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Long-Term Exposure to Ambient Fine Particles and Heart Rate in Northwestern China: Findings from 1.8 Million Adults of the Kashgar Prospective Cohort Study (KPCS)

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Abstract: Elevated heart rate (HR) can be hypothesized to be involved in the pathways by which ambient air pollution, especially fine particulate matter ($PM_{2.5}$), causes cardiovascular morbidity and mortality. However, evidence concerning long-term $PM_{2.5}$ exposure and HR is still limited. Therefore, in this study, we assessed the associations of $PM_{2.5}$ with HR levels and tachycardia prevalence and explored potential modifiers of the associations. We used baseline data of 1,802,207 adults from the Kashgar Prospective Cohort Study (KPCS). $PM_{2.5}$ exposure was assessed based on satellite sensing data, meteorological factors, multi-resolution emission inventory, and measurements from ground-based surface monitors measurements. HR was measured using a calibrated electronic sphygmomanometer, and tachycardia was defined as resting heart rate (RHR) equal to or greater than 80 beats per minute. Linear regression and logistic regression models were employed to evaluate the associations of $PM_{2.5}$ levels with RHR levels and tachycardia prevalence, respectively. Stratified analyses by sex, age, ethnicity, smoking status, alcohol use, and physical activity were also performed. The mean (standard deviation) age of the study participants was 39.4 (15.5) years old. In the adjusted models, an interquartile range (8.8 $\mu g/m^3$) increase in $PM_{2.5}$ levels was associated with 0.515 (95% confidence interval: 0.503–0.526) bpm increase in RHR levels and with 1.062-fold (95% confidence interval: 1.059–1.064) increase in the odds of tachycardia. The results were robust against several sensitivity analyses. In addition, we observed the above associations were stronger in participants that were men, of Uyghur ethnicity, smoking cigarettes, drinking alcohol, and having physical inactivity, compared to their counterparts. In summary, our findings indicate that long-term exposure to ambient $PM_{2.5}$ may be hazardously associated with HR, and women, Uyghur people, and those with unhealthy lifestyles may be more vulnerable to the hazardous effects.

Keywords: air pollution; $PM_{2.5}$; heart rate; tachycardia; Xinjiang; Northwestern China

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1. Introduction

Air pollution, especially fine particulate matter (with aerodynamic diameter equal to or less than 2.5 μm, $PM_{2.5}$), remains the leading environmental threat to people's health

worldwide [1]. Accumulating studies have documented that long- and short-term exposure to $PM_{2.5}$ can cause many health conditions [2]. The existing evidence generally supported that $PM_{2.5}$ is a risk factor for cardiovascular morbidity and mortality [3,4]. However, the underlying mechanisms are still unclear. A large number of studies have suggested that elevated resting heart rate (RHR) is an independent risk factor of cardiovascular diseases [5,6]. Thus, it is biologically plausible that RHR might be a mediator between $PM_{2.5}$ exposure and cardiovascular diseases.

Mechanistic evidence indicates that $PM_{2.5}$ exposure can induce systemic inflammation [7], oxidative stress [8], autonomic dysfunction [9], and epigenetic changes [10], which are involved in the pathogenesis of the development of elevated RHR levels and tachycardia [11,12]. In fact, many past epidemiological studies have examined the association between $PM_{2.5}$ and RHR, and most of them focused on the effects of short-term $PM_{2.5}$ exposure but generated mixed results [13–17]. For example, a study performed among adults in Taiwan, China, reported that short-term exposure (7-day average concentration) to $PM_{2.5}$ was associated with elevated RHR levels [17]. Similarly, a study of 28 young adults from the USA reported that a 10-$\mu g/m^3$ increase in the same day of $PM_{2.5}$ levels was associated with a 2.1 beats per minute (bpm) increase in HR [16]. However, there are also studies that reported null or even inverse associations [13–15].

For the association between long-term $PM_{2.5}$ exposure and HR, only a few studies were performed and were limited to specific or local populations [18,19]. For example, a large cross-sectional study in reproductive-age Chinese adults reported that greater $PM_{2.5}$ levels were associated with higher RHR levels and tachycardia prevalence [18]. Similar positive association was reported in adult population in north China [19]. To the best of our knowledge, no study has explored the effects of $PM_{2.5}$ on HR among people living in northwestern China, where air pollution sourced from natural dust is always severe.

Kashgar prefecture is located in the westernmost part of Xinjiang, China, which is an area surrounded by deserts and thus was highly polluted by dust storms [20]. Over 90% of the residents were of Uyghur ethnicity and the prevalence of cardiovascular disease is always reported to be high [21]. In addition, due to relatively lower economic levels, less medical resources, and less healthcare knowledge [22], people in this region may be more vulnerable to the hazardous effects of $PM_{2.5}$. Therefore, we hypothesized a hazardous association between long-term exposure to $PM_{2.5}$ and RHR levels and tachycardia prevalence, and tested the hypothesis using a large sample of the general population in Kashgar region. We also explored if there existed potential modifiers for the associations.

2. Materials and Methods

2.1. Study Population

Data for this study were extracted from the Kashgar Prospective Cohort Study (KPCS), an ongoing longitudinal study based on the Free Universal Health Examination Program. Details on the protocols of the study have been published elsewhere [23]. Briefly, the program was launched by the government in 2016 to facilitate health promotion and management, which provides annual free health examinations for all residents in the Kashgar prefecture (including Kashi city and 11 surrounding counties) (Figure 1). Participants underwent standardized questionnaire interviews in the community (for urban areas) and village (for rural areas) healthcare centers. Anonymized data were collected from the participants, including demographics, socioeconomic status, lifestyles, and medical history. In addition, a series of medical examinations were conducted by professionals and trained physicians to collect data on anthropometric measurements, personal health status, and laboratory measurements. Residents were encouraged to participate in the health examination program annually.

KPCS is a dynamic cohort with no end date. KPCS used participants' data collected between January and December in 2017 as baseline data because the health examination program in 2016 was still in its pilot period and covered a small part of residents. In 2017, a large proportion of residents participated in the examination, and we included them as the

baseline data of our cohort to maximize the sample size. For the current analysis, baseline data of 2,050,614 individuals from KPCS were initially included. Then, we excluded 109,841 individuals aged less than 15 years old, and further excluded 138,420 individuals with missing outcomes and 146 individuals with missing covariates, leaving a total of 1,802,207 participants for the final analysis. Each participant signed a consent form to authorize the government to use data from this health examination program. We got permission from the government to derive data collected via questionnaires and health examinations, and the study protocol was approved by the Ethical Committee of the First People's Hospital of Kashi.

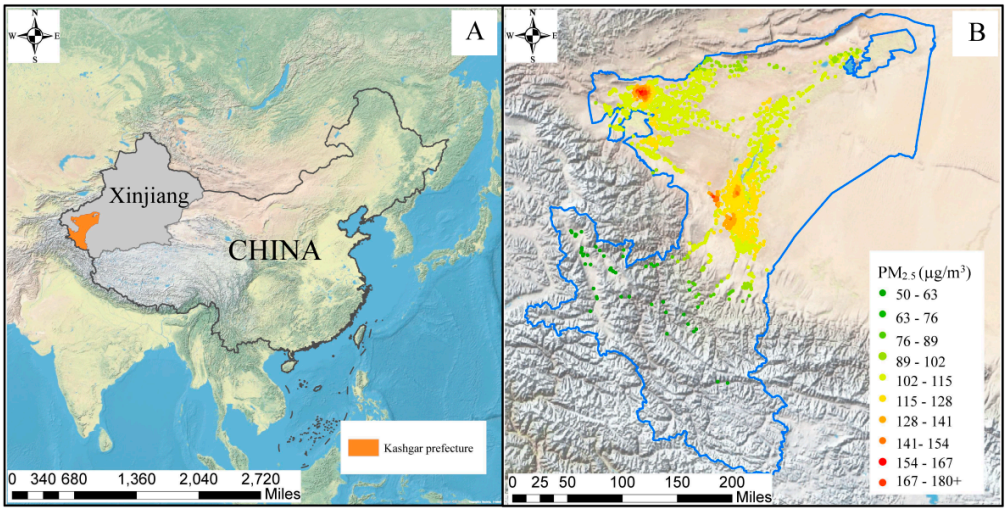

Figure 1. Map of China showing study location (**A**) and $PM_{2.5}$ concentrations (**B**).

2.2. Exposure Assessment

The annual $PM_{2.5}$ data were obtained from the widely used ChinaHightAirPollutants (CHAP) dataset developed by Wei et al. [24,25]. The dataset was predicted based on satellite sensing data, meteorological factors, multi-resolution emission inventory, and ground-based surface monitor measurements at a resolution of 0.01° (≈1 km). The cross-validation coefficient of determinations (CV-R^2) and root-mean-square errors were 0.92 μg/m^3 and 10.76 μg/m^3, respectively. Then, we calculated one-year (2016) average concentrations of $PM_{2.5}$ before the survey year (2017) and assigned them to each of the study participants as main exposure. Two- (2015–2016) and three- (2014–2016) year average concentrations were also calculated and used in sensitivity analyses.

2.3. Outcome Assessment

Participants were instructed to refrain from physical work, exercise, and smoking on the day of the health examination. RHR was measured by trained physicians using a calibrated electronic sphygmomanometer while the participant was in the supine position, with an appropriate cuff at heart level after five to ten minutes of rest. Two or more measurements were averaged. If the difference between the first two measurements was greater than five bpm, another measurement was performed and the results were averaged. We defined tachycardia as an RHR > 80 bpm [26,27].

2.4. Confounders

We collected data on socio-demographics, socioeconomic status, and behavioral habits through the completion of a standardized questionnaire. Sociodemographic information consisted of age (in years), sex (man/woman), and ethnicity (Han/Uyghur/other). Variables on socioeconomic status included economic status (poor household/non-poor household), occupation (unemployed/farmer/worker/office clerk/other), and education level (schooling ≤ 9 years/schooling > 9). Data on behavioral habits included cigarette

smoking (yes/no), alcohol use (yes/no), physical inactivity (yes/no), and dietary pattern (omnivorous/plant-based/meat-based). Health information, including body mass index (BMI), hypertension, diabetes, cardiovascular disease, and renal disease, were obtained through medical records. Meteorological factors including 1-year (2016) average levels of humidity and temperature were retrieved from the ERA5-Land dataset (https://cds.climate.copernicus.eu accessed on 2 December 2022), which was estimated at a 0.1° (≈10 km) resolution using machine learning methods based on ground observation data and remote sensing data.

For a variable to be considered as a confounder, the following criteria had to be met. First, the variable had to be a risk factor for elevated RHR or tachycardia. Second, it had to be related to $PM_{2.5}$ exposure. Third, it could not be a mediator on the pathway between $PM_{2.5}$ exposure and elevated RHR or tachycardia [28]. We applied a directed acyclic graph (DAG, Figure S1) to retain a minimally sufficient set of confounders in the adjusted models. The following confounders were included: age, sex, ethnicity, education level, economic status, occupation, residential setting, physical inactivity, humidity, and air temperature.

2.5. Statistical Analysis

We employed linear and logistic regression models to evaluate the associations of $PM_{2.5}$ exposure with RHR levels and tachycardia prevalence, respectively. We also used natural cubic spines to plot the concentration-response curves of $PM_{2.5}$ exposure to RHR levels and tachycardia prevalence. Associations of $PM_{2.5}$ concentrations with tachycardia and RHR levels were presented both corresponding to an interquartile range (IQR) difference in $PM_{2.5}$ exposure and by quartiles because natural cubic regression splines indicated slightly nonlinear relationships (Figure 2). Effect estimates of the associations were presented as beta (β) and odds ratios (ORs) with their 95% confidence intervals (CIs). We adjusted the main models for the variables listed in the confounders section. Among them, humidity and air temperature were incorporated as natural splines with four degrees of freedom, selected based on Akaike information criterion for three to five degrees of freedom. In addition, stratification analyses were performed to test effect modification by sex, age, ethnicity, smoking status, alcohol use, and physical activity [29]. We assessed differences in the association between subgroups using a two-sample z-test, based on the point estimates and SEs [30].

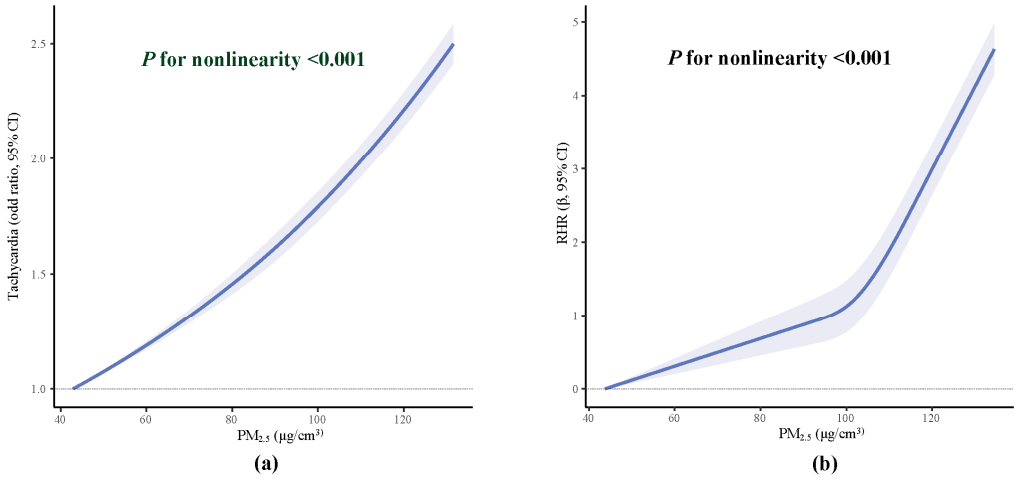

Figure 2. The concentration-response curves for $PM_{2.5}$ exposure on tachycardia (**a**) and RHR (**b**). Adjusted for age, sex, ethnicity, education level, economic status, occupation, residential setting, physical inactivity, humidity, and temperature. Abbreviation: RHR: resting heart rate; β: regression coefficient.

We performed a set of sensitivity analyses to test the robustness of our results. First, we re-calculated 2-year (i.e., 2015–2016) and 3-year (i.e., 2014–2016) average concentrations of $PM_{2.5}$ rather than the current 1-year average to test potential exposure misclassification.

Second, we repeated the analysis by additionally adjusting for smoking status, alcohol use, hypertension, and body mass index to test potential confounding effects of risk factors for tachycardia [29]. Third, we repeated the analysis by excluding participants with cardiovascular disease, renal disease, and diabetes to test the potential confounding effects of the existing diseases.

All statistical analyses were performed in R 4.1.5 (R Core Team, Vienna, Austria). A $p < 0.05$ for a two-tailed test was considered statistical significance.

3. Results

3.1. Baseline Characteristics

A total of 1,802,207 participants were included in the current study. Mean (SD) age of the participants was 39.4 (15.5) years old (Table 1). About half of the participants were women, 96.4% were of Uyghur ethnicity, 86.9% had less than 9 years of schooling, 75.7% were farmers, and 24.9% lived in urban areas. One-year average $PM_{2.5}$ levels ranged from 49.7 to 183.5 $\mu g/m^3$ with a mean (SD) value of 102.3 (10.9) $\mu g/m^3$.

Table 1. Characteristics of the study population.

Characteristics	Non-Tachycardia (N = 1,236,049)	Tachycardia (N = 566,158)	Overall (N = 1,802,207)	*p*-Value
Age {y, [mean (SD)]}	39.1 (15.1)	40.0 (16.3)	39.4 (15.5)	<0.001
Woman [n (%)]	586,939 (47.5)	337,745 (59.7)	924,684 (51.3)	<0.001
Ethnicity [n (%)]				<0.001
Han	38,328 (3.1)	15,189 (2.7)	53,517 (3.0)	
Uyghur	1,183,170 (95.7)	545,876 (96.4)	1,729,046 (95.9)	
Other	14,551 (1.2)	5093 (0.9)	19,644 (1.1)	
Years of schooling ≤ 9	1,074,860 (87.0)	490,559 (86.6)	1,565,419 (86.9)	<0.001
Poor household [a]	347,365 (28.1)	149,656 (26.4)	497,021 (27.6)	<0.001
Occupation [n (%)]				<0.001
Unemployed	51,243 (4.1)	28,830 (5.1)	80,073 (4.4)	
Worker	71,885 (5.8)	32,572 (5.8)	104,457 (5.8)	
Farmer	943,610 (76.3)	420,013 (74.2)	1,363,623 (75.7)	
Office clerk	49,169 (4.0)	22,019 (3.9)	71,188 (4.0)	
Other	120,142 (9.7)	62,724 (11.1)	182,866 (10.1)	
Urban residence [n (%)]	304,434 (24.6)	144,237 (25.5)	448,671 (24.9)	<0.001
Cigarette smoking [b] [n (%)]	171,405 (13.9)	55,860 (9.9)	227,265 (12.6)	<0.001
Alcohol use [n (%)]	77,682 (6.3)	25,940 (4.6)	103,622 (5.7)	<0.001
Physical inactivity [c] [n (%)]	1,020,768 (82.6)	467,998 (82.7)	1,488,766 (82.6)	0.20
Dietary pattern [n (%)]				<0.001
Omnivorous	1,116,179 (90.3)	512,102 (90.5)	1,628,281 (90.3)	
Plant-based	80,486 (6.5)	35,968 (6.4)	116,454 (6.5)	
Meat-based	39,384 (3.2)	18,088 (3.2)	57,472 (3.2)	
BMI {kg/m^2, [mean (SD)]}	24.4 (5.3)	24.7 (5.6)	24.5 (5.4)	<0.001
Renal disease [n (%)]	4345 (0.4)	2542 (0.4)	6887 (0.4)	<0.001
Diabetes [d] [n (%)]	44,493 (3.6)	33,722 (6.0)	78,215 (4.3)	<0.001
Hypertension [e] [n (%)]	146,645 (11.9)	94,460 (16.7)	241,105 (13.4)	<0.001
Cardiovascular disease [n (%)]	98,699 (8.0)	50,859 (9.0)	149,558 (8.3)	<0.001
$PM_{2.5}$ {$\mu g/m^3$, [mean (SD)]}	102.0 (10.9)	103.0 (11.0)	102.3 (10.9)	<0.001
Resting heart rate {bpm, [mean (SD)]}	71.46 (7.7)	88.78 (7.0)	76.90 (11.0)	<0.001

Abbreviation: BMI: body mass index; RHR: resting heart rate; SD, standard deviation; $PM_{2.5}$, particulate matter with an aerodynamic diameter less than or equal to 2.5 μm. [a] Poor household was defined as a net annual household income $\leq$ 2952 Yuan per person. [b] Cigarette smoking was defined as having smoked at least 100 cigarettes in a lifetime. [c] Physical inactivity was defined as exercise frequency < 1/week. [d] Diabetes was defined as a fasting blood glucose of 7.0 mmol/L or higher and/or having antidiabetic therapy. [e] Hypertension was defined as mean systolic blood pressure > 140 mmHg, mean diastolic blood pressure > 90 mmHg, and/or being on antihypertensive drugs within 2 weeks.

The mean (SD) RHR level was 16.9 (11.0) bpm, and 566,158 participants (31.4%) were classified as having tachycardia. Compared with participants with normal RHR levels, those with tachycardia were more likely to be men (52.5% vs. 40.3%), have low economy levels (28.1% vs. 26.4%), to be farmers (76.3% vs. 74.2%), live in rural areas (75.4% vs. 74.5%), drink alcohol (6.3% vs. 4.6%), and smoke cigarettes (13.9% vs. 9.9%).

3.2. Associations of $PM_{2.5}$ with RHR Levels and Tachycardia Prevalence

The tests of linearity showed that the association between $PM_{2.5}$ levels and tachycardia prevalence was almost linear (Figure 2). We observed that higher $PM_{2.5}$ levels were associated with higher RHR levels and a greater tachycardia prevalence. More specifically, in the adjusted models, an IQR increase in $PM_{2.5}$ levels was associated with 0.515 (95% CI: 0.503–0.526) bpm increase in RHR levels and with 1.062-fold (95% CI: 1.059–1.064) increase in odds of tachycardia. When we categorized $PM_{2.5}$ levels into quartiles, we found that, compared with the bottom quartile of $PM_{2.5}$, those at the 2nd, 3rd, and 4th quartiles were associated with 1.079- (95% CI: 1.069–1.090), 1.207- (95% CI: 1.194–1.220), and 1.308- (95% CI: 1.292–1.323) fold increased odds of tachycardia, respectively, and with 0.140 (95%: 0.092–0.187) bpm, 1.349 (95% CI: 1.295–1.403) bpm, and 2.586 (95% CI: 2.528–2.644) bpm increases in RHR levels, respectively (Table 2). Similar effect estimates were observed in crude models (Table S1).

Table 2. Adjusted associations of $PM_{2.5}$ with tachycardia and RHR.

	Tachycardia		RHR (bpm)	
$PM_{2.5}$	**OR (95% CI) [a]**	***p*-Value**	**β (95% CI) [a]**	***p*-Value**
Categories				
Q_1	1 (Reference)		0 (Reference)	
Q_2	1.079 (1.069, 1.090)	<0.0001	0.140 (0.092, 0.187)	<0.0001
Q_3	1.207 (1.194, 1.220)	<0.0001	1.349 (1.295, 1.403)	<0.0001
Q_4	1.308 (1.292, 1.323)	<0.0001	2.586 (2.528, 2.644)	<0.0001
Per IQR increase (8.8 μg/m^3) (14 bpm)	1.062 (1.059, 1.064)	<0.0001	0.515 (0.503, 0.526)	<0.0001

[a] Adjusted for age, sex, ethnicity, education level, economic status, occupation, residential setting, physical inactivity, humidity, and temperature.

When we alternatively used 2-year (Table S2) and 3-year (Table S3) average concentrations of $PM_{2.5}$, the results were consistent with those obtained in the main models. Similar results were also observed when we additionally adjusted the main models for other predictors of tachycardia (Table S4). When we excluded participants with diseases that may affect RHR, the results were also not substantially changed (Table S5).

3.3. Subgroup Analyses

Stratified analyses showed that the associations of $PM_{2.5}$ with RHR levels and tachycardia prevalence were significantly stronger in participants being men, of Uyghur ethnicity, smoking cigarettes, drinking alcohol, and had physical inactivity, compared to their counterparts (all p values for difference < 0.05). No significant effect modification was observed for sex (Table 3).

Table 3. Association of $PM_{2.5}$ with tachycardia and RHR stratified by sex, age group, ethnicity, smoking status, alcohol use, and physical inactivity.

Strata	**Tachycardia**		**RHR (bpm)**	
	OR (95% CI) [a]	***p*-Value for Effect Modification**	**β (95% CI) [a]**	***p*-Value for Effect Modification**
Sex		<0.0001		<0.0001
Man	1.076 (1.072, 1.080)		0.632 (0.616, 0.649)	
Woman	1.052 (1.049, 1.055)		0.430 (0.417, 0.443)	

Table 3. *Cont.*

Strata	Tachycardia		RHR (bpm)	
	OR (95% CI) [a]	*p*-Value for Effect Modification	β (95% CI) [a]	*p*-Value for Effect Modification
Age		0.726		<0.0001
Age ≤ 39	1.064 (1.061, 1.068)		0.591 (0.575, 0.607)	
Age > 39	1.065 (1.062, 1.069)		0.546 (0.531, 0.560)	
Ethnicity		0.027		0.003
Han	1.062 (1.059, 1.064)		0.455 (0.413, 0.497)	
Uyghur	1.073 (1.063, 1.083)		0.522 (0.511, 0.532)	
Cigarette smoking		<0.0001		0.003
No	1.060 (1.058, 1.063)		0.455 (0.413, 0.497)	
Yes	1.075 (1.069, 1.081)		0.522 (0.511, 0.532)	
Alcohol use		0.010		<0.0001
No	1.060 (1.058, 1.063)		0.497 (0.485, 0.509)	
Yes	1.072 (1.064, 1.081)		0.639 (0.599, 0.679)	
Physical inactivity		<0.0001		<0.0001
No	1.060 (1.057, 1.062)		0.504 (0.493, 0.514)	
Yes	1.071 (1.065, 1.076)		0.591 (0.565, 0.617)	

[a] Adjusted for age, sex, ethnicity, education level, economic status, occupation, residential setting, physical inactivity, humidity, and temperature, except the variables were stratified.

4. Discussion

In this large population-based study, we found that exposure to greater $PM_{2.5}$ levels was associated with higher RHR levels and tachycardia prevalence. Several sensitivity analyses documented that the associations were robust. In addition, we observed that participants' sex, ethnicity, and several lifestyles modified the association of $PM_{2.5}$ with RHR and tachycardia.

Several past epidemiological studies conducted in China and other countries have also examined $PM_{2.5}$ exposure with RHR and tachycardia, with most focusing on short-term exposure [13–16]. Consistent with our findings, a nationwide cross-sectional survey of over 10 million reproductive-age adults in China showed that per 10 μg/m^3 increase in 3-year average $PM_{2.5}$ levels was associated with 0.076 bpm elevation in RHR and 1.8% increase in the odds of tachycardia [18]. Another cross-sectional analysis of 27,047 adults from three cities in northern China reported that an IQR increase in 3-year average $PM_{2.5}$ levels was associated with 3.63% (95% CI: 3.07–4.19%) increase in RHR [19]. An Indian study investigated $PM_{2.5}$ exposure sourced from cooking biomass fuel combustion with RHR and reported a positive association between them [31]. Our findings were also consistent with those from short-term exposure studies [16,17,32,33]. For example, in a study of 49 adults living in Taiwan province, China, Tsou et al. observed that an IQR (7.4 μg/m^3) increase in 7-day average $PM_{2.5}$ levels was significantly associated with a 0.229% increase in RHR [17]. A similar positive association was also observed in short-term exposure studies performed in the U.S.A, Canada, and Germany [16,32,33]. However, several short-term exposure studies also reported null or inverse associations of $PM_{2.5}$ with RHR [13–15]. Nevertheless, our current results combined with those from prior long-term exposure studies documented that exposure to greater levels of $PM_{2.5}$ was associated with higher RHR levels and higher odds of tachycardia [18,19].

The exact mechanisms by which long-term exposure to $PM_{2.5}$ cause the development of tachycardia or elevated RHR levels were still not completely understood, but several hypotheses have been proposed. The autonomous nervous system plays a critical role in modulating HR, and prior evidence indicates that $PM_{2.5}$ exposure can cause systemic inflammation, vascular dysfunction, and oxidative stress [7–10], which further affect the autonomous nervous system to favor sympathetic over parasympathetic tone and consequently increase HR levels [34]. More specifically, inhalation of airborne particles could induce excessive generation of reactive oxygen species and/or deficiency in antioxidant capacity, which leads to oxidative stress in the lungs [35]. Oxidative stress in the lungs further induces proinflammatory cytokines like tumor necrosis factor-α (TNF-α), inter-

leukin (IL)-1 and IL-8 that can enter into the peripheral circulatory system, affecting the cardiovascular system [35]. These products may play a role in autonomic imbalance with an increased sympathetic tone and a reduced parasympathetic [36]. In addition, $PM_{2.5}$ and its metal and nano-sized particles may translocate across the alveolar membrane and enter into the circulatory system, thus directly hurting vascular tissue [37]. Furthermore, $PM_{2.5}$ exposure could cause changes of DNA methylation [38], which has also been involved in the pathogenesis of elevated RHR levels [10].

In a stratified analysis, we observed that the association between $PM_{2.5}$ and HR levels was stronger in men than in women, indicating that men may be more vulnerable to the adverse cardiac effects of $PM_{2.5}$. Our finding disagrees with those from Xie et al. [18]. Nevertheless, our finding is explained. A possible explanation is that men are more likely to spend more time outdoors, especially in the study area, and women tend to work at home while men tend to work outside [39]. In addition, men generally had more unhealthy lifestyles like cigarette smoking and alcohol drinking, which are well-documented risk factors for elevated HR [29]. Moreover, our findings showed that participants drinking alcohol, smoking cigarettes, and/or doing less physical activity had stronger positive associations of $PM_{2.5}$ with elevated RHR than their counterparts, although they were inconsistent with some prior studies that failed to find cigarette smoking and alcohol drinking were significant effect modifiers [18,19]. A plausible explanation for this may be that these unhealthy lifestyles have been well demonstrated to be risk factors of heart disorders, including changes in HR [29], and they may consequently interact with $PM_{2.5}$ to increase HR levels. In subgroup analysis by ethnicity, we found that the RHR of the Uyghur population was more likely to be affected by $PM_{2.5}$. To the best of our knowledge, no prior study has compared the ethnicity difference of effect estimates between the Han and Uyghur ethnicities. A possible explanation may be that differences in genetic backgrounds, life habits, and diets interactively contributed to the effect modification of ethnicity.

In interpreting our studies, several limitations should be taken into consideration. First, our study was cross-sectional, which limited the causality between $PM_{2.5}$ exposure and RHR. However, the possibility of reverse causality, i.e., people with elevated HR levels chose to move to places with higher $PM_{2.5}$ levels, was low. Second, we assessed $PM_{2.5}$ levels at the village level rather than individual level for part of the participants, which might have caused exposure misclassification. However, the exposure misclassification is likely to be non-differential with respect to heart rate and thus bias the results towards the null [40]. This means that if we have individual exposure data, the effect estimates would be greater than those observed in our current study. Third, most of the confounders were collected using a questionnaire, thus memory bias is not avoided. In addition, although we have included a set of confounders, some potential confounders (e.g., noise, green space, and indoor air pollution) were not collected, thus residual confounding is still possible. Fourth, HR was only measured for one time, which might not reflect the participants' real condition as HR can be easily affected by many factors. Fifth, our study was performed in a region where $PM_{2.5}$ levels were very high, thus the generalizability of our findings to other populations living in low air pollution regions (e.g., Europe, North America, and southern China) was compromised. However, our findings provide references for Middle Asian countries (e.g., Pakistan, Tajikistan, and Afghanistan) adjacent to the Kashgar region, which were surrounded by desert; air pollution is severe too.

Despite the above limitations, our study still has several apparent strengths. This is one of the few studies that has evaluated long-term exposure to $PM_{2.5}$ and HR and tachycardia and observed positive associations between them. Specifically, our study provided the first piece of evidence on air pollution and HR in a heavily polluted region surrounded by desert. In addition, the sample size of our study is huge, which equals nearly half of the residents in the Kashgar region. Thus, the representativeness and statistical power are well guaranteed.

5. Conclusions

In summary, in this large study, we are the first to examine the potential effects of air pollution on HR and found that exposure to greater levels of $PM_{2.5}$ was associated with higher odds of tachycardia and higher levels of RHR. In addition, people who were male, of Uyghur ethnicity, and had unhealthy lifestyles were more vulnerable to the hazardous effects of $PM_{2.5}$. However, considering the study's cross-sectional nature, potential exposure misclassification, uncontrolled confounders, and limited generalizability, future better-designed longitudinal studies are warranted to validate our findings.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/atmos14020394/s1, Figure S1: Directed acyclic graph for the association of $PM_{2.5}$ with HR; Table S1: Unadjusted associations of $PM_{2.5}$ with tachycardia and RHR; Table S2: Associations of $PM_{2.5}$ with tachycardia and RHR, using the 2015–2016 average concentration of $PM_{2.5}$; Table S3: Associations of $PM_{2.5}$ with tachycardia and RHR, using the 2014–2016 concentration of $PM_{2.5}$; Table S4: Associations of $PM_{2.5}$ with tachycardia and RHR, additionally adjusted for smoking status, alcohol use, hypertension, and body mass index; Table S5: Associations of $PM_{2.5}$ with tachycardia and RHR, excluding participants with cardiovascular disease, renal disease, and diabetes (n = 218,496).

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