or physical disabilities that inhibit the completion of questionnaires or other steps.

Sample Size

The sample size required to estimate the prevalence of any health conditions in the province with 1% margin of error was calculated. A 50% baseline prevalence to maximize the required sample size was assumed. As such, a sample size of 30,000 will provide a power greater than 90% for estimations, and was chosen for this study (Figure 2).

Sampling Method

Primary care centers, called “Health Houses,” have long been established throughout Iran. Each Health House covers a target population of about 1500 individuals, archiving the population census and their health records. The population census at the Health Houses were used as the sampling frame, with the aim to recruit 30 random individuals from each Health House. To obtain a geographically representative sample, the population of all 27 counties in the province were stratified and a random sample of Health Houses in each county were selected. The number of Health Houses included from each county was determined based on the proportion of the total province population living in that county. Consequently, 1,079 random Health Houses (780 urban and 299 rural), were selected across the province, and thereafter, 30 individuals who fulfilled the eligibility criteria were randomly selected from the population covered by each Health House.

Data Collection

I. Invitation

Based on the above-mentioned sampling methods, trained staff performed face-to-face recruitment of potential participants, explained the aims of the study and if they
accepted to participate, they were instructed to visit a pre-determined study site. The study sites were health centers, Health Houses, schools and mosques, located in close proximity of the participants’ homes.

I. Registration

Upon arrival at the study site, written informed consent was obtained from each participant, who was then registered using credible personal identification documents. A unique 11-digit code was assigned to each individual; all questionnaires and biological samples were labeled by these codes.

III. Biological Sampling, Laboratory Assessment and Biobanking

After registration, 15 mL blood, including one clot tube (6 mL) and one EDTA tube (9 mL) (KANG JIAN, China), was obtained from participants by trained staff, using Vacutainers (Greiner Bio-One International GmbH, Kremsmunster, Austria). All participants were fasted for 8 to 12 hours at the time of sampling. Blood was transferred to the reference lab within three hours of sampling, stored in Cool boxes (Pole Ideal Pars, Iran), at 4°C.

Blood samples were centrifuged at 3000 rpm (Sigma, Germany) for 10 minutes to separate the serum. Later, serum levels of fasting blood sugar (FBS), urea, creatinine (Cr), triglycerides (TG), cholesterol (Chol), high-density lipoproteins (HDL), alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST) and gamma-glutamyl transferase (GGT) were measured by BT 1500 AutoAnalyzer (Biotecnica Instruments, Italy), using commercial kits (Pars Azmun, Iran). A complete blood count (CBC) was performed by hematology AutoAnalyzer (Nihon Kohden 6510-k, Japan). Also, a serum sample (500 μL) was transferred at -20°C to IBTO in Tehran for serologic evaluation of hepatitis B and C viruses. Blood chemistry and serology results were returned to participants. In case of any abnormal findings, participants were referred to family physicians or specialists for further evaluation.

In addition to the biochemical and hematological tests, fractioned samples of whole blood (1 tube), plasma (3 tubes), buffy coat (1 tube) and serum (1 tube) were biobanked for each individual in sterile barcoded cryotubes (Micronic, Netherlands) at -80°C.

IV. Anthropometric Measurements

Given the lower occurrence of measurement errors in the morning, anthropometric measurements were made after blood collection while participants were still fasted. Weight (kg) and height (cm) were measured by the Seca 762 Mechanical Flat Scale and Seca 206 Bodymeter Measuring Tape with Wall Stop, respectively. The Seca 203 Circumference Measuring Tape was used for waist, hip, and wrist circumferences (cm). All measurements were made following National Institutes of Health protocols.12 Breakfast was provided prior to the completion of the following steps.

V. Questionnaires

The KCHS questionnaire set consisted of five major sections: general, medical, nutrition, gastrointestinal, and psychological. While the general and medical sections were completed for all participants, other sections were only completed for a subsample. Questionnaires were completed by trained interviewers. An explanation of each section is as follows.

V-A. General Section

The general questionnaire included information on demographic characteristics, socioeconomic status, sleep quality, and physical activity (International Physical Activity Questionnaires [IPAQ]).13

V-B. Medical Section

This section contained questions regarding the personal and family history of chronic diseases, medication use, lifestyle and personal habits, and risk factors of blood-borne disease transmission. In addition, a fertility questionnaire unique to each gender was administered to all participants. As part of the medical evaluation, blood pressure was measured twice in each arm, in the sitting position, using aneroid sphygmomanometers (Riester, Germany).

V-C. Nutrition Section

Ten percent of participants were randomly selected to complete an 86-item qualitative food frequency questionnaire (FFQ), with 9 response categories used to indicate their usual food consumption frequency in the year prior to recruitment. Among the selected participants, 2,831 (9.3% of total) individuals completed this section.

V-D. Gastrointestinal Section

Ten percent of participants were randomly selected
to complete the irritable bowel syndrome (IBS) and gastroesophageal reflux disease (GERD) questionnaires, containing 21 and 10 questions, respectively. Overall, 1,853 (6.1%) participants completed this section.

**V-E. Psychological Section**
To complete the psychological section, 25% of participants were randomly selected, of whom, 6,935 (22.7%) individuals completed the following four questionnaires: Depression Anxiety Stress Scales (DASS), Life Events Checklist (LEC), Post-traumatic Stress Disorder Checklist (PCL), and War Exposure.

**Quality Assurance and Quality Control**
The main tool used to control the quality of data collected, was a smart data server that minimized common errors in data entry, including missing and out-of-range values. To ensure consistent data collection, the same equipment and devices were used at all study sites and executing teams were trained by the same instructors. Also, to ensure the compliance of study procedures with the KCHS protocol, the executive teams were frequently evaluated through unexpected visits.

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**Results**
A total of 30,506 participants were enrolled in the study, of whom 19,604 (64.3%) were female. The mean ± SD age of participants was 41.7 ± 11.9 years. Demographic characteristics of the participants are presented in Table 1. The majority of participants were of the Arab ethnicity (49.0%), were married (83.0%), and resided in urban areas (73.1%).

Health-related characteristics of study participants are described in Table 2. Overall, 10.8% and 5.2% of participants had smoked cigarettes and hookah in their lifetime, respectively; 2.1% had consumed alcohol, and 2.8% had used drugs. The prevalence of cigarette and hookah use were higher in males, compared to females (22 and 5-folds, respectively), and the prevalence of alcohol and drug use was much less among females ($P<0.001$). Among all participants, 42.9% had moderate, and 31.1% had low physical activity levels; the remaining 26% were classified as high. While the prevalence of high physical activity was similar in both genders, the moderate level was more prevalent among females, compared to males ($P<0.001$) (Table 2).

The mean ± SD of body mass index (BMI) was 27.63 ± 5.3, and higher in females ($P<0.001$). For total cholesterol, the mean ± SD was 193.1 ± 47.5; which was higher in females ($P<0.001$). In contrast, the triglyceride levels were relatively higher in males ($P<0.001$). Also, mean systolic and diastolic blood pressures were higher among male

| Characteristics | Total, No. (%) |
|-----------------|----------------|
| Gender          | Male 10902 (35.7) Female 19604 (64.3) |
|                 | Arab 14929 (49.0) Bakhtari 6738 (22.1) |
| Ethnicity       | Fars 5621 (18.5) Lur 2928 (9.7) Other 226 (0.7) |
| Place of residence | Urban 22292 (73.1) Rural 8214 (26.9) |
| Age group (years) | 20-29 5645 (18.5) 30-39 8381 (27.5) 40-49 7579 (24.9) 50-59 6287 (20.7) 60-65 2557 (8.4) |
| Marital status  | Married 25325 (83.0) Single 3644 (12.0) Divorced/widowed 1537 (5.0) |
| Educational level | None (Illiterate) 6607 (21.7) Elementary school 8237 (27.0) Middle school 5246 (17.2) High school diploma 6693 (21.9) University degree 3718 (12.2) |

**Discussion**
This is the first cross-sectional study assessing the prevalence and associated risk factors of NCDs, psychological disorders, and hepatitis B and C infections in the Khuzestan province of Iran. The findings of this study can help identify and better understand the health obstacles in the region and emerging health threats, in order to improve pertinent health policies. The main limitation of this study was the higher response rate in females in comparison to males. However, this limitation can be adjusted for in data analysis by reporting gender-specific or gender-standardized estimates. Given the importance of biobanking in the future of medicine, the samples stored in KCHS will serve as a valuable foundation for future research, especially in the identification of disease biomarkers and genetic variations of NCDs.

**Authors’ Contribution**
HP, AAS, BC, ZM and SE contributed to the design, study execution and manuscript writing. AS, ZR, LD, YP, FA, MN, AM, SM and FH contributed to data collection and manuscript writing. MS, AE, RG and SH contributed to data analysis and manuscript writing.

**Conflict of Interest Disclosures**
Authors have no conflicts to declare.
Table 2. Health-related Characteristics of KCHS Participants

| Characteristics                           | Male       | Female    | Total     | P value  |
|------------------------------------------|------------|-----------|-----------|----------|
| Cigarette smoking, ever<sup>a</sup>      | 3041 (28.0)| 255 (1.3) | 3296 (10.8)| <0.001   |
| Hookah smoking, ever<sup>a</sup>         | 1158 (10.6)| 435 (2.2) | 1593 (5.2) | <0.001   |
| Alcohol use, ever<sup>a</sup>            | 617 (5.7)  | 31 (0.2)  | 648 (2.1)  | <0.001   |
| Drug use, ever<sup>a</sup>               | 809 (7.4)  | 42 (0.2)  | 851 (2.8)  | <0.001   |
| Physical activity<sup>b</sup>            |            |           |           |          |
| Low                                      | 4686 (43.1)| 4763 (24.3)| 9615 (31.1)| <0.001   |
| Moderate                                 | 3445 (31.7)| 9615 (49.2)| 13060 (42.9)|          |
| High                                     | 2732 (25.2)| 5182 (26.5)| 7914 (26.0)|          |
| Body mass index (BMI)<sup>b</sup>       | 26.50 ± 4.7| 28.25 ± 5.5| 27.63 ± 5.3| <0.001   |
| Systolic blood pressure (mm Hg)<sup>b</sup>| 118.34 ± 14.8| 114.42 ± 15.0| 115.82 ± 15.1| <0.001   |
| Diastolic blood pressure (mm Hg)<sup>b</sup>| 76.48 ± 10.6| 73.13 ± 11.2| 74.33 ± 11.1| <0.001   |
| Fasting blood sugar<sup>b</sup>          | 110.99 ± 48.0| 110.33 ± 47.5| 110.57 ± 47.6| 0.247    |
| Total cholesterol<sup>b</sup>            | 191.45 ± 48.6| 194.05 ± 46.8| 193.12 ± 47.5| <0.001   |
| High-density lipoproteins<sup>b</sup>    | 46.43 ± 10.4| 53.46 ± 11.8| 50.95 ± 11.8| <0.001   |
| Triglycerides<sup>b</sup>                | 169.94 ± 117.73| 141.01 ± 90.6| 151.36 ± 102.1| <0.001   |

<sup>a</sup>Data are presented as number and percentage.
<sup>b</sup>Data are presented as mean ± standard deviation (SD).

Ethical Statement
The study protocol was approved by the ethics committee of the National Institute for Medical Research Development (IR.NIMAD.REC.1394.002).

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