Title: Can the accurate epidemiological study help to search the etiology of Kawasaki disease?

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Authors: Ji Whan Han, M.D., Ph.D.

Affiliation: Department of Pediatrics, Yeouido St. Mary’s Hospital, The Catholic University of Korea, Seoul, Korea

Correspondence

Ji Whan Han, M.D., Ph.D.
Department of Pediatrics,
Yeouido St. Mary’s Hospital, The Catholic University of Korea
10, 63-ro, Yeongdeungpo-gu, Seoul 07345, Korea

Phone: +82-2-3779-1034, Fax: +82-2-783-2589

E-mail: han59@catholic.ac.kr, hanji59@gmail.com

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The first patient with Kawasaki disease (KD) was discovered by Dr. Tomisaku Kawasaki in 1961. The data of fifty patients with KD were collected and published in a Japanese journal Arerugi and American journal Pediatrics by him in 1967 and 1974, respectively. After that, many Japanese and North American pediatricians could recognize KD well.

We still do not know the etiology of KD despite many trials to find out the etiology of KD. Epidemiological studies of a disease can give us new understanding or insight on pathophysiology or risk factors of the disease. The Japanese nationwide epidemiological surveys on KD have been performed biennially, and more than 300,000 patients who suffered from KD when they were young children have been registered to the Japanese Department of Health, Labour and Welfare since 1970. Whereas nationwide epidemiological surveys on KD have been performed triennially in South Korea and Taiwan since 1994 and 1996, respectively.

The most useful method to know the epidemiology of KD is the nationwide survey with well-organized questionnaire like the one used in South Korea and Japan. It can provide us with incidence rates, laboratory findings, coronary artery complications and others. Therefore, we can possibly guess the pathophysiology and risk factors of KD by using these data. Two most important things for getting true data from nationwide surveys are the exact diagnosis of KD and active responses to the surveys by pediatricians who care patients with KD. However, Kawasaki disease can be erroneously diagnosed by health-care providers (general practitioners and pediatricians) and parents of the patients with KD in many countries, including South Korea. Over- and under-diagnosis of KD can significantly influence the accuracy of data of epidemiological surveys on KD. Accurate epidemiological surveys on KD are necessary worldwide for better understanding and proper management of KD.
In South Korea and Taiwan, the National Health Insurance Service (NHIS) data are utilized for epidemiological surveys on KD. The strong point is that NHIS programs of South Korea and Taiwan cover more than 99% of the population due to government’s compulsory policy. The weak point is that NHIS data can be inaccurate. For instance, the number of patients with KD who did not receive intravenous immunoglobulin could be excluded from NHIS data. In United States (US), the passive national surveillance system reports to the Center for Disease Control and Prevention, and the inpatient database of children and nationwide inpatient samples have been used for the epidemiological surveys since mid-1970s.

The incidence of KD is much higher in Northeast Asia than in North America and Europe and it is increasing steadily. The latest incidences of KD were 308 in Japan (2014), 194.7 in South Korea (2014), 111.6 in Beijing, 71.9 in Shanghai (2014) and 82.8 per 100,000 less than 5-year-old children in Taiwan (2010). In North America, the incidences of KD were 19.6 in Canada (2014) and 19.1 per 100,000 less than 5-year-old children in US (2015). Interestingly, outside Northeast Asian countries, the incidence of KD has not been changed significantly since 1973. It might be due to omissions in diagnosing or reporting patients with KD. In North America and Europe, the main ethnic group of the patients with KD is Asian. In Hawaii, the incidence of KD in Japanese Americans is as high as Japan. These data indicate that genetic susceptibility is closely related to the occurrence of KD.

The guideline for the diagnosis of KD has been revised since the first Japanese guideline was published in 1984. The American Heart Association’s guideline in 2017 newly recommended that KD can be diagnosed in the presence of 4 days of fever together with at least 4 other principal clinical features of KD, although experienced clinicians who have...
treated many patients with KD may establish the diagnosis with 3 days of fever in rare cases.\(^9\) These recommendations can empower the specialist to treat the patients with KD as soon as possible, and reducing coronary artery complications.

Two interesting findings from the epidemiological surveys on KD are seasonal peaks of incidence and geographical outbreak tendencies that imply that some infectious agents may stimulate the immune system and induce KD in susceptible patients.\(^9\) The meticulous surveillance for the patients with KD by health care providers can make quick diagnosis and treatment of KD, coronary artery complications, such as giant aneurysms, and death.\(^6\)

The important factors for collecting exact epidemiological data are definite diagnosis, precise number of patients with KD, and active participation of clinicians in epidemiological surveys. Among the tools of nationwide surveys on KD, the data from questionnaire are more accurate than NHIS data. In conclusion, the combination of nationwide epidemiological surveys and use of NHIS data on KD will efficiently achieve the true epidemiological study of KD, that would help to search the etiology of KD.
References


