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The arthropathic and functional impairment features of adult Kashin-Beck disease patients in Aba Tibetan area in China

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SUMMARY

Object: The purpose of the study was to analyze the features of arthropathic changes and functional impairments as well as the correlations between them for adult patients suffered with Kashin-Beck disease (KBD) in Aba Tibetan area of Sichuan Province, China.

Method: Nine hundred and eighty-nine adult KBD patients in Aba KBD prevalence area were investigated. The arthropathic changes including arthritic pain (evaluated by visual analog pain score (VAS)), deformity, limited range of joint motion (ROM), as well as daily living and working function were examined, evaluated and analyzed.

Results: Ninety-two percent of patients suffered with multiple affected joints in both upper and lower extremities. The most frequently affected joints were knee (86.1%) and hand (77.2%). The most painful joints were knee (VAS 7.1 ± 1.9) and elbow (VAS 6.8 ± 2.1). Joint deformities most frequently represented as enlargement of interphalangeal joints (93.2%). Limitation of ROM occurred most frequently in hand (76.7%) and elbow (38.4%). Multiple linear regression analysis revealed that only joint pain (regression coefficient: −0.504, 95% confidence interval (CI): −0.820–0.188, $P < 0.001$) and ROM (regression coefficient: 0.017, 95% CI: 0.011–0.024, $P < 0.001$) were independent risk factors affecting daily living and working function.

Conclusion: Most adult patients suffered with multiple affected joints in both upper and lower limbs. The elbow, hand and knee were the most frequently and severely affected joints. The pain and limited ROM were the independent risk factors of daily living and working function.

Introduction

Kashin-Beck disease (KBD) is a chronic and endemic disabling osteoarticular disease affecting the overall growth of a child/adolescent as well as more specifically affecting the joint cartilage of different peripheral joint causing pain, dysfunction and skeletal deformation[1,2]. KBD occurs in childhood and involves pathologic changes of metaphysis and epiphyseal plate, resulting in bony enlargement, deformity, pain and functional impairment of multiple joints. The disease often continues to progress, and the symptoms and signs become more severe in adulthood due to continuous damage to the joint cartilage. This disease is most prevalent in the western area of China, especially in Sichuan and Qinghai provinces and Tibet autonomous regions extending all the way to the Eastern Siberia, Russia, and a small part in Northern Korea[3,4]. The Aba Tibetan area of Sichuan province is an active endemic area of KBD in China with high morbidity, incidence and disability rate[5].

The clinical manifestations of KBD are due to growth retardation and multiple joints damage[3]. Joints of distal extremities such as knees, ankles, elbows, wrists and hands are most frequently affected[1,6]. Most of the KBD patients in Aba area suffered multiple arthropathic changes in major joints, and more than 70% patients had at least four affected joints causing decreased health status and quality of life[7–9].

Several studies have reported the clinical and dysfunctional features of adult KBD patients[5,7,10–12]. However, to our knowledge, there are no reports based on the data from large scale on-the-spot investigation in Aba Tibetan area of Sichuan province in China. This paper gathered the clinical data of our 3 years investigation of adult KBD patients in Aba area, and analyzed the features of their arthropathic changes and functional impairments, and tried to find the risk factors of daily living and working function of the patients.

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We believe these results could provide some theoretical basis and therapeutic targets for relieving symptoms and improving functional status of these patients.

Methods

Sample

From March 2009 to June 2011, local adult residents (above 18 years) who suffered with joint pain or/and enlargement in Rongmuda country, Gaduo country, Gangmuda country, Nanmuda country and Qiutang country in Rangtang County, and Mianchi country in Wenchuan County, Hexi country in Jinchuan County and Nanxin country in Mao County were recruited and investigated. The clinical diagnosis of KBD was made by orthopedists and physicians of the departments of orthopaedics and rheumatology of West China Hospital of Sichuan University, based on the criteria previously described[13]. Patients with tuberculosis of bones and joints, pyogenic arthritis, or severe deformity in limbs caused by trauma were excluded.

This investigation was a part of a key project in The Eleventh Five-Year National Science and Technology Pillar Program of People's Republic of China (2007BA125B04) and was approved by the ethical committee in West China Hospital of Sichuan University in Chengdu, China. All the participants were informed of our arrival following the administrative list and voluntarily recruited and organized by local government staffs in each village. This study was conducted in accordance with the World Medical Association Declaration of Helsinki (www.wma.net/en/30publications/10policies/b3/index.html). Each participant have signed a informed consent before any investigations.

The investigations were performed by survey teams consisted of two doctors and a local physician familiar with the Chinese and western medicine who worked as a translator. Before the each start of our investigations, a 1-day workshop was provided to the investigators and translators regarding proper use of the questionnaires and scales and physical examinations and how to communicate with the local patients with their dialect.

Arthralgia assessment

The visual analog pain score (VAS) was used to evaluate the pain in shoulder, elbow, wrist, hand, hip, knee, ankle joints of each patient. As previously described, VAS range from 0 (no pain) to 10 (severe pain)[14]. The total score of VAS was calculated for analysis of multiple linear regression.

Joints deformity

All the deformities of the joints were inspected and recorded. As previously reported, these deformities included enlargement of interphalangeal joint, flexion deformity of distal phalanx joint (DPJ), brachydactylia, wrist radial deviation, varus/valgus deformity of elbow, varus/valgus/flexion deformity of knee and enlargement of ankle[7]. The number of deformed joints of each patient was recorded for the latter analysis of multiple linear regression.

Rang of joint motion

The active range of joint motion (ROM) measurements were performed on shoulder (abduction and flexion), elbow (flexion and extension), wrist (dorsal extension and palmer flexion), hip (flexion, extension, abduction and external rotation), knee (flexion and extension), and ankle (flexion and extension) with a standard two-legged, transparent 20 cm goniometer using the “anatomical landmark” method to nearest 2°. Because of the complexity of measurements in hand joints, and harsh environmental conditions, we did not specifically measure the ROM of each small joint of the hands, instead, we checked whether the patient could make a clenched fist.

Normal joint range of motion was taken as a reference to determine whether there was a limited ROM in affected joint[13]. Any joint of bilateral shoulder, elbow, wrist, hand, hip, knee and ankle suffered with pain, deformity or limited ROM was considered as an affected joint.

Evaluation of daily activities

According to living and working habits and cultural characteristics of the local residents, we developed and validated a specific scoring system for evaluating daily living and working functional status of KBD patients in Aba Tibetan area, which named as function score for adult Tibetans with Kashin Beck Disease (FSAT-KBD)[15,16]. FSAT-KBD included 12 items, of which items of dressing, face washing, cooking, food taking, Ox dung picking up, heavy objects moving (>10 kg) were mainly focus on upper limb function, and items of cross-legged sitting, squatting, stand up from sitting position, ascending and descending a single-track wood ladder, walking distance and walking aids usage were mainly focus on lower limb function. Point values of 1 (able to complete easily) to 4 (unable to complete) were assigned to each item with minimum to maximum total score of 12–48. By using this scale, the function of upper and lower extremities and the overall function status could be reliably and accurately assessed[15].

Statistic method

Data were analyzed using SPSS version 22.0 (SPSS Inc., Chicago IL). Firstly, patient characteristics were analyzed. The numeric variables were compared by using Student's *t* test or One-way Analysis of Variance (ANOVA) followed by *post-hoc* test (Dunnett's test) for multiple comparisons. Correlation between variables were analyzed by using Spearman correlation. Multiple linear regression was used to analyze risk factors of daily living and working function of the patients for excluding confounders. For all tests, statistical significance was assumed for P values <0.05.

Results

Respondents' characteristics

989 KBD patients were received and completed the investigation, 364 were men (36.8%) and 625 were women (63.2%). The average age was 53.4 ± 14.8 years (19–90 years). The majority of them were Tibetans, accounting for 89.3%, the remaining were Qiang 93 (9.4%), Han 13 (1.3%). The average number of affected joints was 8.8 ± 2.4 (2–14), 5.4 ± 2.1 (2–8) in upper extremities, and 4.2 ± 1.7 (0–6) in lower extremities.

Affected joints

Ninety-two percent of patients suffered with multiple affected joints in both upper and lower extremities. The most frequently affected joints were knee (86.1%) and hand (77.2%), while hip and shoulder were the least frequently suffered joints (14.3% and 20.3% respectively). The most painful joints were knee (VAS: 7.1) and elbow (VAS: 6.8), the least painful joint were also hip (VAS: 3.8) and should (VAS: 4.1) (Table I).

Table I
Levels of arthritic pain ($n = 889$)

	n (Frequency %)	VAS
Upper extremities		
Shoulder	201 (20.3%)	4.1 ± 3.1
Elbow	616 (62.3%)	6.8 ± 2.1
Wrist	734 (74.2%)	4.5 ± 2.2
Hand	764 (77.2%)	5.5 ± 1.7
Lower extremities		
Hip	141 (14.3%)	3.8 ± 2.6
Knee	852 (86.1%)	7.1 ± 1.9
Ankle	472 (47.7%)	4.7 ± 2.1

n: The number of patients.
VAS: visual analog pain score of the joint, presented as mean ± SD.

The joint deformity most frequently represented as enlargement of interphalangeal joints (93.2%) and flexion deformity of DPJs (74.6%), deformity of knee also accounted for 70.3% (Table II).

Limitation of ROM occurred most frequently in hand (76.7%) and elbow (38.4%), ROM of hip and shoulder were least frequently affected (Table III).

Risk factors of daily living and working function

Multiple linear regression analysis revealed that only joint pain (regression coefficient: −0.504, 95% confidence interval (CI): −0.820–0.188, $P < 0.001$) and ROM (regression coefficient: 0.017, 95% CI: 0.011–0.024, $P < 0.001$) were independent risk factors affecting FSAT-KBD scores, while the age, gender and joint deformities did not independently associate with FSAT-KBD scores ($P > 0.05$).

The VAS scores of shoulder, elbow, wrist and hand were mainly correlated with upper extremity functional score, while VAS scores of hip, knee and ankle were mainly correlated with lower extremity functional score (Table IV). Respectively, pains in elbow and hand joints were correlated stronger with upper limb functional scores, while pains in knee and ankle joints were correlated stronger with lower limb functional scores.

The ROM of shoulder, elbow, and wrist all significantly correlated with functional score of upper limb, while ROM of hip, knee and ankle all significantly correlated with k functional score of lower limb (Table V). However, the correlations between ROM of elbow and upper limb function and between ROM of knee and lower limb function were much more stronger.

The ROM of patients' hands were roughly judged by whether a clenched fist could be made. According to the investigation results, the patients were divided into subgroups as “can make a fist with both hand” (group A, $n = 176$), “only can make a fist with right hand” (group B, $n = 176$), “only make a fist with left hand” (group C, $n = 192$) and “can't make a fist” (group D, $n = 474$). The scores of each items of upper limb joints except for “dressing” and “heavy object moving” were significantly different ($P < 0.05$) among the subgroups. The upper limb score of “can make a fist with both hand” subgroup was significantly higher than subgroups of “can't make a fist” and “only can make a fist with left hand” ($P < 0.001$, $P = 0.001$ respectively). And the upper limb score of “can make a fist with right hand” subgroup was significantly higher than subgroup of “can't make a fist” ($P < 0.001$) (Table VI).

Table II
The number and frequency of joint deformities ($n = 899$)

	n (Frequency %)
Upper extremities	
Flexion deformity of DPJ	738 (74.6%)
Brachydactylia	565 (57.1%)
Enlargement of interphalangeal joint	921 (93.1%)
Wrist radial deviation	224 (22.6%)
Deformity of elbow	324 (32.8%)
Lower extremities	
Enlargement of ankle	248 (25.1%)
Deformity of knee	695 (70.3%)

n: The number of patients.

Table III
ROM limitations

	ROM	Frequency of limited ROM
Shoulder		20.1%
Abduction	76 ± 11	18.1%
Flexion	77 ± 14	16.4%
Elbow		38.4%
Flexion	124 ± 14	31.5%
Extension	−21 ± 13	34.8%
Wrist		36.1%
Dorsal extension	20 ± 8	32.4%
Palmar flexion	47 ± 9	26.1%
Hand		
Can't make a fist	–	76.6%
Hip		14.3%
Flexion	131 ± 14	8.4%
Abduction	30 ± 11	10.3%
External rotation	35 ± 13	12.8%
Knee		37.5%
Flexion	110 ± 16	30.1%
Extension	−11 ± 7	32.8%
Ankle		32.3%
Dorsal extension	15 ± 12	28.5%
Plantar flexion	31 ± 11	24.3%

Discussion

Through this relatively large sample investigation of adult KBD patients in Aba Tibetan area, we confirmed that most adult KBD patients suffered with multiple affected joints in both upper and lower extremities. This result was consistent with the results of our previous studies of smaller sample[7,8,17] and with other studies[5,13]. Because KBD always occurs in childhood and most frequently affected the epiphysis and metaphysis of phalanges[3], the joints of hand were very frequently affected in adult KBD patients. In our investigation, interphalangeal joint enlargement was the most common deformity (93.2%), and 66.6% of hands could not make a fist. However, KBD in adult patients did not only affect joints in hands and wrists, but also frequently affected multiple major joints in both upper and lower limbs[1,5,7]. Mathieu *et al.*[13] reported that proximal limb joints suffered much less severe than distal limb joints in adult KBD patients in Tibet. Guo Xiong *et al.*[6] found that limited ROM of knee occurred in 69.3%, and limited ROM of elbow in 63.7% adult KBD patients in Xian Province of China. These features of affected joints were also confirmed in adult KBD patients in Aba Tibetan area of Sichuan Province in this investigation. We found that knee and elbow were the most frequently and severely affected joints while shoulder and hip were the least frequently and most mildly affected joints in these patients.

In this investigation, we used FSAT-KBD which was a specific functional scale for evaluating daily living and working function of local residents to assess the functional status of the patients. This scale was developed based on living and working habits as well as cultural characteristics, it could efficiently and effectively assess the functional status of the multiple joints in both upper and lower limbs which might be affected by KBD[15,16].

In our investigation, we found that both limited ROM and pain were independent risk factors of daily living and working function of adult KBD patient, which was different with the results of Schepman's previous study[5], even though we used the same

Table IV
Spearman correlation (*rs*) between VAS and FSAT-KBD scores

	Shoulder	Elbow	Wrist	Hand	Hip	Knee	Ankle
Dressing	−0.289*	−0.147*	−0.047	−0.052	0.014	−0.028	0.007
Face washing	−0.128*	−0.301*	−0.279*	−0.054	0.003	−0.012	0.006
Cooking	−0.032	−0.076[a]	−0.181[g]	−0.364*	−0.002	0.006	0.004
Food taking	−0.009	−0.227*	−0.171*	−0.323*	−0.009	−0.011	−0.007
Ox dung picking up	−0.207*	−0.106[b]	−0.041	−0.063	0.013	−0.078[c]	0.017
Heavy object moving	−0.069[d]	−0.287*	−0.284*	−0.303*	−0.058	−0.147*	−0.049
Cross-legged sitting	0.004	−0.021	−0.033	−0.028	−0.386*	−0.179*	−0.062
Squatting	−0.012	−0.105[e]	−0.017	0.007	−0.147*	−0.423*	−0.228*
Stand up from sitting position	−0.033	0.005	−0.028	−0.051	−0.088[f]	−0.419*	−0.116*
Ascending and descending a single-track wood ladder	−0.042	−0.025	0.006	−0.054	−0.136*	−0.482*	−0.213*
Walking distance	0.008	0.034	−0.105*	−0.043	−0.148*	−0.388*	−0.227*
Walking aids usage	0.003	0.043	0.061	0.033	−0.128*	−0.211*	−0.208*
Upper limb score	−0.123*	−0.213*	−0.177*	−0.237*	−0.008	−0.014	−0.005
Lower limb score	−0.004	−0.010	−0.013	−0.037	−0.141*	−0.404[Q]	−0.211*
Total score	−0.044	−0.127*	−0.072[g]	−0.103[h]	−0.032	−0.258*	−0.021

*: $P < 0.001$.
a: $P = 0.027$, b: $P = 0.002$, c: $P = 0.031$, d: $P = 0.041$, e: $P = 0.003$, f: $P = 0.008$, g: $P = 0.024$, h: $P = 0.001$.

Table V
Spearman correlation (*rs*) between ROM and FSAT-KBD scores

	Shoulder	Elbow	Wrist	Hip	Knee	Ankle
Dressing	0.314*	0.191[a]	0.047	0.003	0.012	0.018
Face washing	0.213*	0.234*	0.049	0.026	0.007	0.011
Cooking	0.018	0.024	0.133*	0.031	0.018	0.003
Food taking	0.044	0.203*	0.126*	0.017	0.014	0.021
Ox dung picking up	0.235*	0.212*	0.061	0.112[b]	0.038	0.007
Heavy object moving	0.041	0.132*	0.068[c]	0.117*	0.125*	0.015
Cross-legged sitting	0.005	0.037	0.008	0.294*	0.147*	0.052
Squatting	0.018	0.009	0.014	0.136*	0.381*	0.206*
Stand up from sitting position	0.013	0.008	0.018	0.082[d]	0.334*	0.114*
Ascending and descending a single-track wood ladder	0.036	0.019	0.007	0.071[e]	0.461*	0.198*
Walking distance	0.003	0.009	0.103[f]	0.067[g]	0.355*	0.217*
Walking aids usage	0.008	0.011	0.009	0.164*	0.324*	0.133*
Upper limb score	0.123*	0.211*	0.141*	0.007	0.011	0.008
Lower limb score	0.013	0.006	0.017	0.103[h]	0.402*	0.188*
Total score	0.036	0.174*	0.100[i]	0.055	0.206*	0.061

*: $P < 0.001$.
a: $P = 0.013$, b: $P = 0.001$, c: $P = 0.046$, d: $P = 0.029$, e: $P = 0.037$, f: $P = 0.016$, g: $P = 0.042$, h: $P = 0.002$, i: $P = 0.003$.

statistical method. The reasons for this discrepancy may be as the follows. Firstly, we investigated 989 patients, much more than the sample of Schepman's study. Larger sample size may increase the sensitivity of regression analysis. Secondly, the functional scale we used in this study was different with that in Schepman's study. The scale used in Schepman's study was International Classification of Functioning Disability and Health (ICF)[18], which is widely used in western countries. However, the reliability and validity of ICF has not been tested for KBD patients in Aba area, in which the patients lived in a unique lifestyle and with their own work and living habits. The authenticity and accuracy of an assessment of functional status might be impaired by using a scale which was not highly relevant for the living and working habits and cultural characteristics of the participants[19,20]. Thus the validity and reliability of a scale should be validated before used in different groups of people[21–23]. The FSAT-KBD was specific designed for KBD patients in Aba Tibetan area, and its reliability and validity had been validated in our previous study[15]. Thus, we could evaluate the functional status of the patients more accurately with this scale. Thirdly, joint deformity did not become a direct factor affecting daily activities tested by multiple linear regression in our study. The reason may be that even though the adult patients suffered with joint deformity for long time periods, as long as the joint preserved some functional range of motion without severe pain, patients could sustain a certain degree of daily functions.

Our results demonstrate that the upper limb function is mainly influenced by arthritic pain and limited ROM of the elbow, wrist and hand joints. Pain and restricted ROM of knee and ankle were main reason for functional impairment of lower limb. Although arthritic pain and limited ROM of shoulder and hip affected some daily activities to some extent, the incidence of these proximal joint involvement was relatively much lower, thus they were not the main reason for affecting the overall function of upper and lower limbs.

Our study has some intrinsic limitations. Firstly, the study was conducted under tough circumstances. The survey area located in a high altitude mountain plateau (above 3000 m) with cold temperatures and in an area still suffering the effects (aftershocks, poor

Table VI
FSAT-KBD score differences between patients with different degrees of hand activities

	Can make a fist with both hands (A) ($n = 146$)	Only can make a fist with right hand (B) ($n = 176$)	Only can make a fist with left hand (C) ($n = 192$)	Can't make a fist (D) ($n = 475$)	*P*-value
Dressing	3.31 ± 0.92	3.58 ± 0.67	3.14 ± 0.83	3.21 ± 0.92	0.064
Face washing	3.35 ± 0.92[a]	3.17 ± 0.94[b]	2.86 ± 0.87	2.59 ± 1.02	< 0.001
Cooking	3.28 ± 0.72[c]	3.13 ± 1.06[d]	3.08 ± 1.12[e]	2.56 ± 1.11	< 0.001
Food taking	3.35 ± 0.87[f]	3.33 ± 0.78[g]	3.26 ± 0.85	3.02 ± 0.67	0.013
Ox dung picking up	2.58 ± 1.12[h]	2.39 ± 0.77[i]	2.28 ± 0.94	2.06 ± 0.68	0.022
Heavy object moving	1.47 ± 0.56	1.40 ± 0.58	1.36 ± 0.54	1.41 ± 0.56	0.174
Upper limb score	17.34 ± 3.47[j,k]	17.01 ± 3.42[l]	15.98 ± 3.10	14.85 ± 3.51	< 0.001

n: The number of patients.
a: $P = 0.003$ compared to D subgroup, b: $P = 0.011$ compared to D subgroup, c: $P = 0.008$ compared to D subgroup, d: $P = 0.021$ compared to D subgroup, e: $P = 0.028$ compared to D subgroup, f: $P = 0.032$ compared to D subgroup, g: $P = 0.044$ compared to D subgroup, h: $P = 0.037$compared to D subgroup, i: $P = 0.048$ compared to D subgroup, j: $P < 0.001$ compared to D subgroup, k: $P = 0.001$ compared to C subgroup, l: $P < 0.001$ compared to D subgroup.

infrastructure, depopulation and security concerns) of the devastating Wenchuan earthquake in May 2008 in Sichuan. The participants lived in scattered, remote areas and could not be convened together from different villages because of the rugged rural trails, communication and transportation difficulties. These extreme socio-geographic difficulties meant we could only visit one remote village at a time, and we could not survey each KBD prevalence area in Aba. However, we did our utmost to survey the patients in the areas of highest prevalence. Secondly, for safety reasons, we only assessed patients who could themselves mobilize to the meeting point, and did not survey the least mobile or most geographically remote patients. Thirdly, most of the patients surveyed were unable to read or write, so all inquiries and measurements were performed with help of translators. A brief 1 day's training was provided to local physicians carrying out the surveys to improve the reliability.

In summary, most adult KBD patients suffered with multiple affected joints in both upper and lower limbs. The elbow, hand and knee were the most frequently and severely affected joints in Aba region, known as a high prevalence KBD area. Pain and limited ROM of these joints were the primary factors for dysfunction of daily living and working activities. Thus, the symptoms and functional status of these patients might be improved to some extent by using symptomatic analgesia and physical therapy.

Contributors

Dr Zhou Zongke had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study design: Dr Zhou Zongke, Dr Pei Fuxing and Dr Huang Qiang.
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Writing: Dr Huang Qiang.
Statistical analysis: Dr Huang Qiang and Li Yichong (from National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention).

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Conflict of interest

We declare that we have no conflict of interest.

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