The prevalence of rheumatoid arthritis in middle-aged and elderly people in Tibet Autonomous Region of China

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Abstract

Objective

There has been no epidemiological survey of it in Tibet. We estimated the prevalence of rheumatoid arthritis in Luoma Town, Naqu City, Tibet Autonomous Region of China.

Methods

A population-based cross-sectional survey was conducted among 1458 residents of Luoma Town, Tibet Autonomous Region, aged ≥ 40 years. We used questionnaires in face-to-face interviews, anthropometric measurements and rheumatoid factor (RF), autoantibodies binding to citrullinated antigens (ACPA) and C-reactive protein (CRP) test. The definition of rheumatoid arthritis in this study was on the basis of new 2010 ACR/EULAR classification criteria.

Results

782 participants completed all items of rheumatoid arthritis. The overall crude prevalence of rheumatoid arthritis was 4.86%. The prevalence was higher in women than in men (7.14% vs. 2.56%, P = 0.005). Tibetan had a higher age-standardized prevalence of rheumatoid arthritis 6.30% (95% confidence interval: 4.20% − 8.64%) compared with the other areas in China (range: 0.20% − 0.93%).

Conclusion

The prevalence of rheumatoid arthritis is relatively higher than other places in China.

Introduction

Rheumatoid arthritis (RA) is a chronic systematic autoimmune inflammatory disease, characterised by a symmetrical inflammatory polyarthritis of the joints of the hands, wrist, feet and knee which can result in joint swelling, pain, stiffness, and possible loss of function [1]. It seriously affects the quality of life of patients. The disease can occur at any age. Women were more affected than men, with the highest prevalence among women over 65 years of age [2]. Globally, there were almost 20 million prevalent cases from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2017[3]. However, due to the different geographical environment and demographic factors, the prevalence of RA is different in regions. The disease is common in northern Europe and North America, but less common in some parts of the developing world, such as rural West Africa. [4].

China, as one of the largest developing countries, the first epidemiological study on rheumatic diseases in China was not reported until 1983 with a prevalence of 0.3% in Taiwan [5]. A lot of epidemiological surveys about different regions of China were published subsequently, showing and the prevalence of RA in China, ranges from 0.2–0.93% [6]. However, China is a vast country with gradual altitude decreases from the west to the east gradually. At the same time, the current researches are mainly concentrated in the areas of different latitudes in the central-east of China. To our knowledge, little attention has been paid to the prevalence of RA in Western China, especially Tibet. China got the economy and society developed in the last 30 years, and the people's living standard and life-style

have also changed greatly in most areas. But Tibet, a distinct area, with an average elevation over 4000 m above sea level, which spreads all over grassland, bare rock and snow, remains the unique culture and traditional lifestyle-nomadic pastoralism [7, 8]. Since the 18th National Congress of the CPC, the alleviation of poverty in China has made remarkable progress. And medical poverty reduction is also an important part. Medical aid for Tibet Autonomous Region is a significant strategic decision of the country. The government gives top priority to the improvement of Tibetan's livelihoods. Whereas, epidemic data collection and policy making are very difficult due to the population of Tibet, which is widely distributed across high mountain areas. Therefore, this study is necessary and urgent with the aim of describing the prevalence of RA in Tibet area.

Materials And Methods

Participants

This was a cross-sectional survey and the target population was aged 40 years and older living in the Tibet in southwest China, and the sampling methods as follow. Luoma Town was randomly selected from total of 12 towns in Seni Community, Naqu City, Tibet Autonomous Region. Luoma Town located in northern Tibet with an average altitude above 4500 meters. First, one community was randomly selected from Naqu City. Next, one town was randomly selected from the former the community. The cluster (Luoma Town) contents 12 villages, and all households in the cluster were included in this study. All inhabitant, aged 40 years or older, who were self-described residents of Luoma Town were included. Individuals who reported disability, mental disease, malignant tumor, clinotherapy, or egresses works and live away from home over half year were excluded from further participation. The survey was approved by the Pecking University Health Science Center Ethics Committees. Written informed consent was obtained from all participants according to the Declaration of Helsinki.

Questionaire

Trained health local professionals administered the survey questionnaires, as it was anticipated that many study participants would be illiterate and could not speak mandarin. All interviewers, clinical examiners, and laboratory tests were trained under the supervision of the study chief investigators (Hongqiang Gong and Jianhao Lin). Data were collected at local Luoma Town Health Station, with trained interviewers going to enumerate face-to-face and interview. Sociodemographic status (e.g. sex, age, education level, etc.) and ethics were queried.

Clinical and laboratory examinations and Definition of RA

Height was measured with a wall-mounted stadiometer, using the average of 2 measurements taken. Body weight was assessed using a beam balance scale with 0.1-kg precision. Two professionals administered the history-taking. Venous blood was collected from each consented respondent by medically-trained staff from the Chinese Center for Disease Control and Prevention based on a standard protocol. The centrifuged blood samples were stored in a deep freezer in the local health station. After samples were collected completely, the blood-based bioassays were performed at laboratory in Tibet Autonomous Region People's Hospital. We tested the rheumatoid factor (RF), autoantibodies binding to citrullinated antigens (ACPA) and C-reactive protein (CRP). The RF and CRP levels were all determined using turbidimetric inhibition immuno assay, and ACPA was using chemiluminescence. RA was identified according to the American College of Rheumatology/ American College of Rheumatology and European Against Rheumatism (ACR/EULAR) RA classification criteria [9].

Research on rheumatoid arthritis in China

A search was conducted using English Medical Current Content (1980 to 2019), Medline (1980 to 2019) and Pub Med (1980 to 2019). The database was searched using the following search terms: rheumatoid arthritis, epidemiology, China and Chinese. For publication in Chinese, we used the same combinations of keywords, translated into Chinese. Two sources were included (1980 to 2019): http://www.cnki.net (National Knowledge Infrastructure) and http://www.imicams.ac.cn/cbm/(National Academy of Medical Sciences).

Statistical analysis

Data was inputted and managed through Epidata software with double entry and validation, version 3.0 (Epidata Association, Odense, Denmark). We divided all subjects into four age groups (i.e., 40–49 years, 50–59 years, 60–69 years and ≥ 70 years). The levels of education attainment were classified as elementary school and below, middle school, high school and college and higher. All analyses and calculations were performed using SPSS statistical package, version 22.0 (SPSS, Inc., Chicago, LI, USA). We used the mean ± standard error and proportions represented continuous variables and categorical variables respectively. In addition, the age-standardized value of RA was calculated by the direct method for the overall population, males and females respectively, after age standardisation to the Chinese census population in 2010 [10]. Quantitative variables were summarized in terms of means and 95% confidence interval (CI). Differences between subjects were analysed by chi-square tests or Fisher exact tests for categorical data, if appropriate. Univariate and multivariate logistic regression analyses were used to estimate the odds ratio (OR) and CI comparing associated influenced factors on RA occurrence. $P < 0.05$ was considered significant.

Results

Participants

This study was a population-based screening in Luoma Town, Naqu Ctity, Tibet Autonomous Region. There are 2,088 subjects were reported age ≥ 40 years in this town. Of all these subjects, 256 were excluded from our study participation due to death, moving away, egresses working, mental disease, malignant tumor, clinotherapy, and disability. The remanding 1832 subjects were enrolled, and 1458(80%)of these subjects consented to enter into this study and completed it in September and October 2018. The consented participants were younger than those who declined to participate (mean ± SD, 52.30 ± 8.43 versus 58.5 ± 3.42, P = 0.106). 782 participants completed all items of RA and attended to be taken blood samples for laboratory test (Fig. 1). The background characteristics of the all enrolled participants were presented in Table 1. The participants who took blood samples had no-significant difference compared to the subjects who refused to take blood samples, except for the age characteristics. Slightly more than half (50.13%) of included subjects were women and the mean age of whom (52.79 ± 8.74) was almost equal to men (51.81 ± 8.07). The percentage of Tibetan was approximately approach to 100%. For education distribution, most of men and women only receive elementary or seldom have any formal education (97.70%). The mean BMI of women was greater than men, but all of them are overweight.

The prevalence of RA in Tibet

The overall crude prevalence of RA of was 4.86%, and it was more prevalent in women than in men (7.14% vs 2.56%, P = 0.005). The age-standardized prevalence of RA was 6.30% (95% confidence interval (CI): 4.20%-8.64%), men and women was 2.46%(95% CI: 1.04%,4.10%)and 9.59%(95% CI: 5.93%, 13.77%) respectively as shown in Table 2. Meanwhile, the prevalence of women, as well as the general population, increased with age (Fig. 2). We

examined the association of each factor (age, ethnicity, education, obesity) with the odds of RA, for overall and sex-specific. But there was no significant result.

Table 1

The characteristics of participants in this study

	Included Subjects			Subjects who refused to take blood samples		
	Male49.87% (n = 390)	Female50.13% (n = 392)	Total(782)	Male48.52% (n = 328)	Female51.48% (n = 348)	Total(676)
Age,mean ± SD	51.81 ± 8.07	52.79 ± 8.74	52.30 ± 8.43	54.17 ± 9.79	53.47 ± 10.24	53.81 ± 10.0*
Age group,%(n)						
40–50	41.87% (164)	45.13%(176)	43.48% (340)	38.41% (126)	44.54%(155)	41.57% (281)
50–59	36.99% (145)	38.21%(149)	37.60% (294)	34.45% (113)	29.89%(104)	32.1% (217)
60–69	16.58%(65)	13.33%(52)	14.96% (117)	19.51%(64)	16.67%(58)	18.05% (122)
≥ 70	4.59%(18)	3.33%(13)	3.96%(31)	7.62%(25)	8.91%(31)	8.28%(56)
Ethnicity,% (n)						
Tibetan	99.74% (389)	99.74%(391)	99.74% (780)	100%(328)	100%(348)	1000% (676)
Moinba	0%(0)	0.26%(1)	0.10%(1)	0%(0)	0%(0)	0%(0)
Others	0.26%(1)	0%(0)	0.10%(1)	0%(0)	0%(0)	0%(0)
Education,% (n)						
Elementary education and below	98.46% (384)	99.23%(389)	97.70% (763)	48.60% (312)	50.62%(325)	99.22% (637)
Middle/high school	1.28%(5)	0.51%(2)	0.90%(7)	0.62%(4)	0.16%(1)	0.78%(5)
College and higher	0%(0)	0.26%(1)	0.13%(1)	0%(0)	0%(0)	0%(0)
BMI,mean ± SD	25.25 ± 7.02	26.32 ± 17.31	25.82 ± 4.36	25.13 ± 11.63	24.45 ± 4.50	24.78 ± 8.85
BMI = Body mass index. *: $p < 0.05$						

Table 2
The prevalence of Rheumatoid arthritis

	Male	Female		Overall
Crude, %	2.56% (2.318%, 2.82%)	7.14% (6.44%, 7.85%)	$P = 0.005$	4.86% (4.52%, 5.20%)
Age-standardized, %	2.46% (1.04%, 4.10%)	9.59% (5.93%, 13.77%)		6.30% (4.20%, 8.64%)

Discussion

Our cross-sectional study involves a provincial representative sample of the middle-aged and older Tibet inhabitants, and the overall prevalence of RA was estimated as 6.30%. Although there was a difference in age between those who refused to take blood and those who took blood, the average age of the former is higher than the latter. At the same time, as we all know that the prevalence of RA increased with age, therefore the true prevalence may be higher. This amazing rate, which is close to the highest prevalence of RA (up to 6.80%) in the world which was identified in Native American Chippewa Indians [11], is far above a previously reported 0.28% (age-standardized prevalence) in the national epidemiological study in China [12]. The prevalence in the over 45 years old group was much lower than our results also (0.74%). Similarly, both the prevalence of men (2.46%) and women (9.59%) in our research are higher than the study (0.19% in men and 1.28% in women, age > 45) [12]. But the prevalence of women and totality increasing with age, and the peak being after 60 years old, which was consistent with previous reports. A study shown that the prevalence of RA has significant geographic variation [13]. Considering that China is geographically a large area with a multi-ethnic population and substantial regional differences in socio-economic and hygienic conditions, the result may not represent China as a whole [14]. Since 1983, a large number of studies have been performed in different areas of China to investigate the epidemiology characteristics of RA, with the focus on the differences among the different regions [15.16.17-26]. And the prevalence of RA ranges from 0.2%(Shantou) to 0.93%(Taiwan), which were all much lower than our results as well. However, the main concern of these researches was the prevalence in low altitude areas of the east-central China with different latitudes, and the majority of the participants were Han nationality [27].

Previous studies have presented that the prevalence of RA differs in different regions of the world, which suggested the aetiology of this disease was influenced by both gene and environment factors [28]. Tibet is known as the ‘Third Pole’ and is one of the highest and most extreme inhabited areas of the world, which means the geographical environment of Tibet area is different from the inland or coastal areas of China [29]. A research pointed out that the people living in high altitudes featured high bacterial diversity and richness, and Tibetans’ core microbiota comprised Prevotella [30]. At the same time, Scher etc. identified that the presence of Prevotella as strongly correlated with disease in new-onset untreated rheumatoid arthritis (NORA) patients [31]. Therefore, this might be a reason for the high prevalence of RA in Tibet. On the other hand, it is worth noting that nearly all of participants examined in our study were Tibetan residents (99.74%) of Luoma Town with the nomadic lifestyle. In addition, Tibet is an isolated area in the inland of China, where the plateau people live in for generations, which means that they have unique genetic background with low levels of heterozygotes, and high levels of homozygotes [32]. As we all know, 50% of risk of developing rheumatoid arthritis is attributable to genetic factors [33]. Maybe this could explain the much higher prevalence in Tibet compared to the other areas in China. And it is not just a coincidence: the prevalence of RA of native American Chippewa Band (6.8%) is far above that of the rest of the United States (1.07%), too [12, 34]. But more researches sre still needed to confirm it.

Our result demonstrates the prevalence of RA in Tibet with the highest rate. Therefore, Tibet as the key area of national medical poverty alleviation should be paid more attention to the prevention and treatment of RA.

Meanwhile, the government should make policies based on the prevalence, disease burden [35] and local characteristics.

Conclusion

This is the first cross-sectional study of RA from the Tibet Autonomous Region, China. Notable findings include the prevalence of RA in Tibet is highest in China. Future studies should aim to research the reason through gene and altitude environment factors. Lastly, the government should pay attention to the RA in Tibet.

Declarations

Ethics approval

The survey was approved by the Pecking University Health Science Center Ethics Committees.

Consent to participate

Written informed consent was obtained from all participants according to the Declaration of Helsinki.

Availability of data and material

The first author can provide all data.

Conflict of interest statement

The authors declare that they have no conflict of interest.

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Consent for publication

All authors approved the final version to be submitted.

Author contributions

Qingxi Zhang, Qiang Liu, Chutong Lin, Hu Li, Hongqiang Gong, and Jianhao Lin were responsible for the conception and design of the study. Qingxi Zhang, Chutong Lin, Yangjin Baima, and Hu Li acquired the data and performed data analysis and quality assessment. All authors made substantial contributions to the interpretation of the results. Qingxi Zhang drafted the article and all authors revised it critically for important intellectual content

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Figures

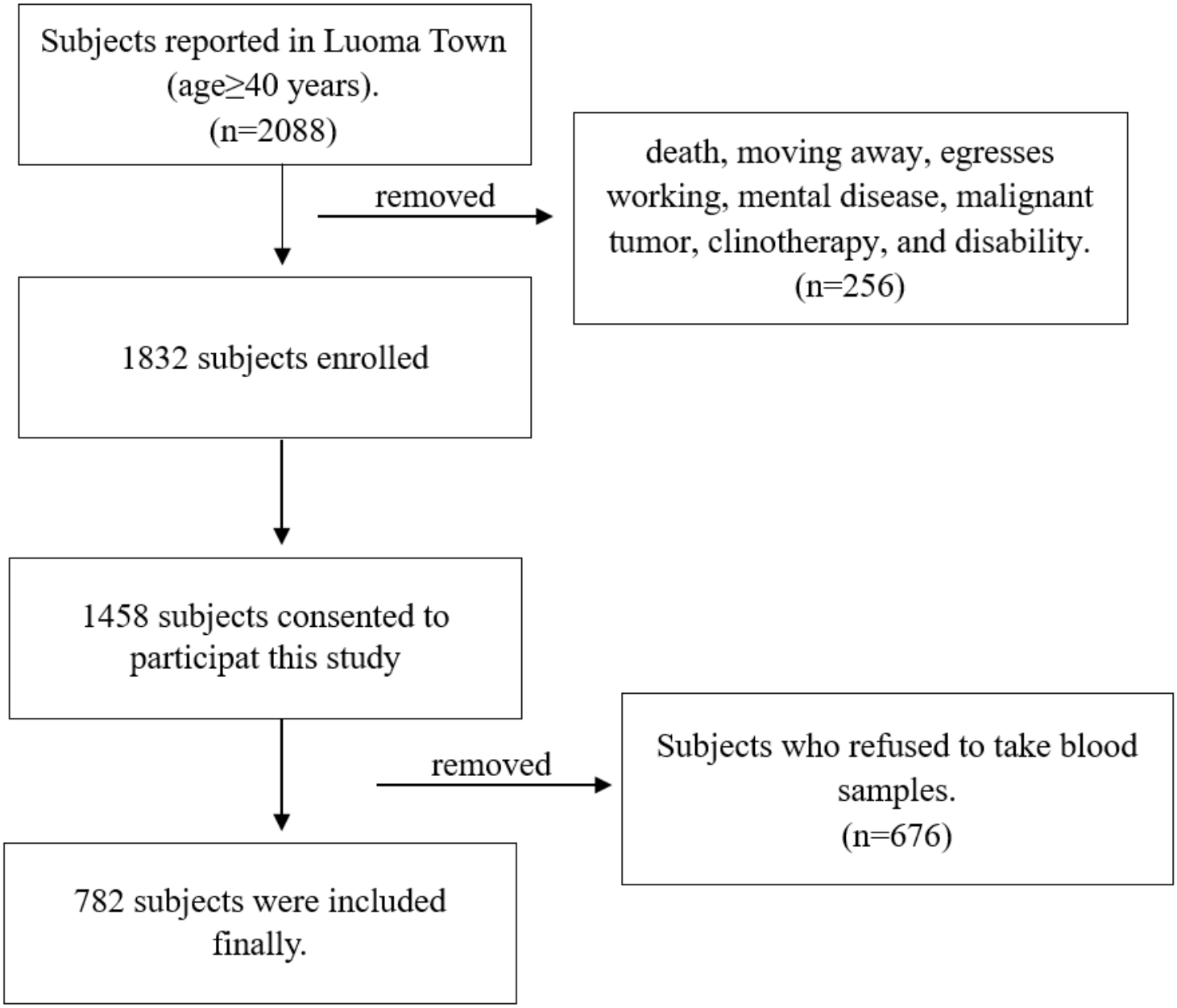

Figure 1

Flowchart of subjects screening.

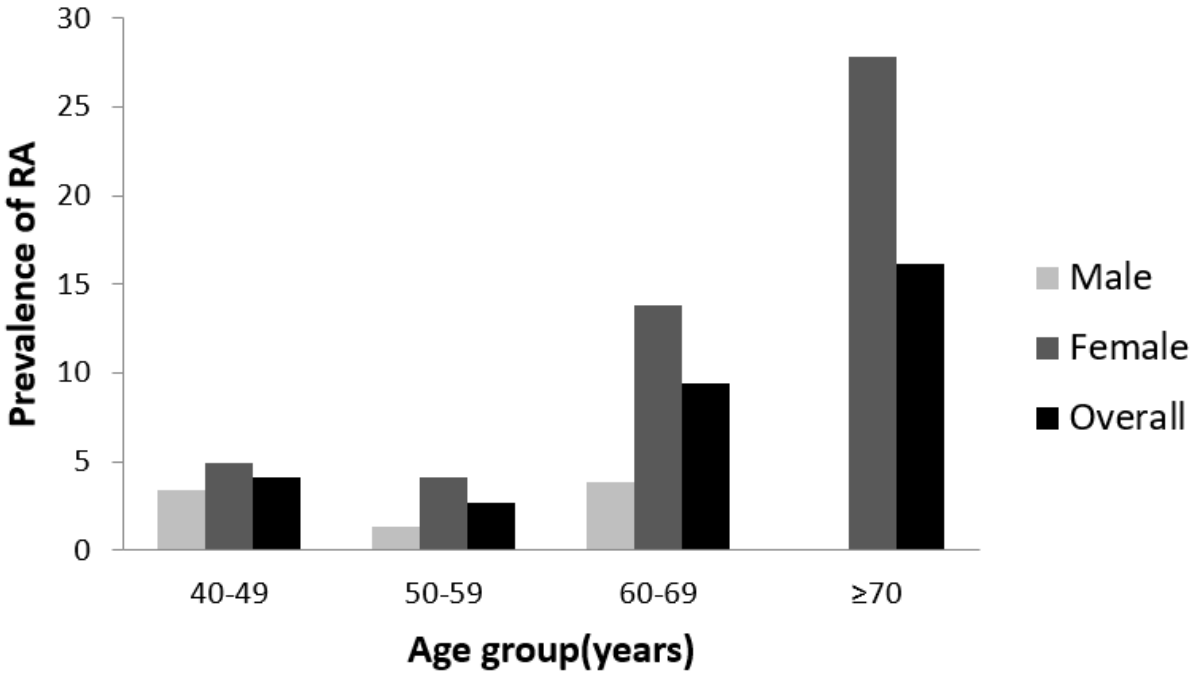

Figure 2

The prevalence of rheumatoid arthritis (RA) in four age groups.