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The prevalence of Keshan disease in China

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ABSTRACT

Background: Sentinel surveillance of Keshan disease (KD) is limited by unable to give the prevalence rates and their estimates. This study was to find the national KD prevalence and the estimated patient numbers to provide evidence toward modifying the policy of KD prevention and control.
Method: Using a probability proportional to population size, randomized, multistage, and cluster sampling, we surveyed 101,127, measured grain selenium levels; and surveyed household income with pre-designed questionnaires.
Results: The national prevalence rates of KD, chronic KD and latent KD were 2.21%, 0.50%, and 1.71% respectively. Chronic KD patients are mainly in the provinces where KD had been seriously epidemic. The KD prevalence rate was higher in females (2.20%) than in males (1.98%). These were also higher in older age groups. The cases younger than 30 years accounted for 13.6%, indicating the possibility that KD is still occurring. Nationally, the estimated numbers of KD and chronic KD patients are 1,675,500 (95% CI, 1,608,500–1,747,300) and 379,800 (95% CI, 346,700–412,800) respectively. Multiple logistic regression analysis indicated that family income was a significant dependent variable (OR: −0.258, 95% CI: −0.332 to −0.185, $p<0.001$). More than 2000 chronic KD patients found in the study were treated in 2009–2011. The limitation of this study was that sampling size was determined at national level.
Conclusion: KD is still a public health issue among the people of the historically severe endemic areas. Selenium supplementation, self-management program for chronic KD patients and translation epidemiology of KD surveillance should be strengthened.

1. Introduction

Keshan disease (KD) is an endemic cardiomyopathy occurring only in China. Its name was derived from the first reported epidemic of the disease, which occurred in 1935 in Keshan county in Heilongjiang province. Because KD occurs only in particular areas in China, it is classified as an endemic disease in China. Nationwide, KD has occurred in 2953 townships in 327 counties in 16 provinces from the northeast to the southwest, a wide zone. These townships, counties, or provinces were delimitated as endemic areas of KD [1]. Although the etiology of KD is not fully understood, it has been recognized by most researchers that KD is strongly associated with selenium deficiency [2]. This theory is based on evidence that the soil in the endemic areas was generally selenium deficient, and the grains grown in the regions were selenium deficient as well. The levels of blood and hair selenium, the activity of serum glutathione peroxidase (GPx), and the antioxidative capacity of the residents living in the endemic areas were low [3–5]. Supplementing selenium to the residents in endemic areas demonstrated a significant reduction in KD incidence in the 1970s through the early 1980s [6]. Clinically, KD patients are divided into four categories based on the onset of attack, clinical features, and heart function [7]. These categories are acute, subacute, chronic, and latent. The typical clinical presentations of KD patients include acute heart failure, congestive heart failure and cardiac arrhythmia. Acute KD patients typically present with cardiogenic shock or acute heart failure and may have cardiomegaly. The onset of sub-acute KD patients is slower than that of acute KD. The patients may develop congestive heart failure in approximately one week. Some patients may also develop cardiogenic shock. Subacute KD patients are often children aged 3–7 years. The symptoms may be similar to those of acute KD patients. Cardiomegaly is common with the heart significantly enlarged. The onset of chronic KD patients takes much longer. Patients present with chronic heart failure, cardiomegaly, dilated cardiac chambers and thinning of the heart walls. Chronic KD is further classified into Chronic II, Chronic III, and Chronic IV according to the

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[2] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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NYHA Functional Classification classes II, III, and IV respectively. Following the late 1980s, we frequently saw patients who experienced no obvious onset of the disease. When they presented to doctors they already became typical cases of chronic KD. We called such cases as natural chronic KD. The onset of the latent KD is subtle with few signs and symptoms and patients have reasonably good heart function (NYHA class I). However, ventricular extrasystole and right bundle branch block or ST–T changes are common. Cardiomegaly is not seen. The cases of latent KD are found only in surveys. In pathology, the typical findings are myocardial degeneration, necrosis, and fibrosis. Chronic KD, some subacute and acute KD patients have cardiomegaly [7,8]. The endemic areas of KD are all rural, and many of them are remote and mountainous, places where people are the most socioeconomically disadvantaged in terms of housing, income, education, transportation, and access to and utilization of health services. KD patients are typically among the poorest of people. This leads to a vicious circle of poverty and illness. KD is a heavy burden to and restricts the economy development of the local communities and health systems of the KD endemic areas.

The national KD surveillance started in 1990. Except for the Xizang Autonomous Region, all the other 15 provinces have fully or partially participated in KD surveillance programs, which used the sentinel method due to limited funding. Before 2008, no national prevalence study of KD with probability sampling had been conducted. The results of the surveillance in recent years (2004–2007) indicated that the national detection rates for chronic KD patients and latent KD patients were approximately 0.6% and 2.85%–4.2%, respectively, at the sentinel sites [9–12]. Sentinel surveillance played an important role in assessing the prevalence status of KD in China. However, data from sentinel surveillance must be interpreted with caution; as such, the data collected were unable to contribute to the generation of national KD prevalence rates and estimated numbers of KD patients [13]. A nationwide cross-sectional study of KD prevalence was carried out in 2008 in order to obtain the national KD prevalence rates and estimated numbers of KD patients. This is extremely important for providing evidence-based technical support toward modifying the policy and strategy, as well as allocating health resources to KD prevention and control [14,15].

2. Methods

2.1. Study design

This was a prevalence study (cross-sectional study) using probability proportional to population size (PPS) randomized multistage cluster sampling. Based on the population, the number of endemic counties and townships in the 15 provinces excluding the Xizang Autonomous Region, the sampling processes were three-stage sampling for 10 provinces, two-stage sampling for 4 provinces, and one-stage sampling for 1 province. The number of survey sites was proportional to the population in the endemic areas in the provinces. One survey site was normally one village. To ensure the quality of sampling and representation of the population, the response rate was required to be higher than 80%, or not less than 500 people must be surveyed at each site.

2.2. Source of data

This project was part of the Endemic Disease Prevention and Control Program of the Public Health Programs of the Central Government. The fieldwork for this program was carried out in April to October 2008. The data on the national rural population in 2007 was purchased from the library of the China Population and Development Research Centre. The national rural population at township level in the KD endemic areas was reported by the Centers for Disease Control and Prevention of the KD endemic provinces in 2006.

2.3. Study scope

The study was conducted at 178 surveillance sites (villages) in 178 townships located in 124 counties in 15 KD endemic provinces (Chongqing, Gansu, Guizhou, Hebei, Heilongjiang, Henan, Hubei, Jilin, Liaoning, Inner Mongolia, Shandong, Shanxi, Shaanxi, Sichuan, Yunnan). The Xizang Autonomous Region was the only KD endemic province that was not included. This was because the endemic area in the Xizang Autonomous Region is very small (1 township) and accounts for only 0.034% (1/2953) nationally.

2.4. Subjects surveyed

The subjects were residents of the sampled survey sites who have been living in the endemic areas for 6 months or more in the past 12 months.

The subjects underwent medical examination, electrocardiograms (ECG) and echocardiography. The suspected KD patients, who had abnormal ECG results, were also examined using chest X-ray. Confirmation of KD diagnosis was based on the Criteria for Diagnosis of Keshan Disease (GB 17021–1997) [7].

2.5. Definition of Keshan disease

Based on the onset, clinical features, heart function, or pathological findings, the cases of KD are defined and classified into four categories as follows:

Acute KD: the onset is fast. Patients present acute heart failure and may have cardiomegaly. Myocardial necrosis is severe. Fibrosis is seldom.

Subacute KD: the onset is not as fast as that of acute KD, and patients may have congestive heart failure in about one week. Some patients may also have cardiac shock. The symptoms may be similar to those of the attack in acute KD patients. Cardiomegaly is common and the hearts dilate significantly, but myocardial degeneration and necrosis are not as severe and widespread as those in acute KD. Myocardial fibrosis is scattered.

Chronic KD: the onset is slow. The patients present chronic heart failure and dilated chambers of the hearts; the heart walls become thinner than normal, and there is widespread myocardial fibrosis. Chronic KD is further classified into Chronic II, Chronic III, and Chronic IV based on the New York Heart Association (NYHA) Functional Classification classes II, III, and IV, respectively. After the late 1980s, we often saw patients who did not have an obvious onset, and when they came to see a doctor, they were already typical cases of chronic KD. Such chronic KD patients are referred to as natural chronic KD cases.

Latent KD: the onset is disguised, and the patients have reasonably good heart function (NYHA class I). Ventricular extrasystole and right bundle branch block or ST–T change are common. Cardiomegaly is not observed.

2.6. Food selenium

At each survey site, 10 staple food samples were collected from 10 families, with 2 food samples in each direction (east, west, south, north, and center) of the site and 1 sample of 50 g from each family. At each site, only one kind of food sample (rice, wheat flour, or corn) was collected. The food selenium concentrations were measured with the fluorometric method and hydride atomic fluorescence spectrometry.

2.7. Questionnaire

Using a pre-designed questionnaire, we surveyed the subjects for sex, age, address, number of people in the family, annual family income, KD history, etc.

2.8. Sample size

The sample size for the estimation of the prevalence of KD is based on simple randomized sampling. The formula for calculating the sample size is:

$$n = \frac{\mu^2_{\alpha/2}\pi(1-\pi)}{\delta^2}$$

Where δ is the sampling error (and was given as 10% π), and μ was given as 1.96 at a confidence level of 95%. Based on the past surveillance data, π was at 0.6%.

The sample size was 63,642. Since a complicated multistage sampling method was used, the design effect was given as 1.5; thus, the calculated sample size was 95,463. The number of subjects actually surveyed was 101,127, which was more than the required number.

2.9. Statistical analysis

SPSS 13.0 for Windows was used to analyze the data. Standard statistical tables and graphs were used to describe the characteristics of the surveyed subjects.