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Prevalence of mild cognitive impairment is higher in hypertensive population: a cross-sectional study in less developed northwest China

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Abstract

Uncertainty remains about the association of hypertension with mild cognitive impairment (MCI) in less-developed areas.

This is a cross-sectional survey conducted in Xinjiang, a less-developed region in China between April and October 2019. We used multi-stage stratified sampling method to obtain study population aged ≥45 years, and we analyzed complete data for 3282 subjects. The Mini-Mental State Examination (MMSE) was used to assess cognitive function. MCI is defined as an MMSE score < 17 for illiterate subjects, <20 for subjects with 1 to 6 years of education, and <24 for subjects with ≥7 years of education.

The prevalence of MCI was significantly higher in hypertensive subjects than in non-hypertensive subjects (22.1% vs 16.1%, $P<.001$) and higher in hypertensives with uncontrolled blood pressure (BP) than in those with controlled BP (27.5% vs 20.7%, $P=.01$). Hypertensive subjects had significantly lower each item score and total score of MMSE, compared to non-hypertensive subjects. Significant negative correlations were observed between systolic and diastolic BP with MMSE scores (P for all $<.001$). Multivariate logistic regression analysis showed that hypertension was the significant risk factor for the presence of MCI (OR = 1.62, 95%CI: 1.34, 2.35, $P<.001$), independent of such factors as gender, age, education attainment, and dyslipidemia.

The prevalence of MCI is higher in hypertensive population, and hypertension is an independent risk factor for MCI in less-developed region, suggesting that hypertensives should be screened for MCI to provide improved diagnoses and optimal therapeutics for cognitive decline prevention, specially in settings with approximate conditions.

Abbreviations: BMI = body mass index, BP = blood pressure, DBP = diastolic blood pressure, MCI = mild cognitive impairment, MMSE = Mini-Mental State Examination, OR = odds ratio, SBP = systolic blood pressure.

Keywords: association, blood pressure, hypertension, less-developed regions, mild cognitive impairment

1. Introduction

With the rapid aging of global population, cognitive impairment such as dementia and Alzheimer disease has become one of the most serious public health problem in both developed and developing countries.[1] Data have demonstrated that mild cognitive impairment (MCI) is a risk for dementia[2] and is considered a prodromal manifestation of dementia and can be identified years before dementia onset.[3] Because the treatment for cognitive impairment, especially Alzheimer disease, is limited, prevention becomes an effective way to delay its onset.[4] People with cognitive impairment progressively lose cognitive functions such as memory, attention, language, and task execution without reaching levels of dementia or Alzheimer disease.[5]

Accumulating epidemiological and mechanistic evidence has shown that hypertension is a possible risk factor for MCI.[6,7] A 2-stage stratified clustering study, conducted in Beijing China in participants aged ≥60 years using the Mini-Mental State Examination (MMSE), reported that the prevalence of MCI is significantly higher in hypertensive (16.5%) than in normotensive individuals (13.1%) and associated with treatment and control rates.[8] Furthermore, accruing evidence shows that in addition to absolute blood pressure (BP) values per se, short- and long-term BP variability, which represents neither a background noise nor a random effect phenomenon that dilutes the prognostic value of BP measurements,[9] is related with cognitive impairment, and dementia onset and progression.[9–12] Nonetheless, the evidence of an association between hypertension and MCI is controversial and not completely understood in low

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middle income regions, especially in populations with a low socioeconomic status.[13] For instance, World Health Organization's study on global ageing and adult health conducted in 6 low-middle income countries, and another study from Peru reported no association between hypertension and MCI.[14,15] A scientific statement from the American Heart Association describes that the relationship between BP and cognitive function remains relatively under-explored in racially or ethnically diverse populations and more research is needed to elucidate the causal link between BP and cognition and to better understand the role of medication in the observed associations.[16] Furthermore, data on this topic from developing regions are important given that increasing trends in cardiovascular diseases coupled with epidemics of hypertension can result in upward trends in dementia prevalence and incidence in this setting. Furthermore, the association between hypertension and MCI may differ in developing regions due to different population age structure, and health care systems as well as higher prevalence of poverty and low education, and suboptimal treatment for chronic conditions.

Therefore, we aimed to investigate the relationship between hypertension and MCI and related factors in the primary care setting of Xinjiang, a less-developed region in Northwest China, where hypertension is highly prevalent (35%–55% in prevalence) and poorly managed (8%–10% vs 15.3% of national average)[17] and burden of dementia is higher than national average in China[18] in order to identify modifiable risk factors of the precursory stage of dementia to establish interventions to prevent or delay the onset of dementia since MCI is considered a preclinical transitional state of dementia for which targeted interventions may be feasible, given the fact that the world population is aging at an unprecedented speed due to increasing life expectancy with most of the increase occurring in low- and middle-income countries.[14]

2. Methods

2.1. Site

Emin County, in Northern Xinjiang, an underdeveloped region in China, is home to a total population of over 160,000, living in the urban, agricultural, and stock-raising setting with higher prevalence of hypertension, characterized by low awareness, treatment, and control rates,[19] which makes it ideal setting for the study about the association of BP and prevalent hypertension with MCI in population from less-developed region.

2.2. Subjects

In order to have higher response rate, the survey was conducted together with the annual health check up programs in Emin between April to May 2019. Multistage stratified random sampling method was used to obtain sample of the population aged ≥45 years. At the first stage, whole county was divided into 10 regions, based on distribution of village and country level hospitals. At the second stage, 3 townships were randomly selected in each region using simple random sampling method. At the third stage, the eligible residents aged ≥45 years from each site were asked to participate in the survey during their annual health checkup at the hospitals using lists compiled from local government registers of households. Inclusion criteria encompassed:

1. local inhabitants aged ≥45 years
2. residing at current address for ≥6 months
3. agreement to participate and sign an informed consent form.

Exclusion criteria included confirmed dementia, confirmed Alzheimer disease, recent cardiovascular event (within previous 6 months) such as any type stroke, malignant tumors, including those in central nervous system by computerized tomography and magnetic resonance imaging, encephalitis or meningitis, injury, trauma, and/or operations in central nervous system; those who are unable to co-operate due to mental reasons or others, moderate to severe obstructive sleep apnea confirmed by polysomnography, and sever diseases on respiratory and/or digestive system. The Independent Ethics Committee of the People's Hospital of Xinjiang Uygur Autonomous Region approved the current study. Signed informed consent was obtained from all of the eligible participants.

2.3. Data collection and measurement

Each participant completed a standardized questionnaire on a face-to-face interview. Data were collected on the participants' demographic characteristics, medical histories, and lifestyles. Trained observers measured the body height, weight, waist circumference, and BP of each participant according to the standardized protocol. While participants were in the standing position, their waist circumference was measured midway between the lower rib margin and the iliac crest. The body height was measured in meters while participants were not wearing shoes. The body weight was measured after participants removed heavy clothing, and 1 kg was deducted for the remaining garments.

2.4. Definition of MCI

Cognitive status was assessed by the MMSE, which is a commonly used measurement recommended by guidelines, specially for hypertensive population.[20] Before starting the study, field workers were trained by experienced neuropsychologist. MCI is defined as an MMSE score <17 for illiterate subjects, <20 for subjects with 1 to 6 years of education, and <24 for subjects with ≥7 years of education. These MMSE score cutoff points demonstrated high efficiency in diagnosing MCI in China.[21,22]

2.5. BP measurement and definitions

Before the BP measurement, each participant was asked to avoid drinking alcohol, smoking cigarettes, and drinking coffee or tea. Each participant's BP records were obtained using with the OMRON HBP-1300 Professional Portable Blood Pressure Monitor (OMRON, Kyoto, Japan) 3 times on the right arm positioned at heart level after the participant was sitting at rest for 5 minutes, with 30 seconds between each measurement with an observer present. The average of the 3 readings was used for analysis. Hypertension is defined as systolic blood pressure (SBP) ≥140mm Hg, and/or diastolic blood pressure (DBP) ≥90mm Hg, and/or use of antihypertensive medicine within 2 weeks, based on the 2018 Chinese Hypertension Guideline.[23] Awareness is defined as self-report of any previous diagnosis of hypertension by a doctor, treatment as self-reported use of a prescription medication for hypertension within 2 weeks at the time of the interview, and control as SBP < 140 mm Hg and DBP < 90 mm Hg.

2.6. Other variables and definitions

Additional covariates were considered, such as sex, age group (45–60 and ≥60 years old), and educational level: illiterate and primary school (≤6 years), junior high school (7–9 years), and senior high and above (≥9 years including technical education, college, and university). We also collected demographic information (gender and age), lifestyle (cigarette smoking and alcohol consumption), disease history (including hypertension, diabetes mellitus, dyslipidemia, and those in exclusion criteria), and use of medications (including anti-hypertensive agents) via a questionnaire. Alcohol intake is defined as consuming alcoholic beverage at least once per week in the past month. Cigarette consumption is defined participants who have smoked at least 20 packets of cigarettes in their lifetime and currently smoke cigarettes and non-smokers as participants who never smoked or smoked <20 packets of cigarettes in their entire lifetime.[17] Body mass index (BMI) was calculated by dividing weight (in kilograms) by height (in meters) squared (kg/m^2). Based on the criteria recommended by the Working Group on Obesity in China, general obesity is defined as normal: BMI < 24.0 kg/m^2, overweight: BMI 24.0–28.0 kg/m^2, and general obesity: BMI ≥ 28 kg/m^2. Diagnosis of diabetes mellitus and dyslipidemia was based on the self-report of participants.

2.7. Statistical analysis

The baseline characteristics were described using descriptive statistics. Nonparametric (Mann–Whitney) test was used to assess between-group differences in the continuous variables including age, BMI, SBP, DBP, and MMSE scores since they were not normally distributed. χ2-test was used to assess between-group differences of categorical variables (such as MCI prevalence). The relationship between BP levels and the MMSE score (continuous variable) was examined using Spearman correlation analysis. Potential risk factors for MCI were assessed by using univariate and multivariate logistic regression analyses to calculate the odds ratios (OR) with respective 95% confidence intervals (95%CI). All analyses were conducted with SPSS, version 19 for Windows (SPSS Inc., Chicago, IL). A two-sided $P < .05$ was defined as statistical significance.

3. Results

In total, 3301 subjects completed the survey with a response rate of 89.1% (3301/3702), and additional 19 subjects were further excluded due to incomplete information on educational status (n=11) and BP measurement (n=8). Finally, complete data for 3282 subjects were analyzed. Study subjects with median age 55.0 (49.0,75.0) years included 50.7% hypertensive (n=16,675) and 55.9% women subjects (n=1833), characterized by more middle aged subjects (65.2%) and lower education attainment (51.4% had primary and lower education, Table 1).

Table 1

Characteristics of study subjects.

Characteristics	Total	Normotensives	Hypertensives	*P* value
Overall (n,%)	3282	1618 (49.3)	1667 (50.7)	
Gender (n,%)				
Men	1449 (44.1)	697 (43.2)	752 (45.1)	.261
Women	1833 (55.9)	918 (56.8)	915 (54.9)	
Age (y)	55.0 (49.0,75.0)	53.0 (48.0, 58.0)	57.0 (51.0, 65.0)	<.001
Age groups (n,%)				
45-59	2140 (65.2)	1234 (76.4)	906 (54.3)	<.001
≥60	1142 (34.8)	381 (23.6)	761 (45.7)	
Ethnicity (n,%)				
Han	1528 (46.8)	826 (51.3)	702 (42.3)	<.001
Kazakh	1279 (39.1)	528 (32.8)	751 (45.3)	
Others	461 (14.1)	256 (15.9)	205 (12.4)	
Education (n,%)				
Primary and lower	1673 (51.4)	737 (45.9)	936 (56.7)	<.001
Junior high	1159 (35.6)	640 (39.9)	519 (31.4)	
Senior high and higher	425 (13.0)	228 (14.2)	197 (11.9)	
Cigarette consumption (n,%)				
Yes	720 (22.0)	377 (23.4)	343 (20.6)	.149
No	2550 (78.0)	1233 (76.6)	1317 (79.3)	
Alcohol intake (n,%)				
Yes	807 (24.7)	410 (25.5)	397 (23.9)	.348
No	2460 (75.3)	1198 (74.5)	1262 (76.1)	
BMI (kg/m^2)	25.9 (23.3, 28.7)	25.0 (22.5, 27.6)	26.8 (24.3, 29.8)	.305
Overall obesity (n,%)				
BMI < 24 kg/m^2	994 (30.9)	620 (39.5)	374 (22.7)	<.001
BMI ≥ 24-27.9 kg/m^2	1217 (37.9)	609 (38.8)	608 (36.9)	
BMI ≥ 28 kg/m^2	1004 (31.2)	340 (21.7)	664 (40.3)	
Diabetes diagnosis (n,%)				
Yes	230 (7.1)	75 (4.7)	155 (9.4)	<.001
No	3018 (92.9)	1527 (95.3)	1491 (90.6)	
Dyslipidemia (n,%)				
Yes	483 (15.3)	136 (8.6)	347 (22.0)	<.001
No	2669 (84.7)	1439 (91.4)	1230 (78.0)	
Systolic blood pressure (mm Hg)	130 (117, 143)	119 (110,127)	143 (135, 156)	<.001
Diastolic blood pressure (mm Hg)	80 (74,90)	76 (70, 80)	90 (80, 95)	<.001

BMI=body mass index.

Table 2

Prevalence of mild cognitive impairment in total hypertensive subjects and those with and without awareness, treatment, and controlled blood pressure (n,%).

Subjects	Mild cognitive impairment	F/P	Total
Normotensives	260 (16.1)	18.15/<.001	1618 (49.3)
Hypertensives	368 (22.1)		1667 (50.7)
Aware	254 (23.0)	1.22/.285	1105 (66.3)
Unaware	114 (20.4)		562 (33.7)
Treated	178 (21.3)	0.545/.487	838 (50.3)
Untreated	189 (22.9)		828 (49.7)
Controlled	73 (20.7)	6.55/.010	352 (21.1)
Uncontrolled	361 (27.5)		1315 (78.9)

Hypertensive subjects were significantly older [57.0 (51.0, 65.0) vs 53.0 (48.0, 58.0), $P<.001$], obese (40.3% vs 21.7%, $P<.001$), diabetic (9.4% vs 4.7%, $P<.001$), and with dyslipidemia (22.0% vs 8.6%, $P<.001$) and with lower education attainment (56.7% vs 45.9%, $P<.001$), compared to non-hypertensive subjects as in Table 1.

As shown in Table 2, the prevalence of MCI was significantly higher in hypertensive subjects than in non-hypertensive subjects (22.1% vs 16.1%, $P<.001$). In addition, hypertensive subjects with non-controlled BP levels showed significantly higher prevalence of MCI, compared to those with controlled BP (27.5% vs 20.7%, $P=.01$). Nonetheless, the prevalence of MCI revealed no significant differences between hypertensive subjects with and without awareness (23.0% vs 20.4%, $P=.285$) and between those who were treated and not treated (21.3% vs 22.9%, $P=.487$).

In Table 3, we compared the each and total score of MMSE between hypertensive and non-hypertensive subjects. The results showed that hypertensive subjects had significantly lower each item score and total score, compared to non-hypertensive subjects (P for all <.001).

In Table 4, we conducted correlation analysis of SBP and DBP with each and total score of MMSE. Significant negative correlations were observed between SBP and DBP with each and total score of MMSE, except for DBP and registration ($P=.150$) and recall item ($P=.667$).

In Table 5, we conducted univariate and multivariate logistic regression analysis for the related factors of MCI including gender, cigarette consumption. and alcohol intake as co-variates

Table 3

Comparison of each and total Mini-Mental State Examination score between hypertensive and normotensive subjects.

Characteristics	Normotensives (1618)	Hypertensives (1667)	P
Orientation	10.0 (9.0, 10.0)	10.0 (8, 10)	<.001
Registration	3.0 (2.0, 3.0)	3.0 (1.0, 3.0)	<.001
Attention and calculation	3.0 (2.0, 5.0)	3.0 (1.0, 5.0)	<.001
Recall	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	<.001
Language and Praxis	9.0 (7.0, 9.0)	8.0 (6.0, 9.0)	<.001
Total score	26.0 (23.0, 28.0)	24.0 (21.0, 27.0)	<.001

even though they did not show significant differences between non-hypertensive and hypertensive subjects, since previous studies reported that female gender, cigarette consumption, and heavy alcohol intake are associated with MCI. The results showed that hypertension was the significant factor for the presence of MCI (OR=1.62, 95%CI: 1.34,2.35, $P<.001$), independent of such factors as gender, age, education attainment, and dyslipidemia.

4. Discussion

This is a population-based, cross-sectional study aimed to investigate the relationship of BP and hypertension with MCI in population from an economically less developed region in Northwest China. Main results encompassed that the prevalence of MCI is significantly higher in hypertensive subjects than in non-hypertensive ones and significantly higher in hypertensive subjects with non-controlled BP than in those with controlled BP. Hypertension is a significant related factor for the presence of MCI with an OR of 1.62, independent of well-defined risk factors for MCI. In addition, hypertensive subjects had significantly lower each item score and total score, compared to non-hypertensive subjects and significant negative correlations were observed between SBP and DBP with each and total score of MMSE.

Current study adds evidence on on-going debate whether hypertension is associated with cognitive impairment in hypertensive population specially from low income regions, since existing data is mixed, with some studies suggesting that exposure to high BP is associated with worse cognitive function but other studies reporting the opposite, a U-shaped, or no

Table 4

Correlation between systolic and diastolic blood pressure with each and total Mini-Mental State Examination score.

		Systolic blood pressure	Diastolic blood pressure
Orientation	Correlation coefficient	−0.089	−0.051
	P	<.001	.006
Registration	Correlation coefficient	−0.063	−0.027
	P	.001	.150
Attention and calculation	Correlation coefficient	−0.097	−0.038
	P	<.001	.037
Recall	Correlation coefficient	−0.056	−0.008
	P	.002	.667
Language and praxis	Correlation coefficient	−0.108	−0.059
	P	<.001	.001
Total score	Correlation coefficient	−0.145	−0.064
	P	<.001	<.001

Table 5

Univariate and multivariate logistic regression analysis for related factors of mild cognitive impairment.

	Univariate			Multivariate		
	OR	95%CI	*P*	OR	95%CI	*P*
Gender (n,%)						
Men	Ref		.001	Ref		
Women	1.32	1.13,1.55		1.40	1.16,1.53	<.001
Age groups						
45–59	Ref			Ref		
≥60	1.75	1.49,2.05	<.001	1.65	1.48,2.12	<.001
Ethnicity						
Han	Ref			Ref		
Kazakh	1.98	1.67,2.35	<.001	2.76	1.71,4.44	<.001
Others	1.40	1.10,1.79	.006	0.95	0.52,2.03	.948
Education						
Senior high and higher	Ref			Ref		
Primary and lower	2.13	1.61,2.81	<.001	1.20	0.61,2.35	.596
Junior high	1.87	1.40,2.50	<.001	2.52	1.37,2.49	.005
Overall obesity						
Normal weight	Ref			Ref		
Overweight	0.765	0.63,0.93	.006	0.81	0.54,1.46	.640
Obesity	0.997	0.82,1.21	.978	0.89	0.51,1.56	.682
Diabetes diagnosis						
No	Ref			Ref		
Yes	1.02	0.75,1.38	.900	1.16	0.55,2.45	.695
Dyslipidemia						
No	Ref			Ref		
Yes	1.24	1.01,1.54	.045	0.97	0.47,1.61	.665
Hypertension						
No	Ref			Ref		
Yes	1.86	1.59,2.18	<.001	1.62	1.34,2.35	<.001
Alcohol intake						
No	Ref			Ref		
Yes	0.82	0.59,1.39	.685	0.70	0.42,1.17	.171
Cigarette consumption						
No	Ref			Ref		
Yes	0.92	0.75,1.13	.405	1.07	0.62,1.85	.807

95%CI: 95% confidence interval, OR: odds ratio.

association.[16] Our results show that hypertension is a risk factor for the presence of MCI in population living in less developed region characterized low income and low educational attainment, which is consistent with previous data.[8,24] The inconsistency of results among previous data may reflect differences in aspects of study design, differences in characteristics of the study populations, and varying age ranges, adjustment for shared determinants that may confound the hypertension-cognition association and reverse causation that may also contribute to the observed association between BP and cognition, especially in studies with cross-sectional design. The wealth of literature suggests low socioeconomic position, which is assessed by using a range of measures including educational attainment, is associated with cognition. Therefore, the population, with approximate conditions with our study subjects from less developed regions characterized by low income and by the disparities in relevant risk factors of MCI between developed and less-developed regions due to the big difference in health awareness and accessibility to health service, may experience a higher prevalence of MCI since almost 57% of subjects with hypertension have primary and lower education attainment. In addition, it has been well-evidenced that only 8% of hypertensive population from less-developed regions of China including Xinjiang have their BP controlled.[17] In fact, it has been shown that poor control of BP and BP variability are associated with adverse cardio-cerebrovascular events and decreased cognition.[25] On the other hand, control of BP and maintaining its stability have shown protective roles in cerebral functions and in prevention of or delay in cognitive decline.[26–28] Therefore, control of BP and maintaining its stability could represent a significant goal in clinical practice to preserve cognition, and prevent or delay the cognitive decline, even if evidence is lacking on superiority of specific anti-hypertensive agents on this aspect currently.

Current study contains some different results, compared with other studies. The prevalence of MCI in hypertensive and non-hypertensive subjects are higher than previous reported data (12%–20%). The study was conducted in multi-ethnic rural region. 53.2% of study subjects are ethnic minorities, and 57% have primary and lower educational attainment, which may have brought some difficulties in understanding the MMSE contents, even if language assistance was provided during the on-site survey. Nonetheless, the consistent higher rates in both groups may reflect the credibility of the results. In addition, we failed to observe differences in the prevalence of MCI between aware and unaware, treated and untreated hypertensives, which is inconsistent with the results of the study conducted in Beijing.[8] Wang et al reported that the awareness, treatment and control rates of hypertension are significantly lower in population from less-developed region like Xinjiang than in those from developed parts of China including Beijiang.[17] The low rates of awareness and treatment may have under-powered data to observe such small effects on MMSE. Thus, this aspect may need a specific aimed study with sufficient sample to be further clarified.

This study is strengthened by larger sample size, strict data collection and analysis procedure, and inclusion of diverse population (e.g., Han, Kazakh, Uygur), and broader age range, which may merit the data quality and generalizability. Nonetheless, it should be kept in mind that current study contains some limitations while interpreting the results. First, cross-sectional design could not allow us to draw casual conclusion between BP, hypertension, and MCI. Nonetheless, it has increasingly accepted that elevated BP is a risk factor for MCI, and thus, current results extend this phenomenon to the developing regions. Cross-sectional design also made it difficult to have data on BP variability, which may have underpowered the strength of the evidence on the effects of BP indices on cognitive status. Cross-sectional nature of the study also would not allow us to determine a causal relationship, or the reverse causation, between hypertension and MCI. However, recent intervention studies found that better BP control is associated with lower incidence of MCI within about 3 years of follow-up, whereas further research is still warranted on this aspect, while considering the limitations of studies conducted.[27] Second, we excluded the subjects with confirmed dementia and Alzheimer disease at enrollment, which may have brought up selection bias for and underpowering of our study results if they were the consequence of hypertension. This will be considered in future studies. Third, we failed to collect the information on occupation or use of pesticides/herbicides, on access to health care, on diet habits, and nutrition intake and failed to objectively measure the blood lipids and glucose levels, which may have brought some bias to our results. However, previous studies have shown that population involving in manual labor (such as agricultural region) or using pesticides/herbicides are at risk for cognitive decline,[29] and thus advocating higher attainment of education and mental labor and the avoiding the use of pesticides/herbicides are still significant parts in prevention of cognitive decline. Fourth, study population is selected from 1 site of Xinjiang, which makes the data difficult to generalize to other parts of China, even of Xinjiang. Nonetheless, the larger sample size, diversity of population, and broader age ranges may add some merits in terms of generalizing the results to other population in Xinjiang, China and even to Central Asia population, since some population from Xinjiang and Central Asia share life style and even genetic background and living a life in developing regions.

In conclusion, the prevalence of MCI is higher in hypertensive population, and hypertension shows an increased OR for MCI, independent of some well-known risk factors. Our results suggest that hypertensive population should be screened for MCI in order to provide improved diagnoses and optimal therapeutics for cognitive decline prevention, specially in settings with approximate conditions.

Author contributions

Nanfang Li put forward the idea, designed the study, participated the survey, and provided critical suggestion in writing the paper. Mulalibieke Heizhati and Lin Wang designed the survey, conducted the on-site survey, analyzed the data, and wrote the paper. Mei Li, Zhikang Yang, Zhongrong Wang, and Reyila Abudureyimu participated in the data collection, data input and provided suggestion in wring the paper.

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