Original article

Prevalence of Kaschin-Beck disease among Tibetan children in Aba Tibetan and Qiang Autonomous Prefecture: a 3-year epidemiological survey

Li-Yan Sun, Li-Jun Yuan, Ying Fu, Jia-Yun Deng, Li-Hua Wang
Harbin, China

Background: **Kaschin-Beck disease (KBD), a special type of osteoarthritis, is a disabling degenerative disease and it can cause severe dysarthrosis of joints. This study was undertaken to investigate the prevalence of KBD among Tibetan children in the Aba Tibetan and Qiang Autonomous Prefecture in Sichuan Province and to provide evidence for KBD control in the western regions of China.**

Methods: **Eleven counties were selected as the monitoring regions and all Tibetan children aged 6-13 years were selected as the study subjects. A questionnaire survey and clinical and radiological examinations (right hand and wrist) were performed. KBD was diagnosed according to the Chinese Radiological Criteria of Kaschin-Beck Disease Diagnosis (GB16003-1995).**

Results: **X-ray analysis showed that all counties belonged to controlled endemic areas, and 4 of them were confirmed as active endemic areas for KBD. The overall detection rate of KBD in the Aba Tibetan and Qiang Autonomous Prefecture was 2.09% in 2007, 2.66% in 2008, and 1.20% in 2009. The majority of pediatric patients were found in Jinchuan and Markang counties.**

Conclusions: **Although the prevalence of KBD showed a decreasing trend in the Aba Tibetan and Qiang Autonomous Prefecture, some new pediatric cases are still emerging. Therefore, comprehensive measures should be taken to prevent the occurrence of the disease in children, and an effective preventive program should be set up in the prefecture.**

World J Pediatr 2012;8(2):140-144

Key words: **epidemiological survey; incidence; Kaschin-Beck disease; pediatric; prevalence**

Introduction

Kaschin-Beck disease (KBD) is a chronic, endemic osteoarthritic disease.[1] Its primary pathological change is selective coagulative necrosis of hypertrophic chondrocytes at the base of the articular and growing cartilage plate. These changes develop constantly and cause severe dysarthrosis on the joints. KBD mainly occurs in children of 5-15 years old.[2,3] It is mostly prevalent in the western regions of China, especially in Sichuan and Qinghai provinces and Tibet autonomous regions. Despite various preventive and control measures, new cases still have been emerging in some distant rural areas of China, especially among some ethnic minority groups.

The etiology of KBD remains unclear. Some researchers believe that T-2 toxin is the main cause of KBD.[4,5] T-2 toxin is one of the most toxic of trichothecene mycotoxins that are produced especially by the genus Fusarium in grains.[6] Besides T-2 toxin, selenium deficiency and high concentrations of organic matter in drinking water are also considered as important risk factors for KBD.[7,8] A recent published study has pointed out that environmental conditions, such as microtrauma and cold, can make KBD worse, although they do not originally cause KBD.[9]

We performed a 3-year cross-sectional study to supervise the prevalence of KBD among Tibetan children in the Aba Tibetan and Qiang Autonomous Prefecture in Sichuan Province, and we also investigated the relative risk factors for KBD. In this

Author Affiliations: Harbin Medical University, Center for Endemic Disease Control, China CDC, Harbin, China (Sun LY, Yuan LJ, Fu Y, Wang LH); Sichuan Provincial Center for Disease Control and Prevention, Chengdu, China (Deng JY)

Corresponding Author: Li-Hua Wang, Harbin Medical University, Center for Endemic Disease Control, China CDC, 157# Baojian Road, Nan'gang District, Harbin, China, 150081 (Tel: 86-451-87503095; Fax: 86-451-87503115; Email: lhwanganna@126.com)

doi: 10.1007/s12519-012-0351-7

paper, we try to provide some information about KBD in Tibetan children aged 6-13 years during 2007-2009: (1) the prevalence rates and incidence rates in different years, and dynamic trends of pediatric KBD in the Aba Tibetan and Qiang Autonomous Prefecture; (2) the grading of pediatric patients in different monitoring regions; and (3) possible causes for different prevalences between regions and years.

Methods

Investigated regions and populations

The investigation was launched in 2007 and ended in 2009. There were 13 counties in the Aba Tibetan and Qiang Autonomous Prefecture, of which 11 were chosen as monitoring regions, including Aba, Rangtang, Ruorgai, Jinchuan, Hongyuan, Markang, Songpan, Jiuzhaigou, Heishui, Maoxian and Xiaojin. Wenchuan county and Li county were excluded because they were greatly affected by the Wenchuan Earthquake in 2008.

There are many ethnic groups in the Aba Tibetan and Qiang Autonomous Prefecture, including Tibetan, Qiang, Han and Hui. The Tibetan population accounted for 54.5% of the whole prefecture population, thus we chose the Tibetan population in the Aba Tibetan and Qiang Autonomous Prefecture as the subjects of our study. From 2007 to 2009, we investigated all Tibetan children aged 6-13 years who were living in the above regions.

Methods

Radiological and clinical examinations of the children were performed every year from 2007 to 2009. Each child was examined by a physician and was required to fill in a questionnaire accordingly. We examined 3801 children in 2007, 3802 in 2008, and 3247 in 2009. All the data and important clinical signs and symptoms, including joint thickening, joint pain, joint deformity, muscle weakness, limitation of motion, and muscle atrophy were recorded in a diagram.

After the completion of the examinations, we selected our eligible subjects. The excluded were children with other joint diseases such as joint inflammation, metabolic bone diseases, neoplasia, osteoporosis, and osteomalacia as well as those who refused to join the survey. To target eligible children, technologists from the Center for Disease Prevention and Control in the Aba Tibetan and Qiang Autonomous Prefecture performed orthophoric radiography of the right hands and wrists of all children. There were 3165 children in 2007, 2521 in 2008, and 2917 in 2009 who completed the examination.

According to the Chinese Radiological Criteria of Kaschin-Beck Disease Diagnosis (GB16003-1995), X-ray manifestations were graded into five stages: stage I, metaphyseal changes; stage II, diaphyseal changes; stage III, metaphyseal and diaphyseal changes; stage IV, metaphyseal and epiphyseal changes; stage V, diaphyseal, metaphyseal and epiphyseal changes.

According to the Chinese Determinative and Hierarchical Criteria of Kaschin-Beck Disease Areas (GB16395-1996), endemic areas were also classified into five types based on prevalence: I: mild area: an X-ray detection rate of <10% in children aged 7-12 years; II: moderate area: an X-ray detection rate of 10%-30% in children aged 7-12 years; III: severe area: an X-ray detection rate of >30% in children aged 7-12 years; IV: new area: no patient history and all patients aged <20 years; V: controlled and historical area: an X-ray detection rate of <5% in children aged 7-12 years and a detection rate of <3% for diaphysis, but this was confirmed previously as an endemic area.

Data analysis

For the diagnosis of KBD, the accuracy of clinical examination is usually lower than that of X-ray examination. Therefore, the X-ray positive rate was used to indicate the prevalence of KBD in endemic areas in this study. We used the percentage of children with metaphyseal changes, namely children in stage I, to represent the incidence rate of pediatric KBD, because children with metaphyseal changes can be regarded as new cases.

Results

Grading of pediatric patients with KBD

Among 3165 children examined in 2007, 66 were confirmed with KBD, with a detection rate of 2.09%. According to the criteria, 53 patients were in stage I, 10 were in stage II, 2 were in stage III, and 1 was in stage V. The constituent ratio of patients in the different stages was 80.30%, 15.15%, 3.03% and 1.52%, respectively. Patients in stage I were mainly seen in Hongyuan and Rangtang counties, and patients in stage II were found in Jinchuan county.

In 2008, 67 (2.66%) of 2521 children were detected with KBD. Among the 67 patients, 24 (35.82%) were in stage I, 42 (62.69%) were in stage II, and 1 (1.49%) was in stage III. In Jinchuan county, the number of stage I patients increased compared to that in 2007. Stage II patients were mainly detected in Jinchuan and Markang counties.

Among 2917 children investigated in 2009, 35 children (1.20%) were diagnosed with KBD. Of the 35 patients, 19 (54.29%) were in stage I, and 16 in stage II. Apart from Jinchuan county, stage I patients were also

detected in Rangtang county. Stage II patients were still found in Jinchuan county. The hierarchical distribution and the stage of pediatric KBD in different years are shown in the Fig. and Table 1.

Prevalence and incidence of pediatric KBD in each county

In 2007, the prevalence of pediatric KBD was predominant in Jinchuan county, followed by Rangtang and Hongyuan counties. And the highest incidence of pediatric KBD was seen in Rangtang county. In 2008, the maximum prevalence of KBD was observed in Markang county and the highest incidence of KBD in Jinchuan county, which made the whole situation totally different from that in 2007. Jinchuan county had the highest prevalence rate of KBD again in 2009. Surprisingly, the maximum incidence rate was noted in Xiaojin county in 2009. The detailed information from the monitoring regions in different years is shown in Table 2.

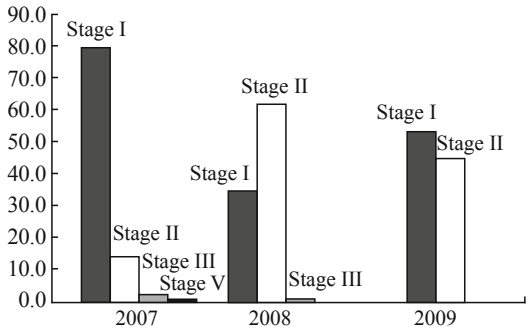

Fig. Constituent ratio of patients with pediatric Kaschin-Beck disease in different years.

Table 1. Stages of pediatric patients with Kaschin-Beck disease from 2007 to 2009

Stages	2007	2008	2009
I	53	24	19
II	10	42	16
III	2	1	0
IV	0	0	0
V	1	0	0
Total	66	67	35

Prevalence of KBD in children

The data of our investigation showed that the prevalence of KBD in children in the Aba Tibetan and Qiang Autonomous Prefecture was higher in 2008 and lower in 2009. Since the annual X-ray detection rate was <5%, the Aba Tibetan and Qiang Autonomous Prefecture was regarded as a controlled endemic area of KBD.

Discussion

The detection rate of KBD reflects its prevalence, while the detection rate in the metaphysis and diaphysis reflects the activity of causative agents. In general, there are active changes in the metaphysis, which can improve, disappear or aggravate over the course of a year. Changes of the metaphysis usually indicate that the cartilage has been damaged within a year, and causative agents remain active. Therefore, patients with these changes can be regarded as new cases. Changes in the diaphysis are relatively stable; they appear later, and cannot be cured. They indicate a long-term cartilage damage (>1 year), and that even when causative agents are stable or disappear, changes in the diaphysis will not disappear accordingly. Such patients are considered as reflactable patients. Those with changes in both metaphysis and diaphysis are also regarded as old cases, and they are under the influence of causative agents all the time.

According to the number and influence of causative agents, endemic areas can be distinguished as active,

Table 2. Prevalence and incidence rates of pediatric Kaschin-Beck disease (KBD) from 2007 to 2009

County	Subjects			Patients with KBD			Prevalence rate (%)			Incidence rate (%)		
	2007	2008	2009	2007	2008	2009	2007	2008	2009	2007	2008	2009
Aba	299	400	402	1	8	3	0.33	2.00	0.75	0.33	0.25	0.75
Rangtang	486	400	468	17	3	7	3.50	0.75	1.50	3.50	0.75	1.28
Ruorgai	519	300	300	9	0	3	1.73	0.00	1.00	1.73	0.00	0.33
Jinchuan	325	223	379	15	19	10	4.62	8.52	2.64	1.85	4.48	0.53
Hongyuan	560	250	250	18	6	2	3.21	2.40	0.80	3.21	1.60	0.40
Songpan	467	250	252	5	3	1	1.07	1.20	0.40	0.21	0.40	0.00
Heishui	101	32	204	1	0	0	0.99	0.00	0.00	0.99	0.00	0.00
Jiuzhaigou	216	250	251	0	4	3	0.00	1.60	1.20	0.00	1.20	0.40
Xiaojin	18	50	50	0	0	1	0.00	0.00	2.00	0.00	0.00	2.00
Markang	95	259	261	0	24	5	0.00	9.26	1.92	0.00	0.76	1.53
Mao	299	107	100	0	0	0	0.00	0.00	0.00	0.00	0.00	0.00
Total	3165	2521	2917	66	67	35	2.09	2.66	1.20	1.67	0.95	0.65

relatively stable, and stable areas. In the active areas, there are a large amount of causative agents with strong effects. Among the patients with X-ray changes, more than 50% of them demonstrate metaphyseal changes. With time, the active areas are likely to turn into the relatively stable areas when the effect of the causative agents is declined. In these areas, the detection rate is higher in the diaphysis than in the metaphysis. Similarly, relatively stable areas become the stable areas if the effect of the causative agents is kept to decline. In the stable areas, the proportion of patients with metaphyeal changes is less than 10%.[10]

In our 3-year cross-sectional study, the activity of causative agents and detection rates in the metaphysis and diaphysis varied greatly in different areas of the Aba Tibetan and Qiang Autonomous Prefecture. In Jinchuan county, although the detection rate of metaphyseal and diaphyseal changes was higher, causative agents were not active all the time. In 2008, Jinchuan county was classified as an active endemic area because the patients with metaphyseal changes accounted for 52.63% of the total number. However, in 2009, it became a relatively stable area with a diaphyseal detection rate higher than the metaphyseal detection rate. In Rangtang and Hongyuan counties, the proportion of patients with metaphyseal changes was higher than 50% all the time, and the causative agents of KBD were active in the study period.

Based on the prevalent features of KBD and the annual fluctuation in the activity of causative agents, Chinese researchers[5] have suspected that there is a special, affirmative biological causative agent in the environment, which has a decisive influence on the occurrence of KBD. This agent can induce biological changes in cartilage in a short time. The activity of this agent may increase quickly when the social and natural environment is suitable. As such the agent can cause a sharp increase in number of new KBD cases. In contrast, once the causative agent is removed, the disease turns to be stationary.[6,11] The other types of endemic diseases caused by geochemical factors do not show such features.

The present study showed a geographical distribution of KBD over the years. In Jinchuang and Markang counties with a higher prevalence of KBD, which are situated in Southwest Aba, this can be explained by factors leading to suspicious causative agents.

The first factor is the natural environment, which cannot be altered. Temperature and humidity may influence the incidence of KBD. Local temperature and humidity fit the growth and reproduction of Fusarium, which can contaminate grain. The large difference in temperature between day and night is conducive to T-2 toxin production,[12] which can cause food poisoning. Fusarium contaminates food itself and can produce T-2 toxin under the right circumstances. The second factor is the way that food is supplied, processed and stored. Fertile land and abundant sunshine make self-produced food sufficient for local residents. Therefore, the local farmers take self-produced wheat or barley as their staple food. Generally, they mill flour from wheat or barley every 6 months, and the flour is stored in large wooden cabinets. During the milling process, the generated heat turns the water in grain into steam in flour. If the flour is stored before adequate drying, when the temperature decreases, the steam in flour will gather and turn back into water. After a long time, when the temperature and humidity in the wooden cabinets reach the correct point, Fusarium begins to produce T-2 toxin. The final factor is the lower selenium level in residents' food and drink.[13,14]

According to the disease status in 2007 and 2008, our team took some preventive measures against potential causes of pediatric KBD. The measures included encouraging local residents to eat food from non-KBD areas, improving selenium level in children's nutrition, and moving residents to non-KBD areas. These might contribute to the sharp decrease of KBD prevalence in the Aba Tibetan and Qiang Autonomous Prefecture in 2009.

Epidemiological studies are usually not accurate enough because of insufficient or biased samples.[15] To avoid this problem, we examined all Tibetan children of 6-13 years old in our monitoring regions. However, we still have to take several limitations into consideration. We could not evaluate the occurrence rate of incorrect classifications because of technical misinterpretation of images. We even could not ignore the misdiagnosis of non-KBD cases. Although the criteria for KBD have been described clearly, some other types of pediatric osteoarthritis are misdiagnosed as KBD. In addition, we could not ignore the missing of some investigations especially in 2008 when the Earthquake happened in Sichuan Province.

KBD is difficult to deal with. Therefore, primary prevention is the most effective measure to reduce the incidence of KBD. Our future study is going to evaluate the effect of the preventive measures mentioned above.

In conclusion, in the monitoring counties of the Aba Tibetan and Qiang Autonomous Prefecture, the detection rate of KBD in children was less than 10%. All counties could be confirmed as mild or controlled endemic areas. For example, Hongyuan and Rangtang counties are considered controlled endemic areas, but the causative agents of KBD there are still active. Effective preventive and control strategies are necessary in these areas. Jinchuan and Markang counties are

relatively severe and active areas for KBD and need to be monitored persistently. In the rest counties the prevalence of KBD has been controlled but efforts should be made to prevent its recovery when major natural disasters such as floods or earthquakes take place.

Funding: This study was supported by a grant from the National Science and Technology Support Program (N2007BAI25B03).
Ethical approval: Not needed.
Competing interest: None declared.
Contributors: Wang LH is the guarantor and proposed the study. Sun LY collected the data and wrote the paper. Sun LY, Yuan LJ, Fu Y and Deng JY carried out the study.

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Received February 7, 2011
Accepted after revision July 1, 2011