Brief Report

Epidemiological Survey of Kawasaki Disease in Sichuan Province of China

by Xiao-hui Li, Xiao-jing Li, Hui Li, Ming Xu, and Ming Zhou
Chengdu Children’s Hospital, Chengdu, Sichuan, China

Summary

Objectives: To investigate the incidence and epidemiological characteristics of Kawasaki Disease (KD) in Sichuan province of China.

Methods: The questionnaire and diagnostic guideline for KD provided by Japan Kawasaki Disease Research Center (JKDRC) were used for the questionnaire investigation in pediatric departments of all hospitals in Sichuan province for data of KD diagnosed in their hospitals from 1 January 1997 to 31 December 2001.

Results: Of the 212 hospitals investigated, 91.5% responded to the questionnaire investigation, with a total of 1811 cases of KD identified. The incidence per 100,000 children <5 years of age was 4.26 in 1997, 5.21 in 1998, 8.57 in 1999, 7.70 in 2000 and 9.81 in 2001, respectively. The average incidence throughout the 5 years was 7.06 per 100,000. The ratio of male to female was 1.62:1. The age distribution showed a peak near 1–2 years of age. Cardiac sequelae were seen in 17.0% of the patients. Only 66.2% patients with KD had been treated with intravenous immunoglobulin.

Conclusion: The incidence of KD in Sichuan province was lower than that reported in Japan and Beijing, higher than that in Guangdong, Jiangsu and Shanxi province of China.

Key words: Kawasaki disease, epidemiology, children, Sichuan.

Kawasaki disease (KD) that was also named as mucocutaneous lymph node syndrome was first reported by Kawasaki of Japan in 1967. Now, it has already been distributed in area of different geographic region and climate all over the world, being a common disease mainly seen in children with generalized non-specific vasculitis, especially damaging the coronary artery and has been regarded as one of the major acquired cardiopathy in childhood [1].

During the recent three decades, the Japan Kawasaki Disease Research Center (JKDRC) has carried out 16 epidemiological surveys in Japan. By year 2000, the incidence was 140.3 per 100,000 children in those aged under 4 years [2]. In America, the incidence was 6–9 per 100,000 children aged under 5 years [3]. In China, the first investigation on the incidence of KD in hospitalized children was performed by Liang [4] and so far, there is no nationwide KD epidemiological survey carried out in China.

In year 2002, cooperating with JKDRC, we carried out an epidemiological survey in hospitals of Sichuan province, to learn about the incidence of KD in different districts, climate and ethnics, and investigate its epidemiological characteristics.

Subjects and Methods

Subjects
Patients with KD hospitalized in pediatric departments of all the hospitals in Sichuan province from 1 January 1997 to 31 December 2001.

Methods
According to the method used by national survey on childhood KD in Japan, a questionnaire investigation on all hospitals with pediatric department in Sichuan province was carried out with the questionnaire form and diagnostic criteria for KD provided by JKDRC.

The questionnaire included the following items: patient name, gender, age, date of disease onset, date of diagnosis, date of presentation, clinical symptoms, ultrasonic cardiogram findings, laboratory tests, therapy and prognosis.
Pediatricians who had taken part in the present investigation were asked to review the patients’ hospital records and take note of data of diagnosed KD patients or suspected KD patients during the 5 years from 1 January 1997 to 31 December 2001. Specialized interview by investigators were carried out to learn about the status, offer guide for those working with the questionnaire to ensure accuracy of the recovered questionnaire and sending it back in time. All the recovered questionnaire were summarized and analyzed.

**Diagnostic criteria**

According to the fourth modified version of KD diagnostic criteria by JKDRC, typical patient should at least have five of the following six cardinal symptoms: (i) Fever persisting for more than 5 days. (ii) Changes of peripheral parts of the extremities. (iii) Polymorphous exanthema. (iv) Bilateral conjunctival congestion. (v) Changes of lips and oral mucosa. (vi) Acute non-purulent cervical lymphadenopathy. Diagnostic criteria for atypical patients were: the patient has four of the six cardinal symptoms plus coronary artery lesion(s) confirmed by two-dimensional echocardiography (2-DE) or coronary angiography.

**Statistical analysis**

Parametric data were expressed as mean ± SD, categorical data were compared with χ² test. Ratio of patient number/population under 5 years of age of the same year was used as incidence of KD.

**Results**

**Recovering of the questionnaire forms**

Of the 212 hospitals, 194 (91.5%) responded to our questionnaire investigation, with a recovery rate of 91.5%. In 112 of the 193 hospitals, more than one case of KD was identified. A total of 1811 KD patients were reported throughout the province. 300 cases were excluded, of which, 135 had only four cardinal symptoms and 2-DE was not performed, the remaining 165 patients had less than four of the six cardinal symptoms. Thus, there were 1511 eligible KD patients with an eligible rate of 83.4%.

**Epidemiological characteristics**

In the 1511 KD that met the diagnostic criteria of KD during 1997–2001, there were 943 males and 568 females with a male to female ratio of 1.66 : 1. There was an increment of incidence year by year; Table 1 shows the incidence trend. Most of the patients were 1 to 5-years old, 62.0% were under 3 years of age and 88.2% were under 5 years of age. Seasons that most KD happened in were during March through May and least in September. A total of 961 patients were from urban area and 550 from the countryside, with a ratio of 1.75 : 1. The KD identified mostly occurred in the big cities, while only three cases were reported in the very cold and remote area. In the cities, KD was mainly diagnosed in large general hospitals and children’s hospital.

**Diagnosis, therapy and outcome**

According to the diagnostic criteria of KD, 666 cases (44.1%) had all six cardinal symptoms, 768 cases (50.8%) had five of the six cardinal symptoms and 77 (5.1%) had four of the six cardinal symptoms (Table 2). 2-DE findings showed that 257 (17.0%) patients had coronary artery lesions (CAL). In which, 111 (7.6%) were bilateral. The proportion of patients with coronary artery lesions was higher in males than in females.

A total of 1072 of the KD patients received intravenous immunoglobulin (IVIG) therapy, accounting for 70.9% of the total KD reported. In which, 417 cases (38.9%) received the dose of 1 g kg⁻¹ d⁻¹, 98 cases (9.1%) received 2 g kg⁻¹ d⁻¹, 335 cases (31.2%) received 400–500 mg kg⁻¹ d⁻¹ x 3 days, other therapeutic regime was used in 222 cases (20.7%). Aspirin alone was used in 439 cases (29.1%).

Results of the present study also indicated that there exists association between platelet
count and coronary artery lesions, when platelet count were $300-400 \times 10^9/l$, $400-500 \times 10^9/l$, $500-600 \times 10^9/l$ and $>600 \times 10^9/l$, the proportion of coronary artery lesions was 16.3, 18.0, 20.3 and 26.6%, respectively.

In the present survey, only 3 of the 1511 patients (0.20%) died; two of them died from myocardial infarction, one from heart failure.

**Discussion**

Sichuan is the largest province in west China with a population of 83,290,935 in year 2000. A total of 212 hospitals of Sichuan province participated in the present questionnaire survey. The response rate to our questionnaire was 91.5%. 1511 cases met the diagnostic criteria. The incidence per 100,000 children <5 years of age from year 1997 through 2001 was 7.06, 22.9, 5.93, 2.34, and 2.53, respectively. The ratio of male to female was 1.66:1. The peak of onset of KD was 1–2 years of age. Coronary artery damages were seen in 17.0% of the patients. A 70.9% of patients with KD had been treated with IVIG. Results of the present investigation generally reflect the KD incidence in Sichuan district.

A total of 2627 hospitals took part in the 14th national KD epidemiological survey in Japan during 1995–96. 1777 hospitals responded to the questionnaire investigation, the respond rate to the questionnaire was 67.6%. KD identified in 1995 and 1996 was 6107 and 6424 cases, respectively, incidence of those under 5 years of age was 22.9/100,000 and 108.0/100,000, respectively, ratio of male to female was 1.37:1, the peak of onset seen at about 6 months of age. Twelve percent had complicated cardiac complications.

Comparing with the epidemiological data of Japan, the incidence in Sichuan province has a trend of increment year by year, however, significantly lower than that of Japan. The reasons probably could be that all the suspected KD patients received 2-DE examination in Japan, thus, more patients entered into statistical analysis; however, in the present survey, many suspected KD patients had not received examination of 2-DE and thus, more patients were excluded.

In the recent years, under the support of Professor Yangawa H. of Japan and Kawasaki T. of JKDRC and under the guidance of Dr Zhang Tuo Hong, regional epidemiological investigations had been carried out in Shanxi, Jiangsu, Guangdong and Beijing of China.

Comparing with the KD epidemiological investigation carried out in China, the incidence of KD in Sichuan province is lower than that of Beijing, but higher than that of Guangdong, Shanxi and Jiangxu province, probably due to the different recovering rate to the questionnaire, and the proportion of 2-DE performed for those suspected of having KD. The present investigation also revealed that the KD patients were relatively concentrated in the large general hospitals and children’s hospital in the large and middle size cities, such as Chengdu, Luzhou and Nancong and few in the very cold district, such as Ganzhi and Aba canton, demonstrating there is geographic distribution variation. The results from other provinces also showed significant district variation, the 5 years’ average incidence in Beijing was 22.9/100,000, the highest incidence in Guangdong province was seen in Shengzeng and Zhuhai, reaching 18.73/100,000 in Shengzeng, next to it was 9.87/100,000 of Guangzhou, while only 1.23/100,000 in the north part of Guangdong province. In Jiangsu, more KD was seen in Nanjing and Xi’an. The reason could be: (i) Many patients were referred to the large general hospitals and children’s hospitals in large and middle size cities; (ii) related to the poor living condition, geographic environment and diet habit in the remote area.

Seventeen percent of the KD patients in Sichuan province had complicated cardiac lesions, which was lower than that in Guangdong and Beijing, higher than that in Jiangsu, and similar to that in Shanxi province. The present investigation showed that the proportion of coronary damage diagnosed at $\geq 7$ days was 11.2%, while that at $>7$ days was 18.5%, suggesting that early diagnosis and early intervention had important impact on the development of coronary artery damages.

### Table 3

Comparing with other province of China in KD epidemiological investigation

<table>
<thead>
<tr>
<th>Province</th>
<th>Year</th>
<th>No of cases</th>
<th>Incidence cases/100,000</th>
<th>CAL(%) (no of cases)</th>
<th>Recovering rate of questionnaire (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sichuan</td>
<td>1997–2001</td>
<td>1511</td>
<td>7.06</td>
<td>17.0 (257)</td>
<td>91.5</td>
</tr>
<tr>
<td>Beijing</td>
<td>1995–99</td>
<td>710</td>
<td>22.9</td>
<td>21.5</td>
<td>95</td>
</tr>
<tr>
<td>Guangdong</td>
<td>1995–99</td>
<td>457</td>
<td>5.93</td>
<td>32.5 (113)</td>
<td>71.2</td>
</tr>
<tr>
<td>Shanxi</td>
<td>1993–97</td>
<td>376</td>
<td>2.34</td>
<td>18.6 (70)</td>
<td>70</td>
</tr>
<tr>
<td>Jiangsu</td>
<td>1993–97</td>
<td>509</td>
<td>2.53</td>
<td>13.6 (69)</td>
<td>49.7</td>
</tr>
</tbody>
</table>
A total of 1072 of the KD patients received IVIG therapy, accounting for 70.9% of the total KD identified. In which, 417 cases (38.9%) received the dose of $1\, \text{g/kg} \cdot \text{d}^{-1}$, 98 cases (9.1%) received $2\, \text{g/kg} \cdot \text{d}^{-1}$, 335 cases (31.2%) received $400-500\, \text{mg/kg} \cdot \text{d}^{-1} \times 3\, \text{days}$, other therapeutic regime was used in 222 cases (20.7%). Aspirin alone was used in 439 cases (29.1%). Results of investigation in Beijing [5] showed that cardiac examination findings were available in 701 cases, accounting for 98.7% of their total patients, 253 of them (35.9%) had cardiovascular complications. 614 cases received IVIG therapy, accounting for 86.5% of the total KD patients, of which 93% received the dose of $400\, \text{mg/kg} \cdot \text{d}^{-1}$ for 3 days, 5.4% was treated with the dose of $1\, \text{g/kg} \cdot \text{d}^{-1}$ for 2 days and 1.6% with $2\, \text{g/kg} \cdot \text{d}^{-1}$ for 1 day. The data from Guangdong [6] showed that 2-DE was performed in 64.8% of the patients, and coronary artery abnormalities were discovered in 32.5% of them; no data related to IVIG therapy were available. Difference in the proportion of coronary artery damage may be related to the date of diagnosis and therapy, and the therapeutic regime.

Results of the present investigation also revealed that the higher the platelet count was, the more coronary artery damage would be. The data from Guangdong [6] also showed that 72.3% of their KD patients had thrombocytosis and only 1.7% had thrombocytopenia, suggesting that there exists certain association between platelet count and the development of coronary artery damages.

The mortality of KD in Sichuan province was 0.20%, similar to that in Guangdong and Jiangsu, higher than that in Beijing (without death) and lower than the 1% mortality of Shangxi, demonstrating the good outcome of KD.

References