scientific reports

OPEN

Using five exposure metrics to explore the association between ambient PM$_{2.5}$ and the hospital admissions for COPD in Tianshui city, China

Deshun Li[1], Jiyuan Dong[3], Xiaoju Liu[2], Juan Shu[2], Lisha Zhu[1] & Hairong Bao[2✉]

Numerous studies have identified air pollutant as a primary risk factor for chronic obstructive pulmonary disease (COPD), particularly for fine particulate matter (PM$_{2.5}$). However, the daily average levels of PM$_{2.5}$ may not accurately reflect the actual exposure level due to the fluctuating air pollutant levels throughout the day and different human activity patterns. Few studies have comparatively analyzed the association between different exposure metrics of PM$_{2.5}$ and COPD hospitalization. We aimed to explore the association between PM$_{2.5}$ and COPD admission in Tianshui city using five different exposure metrics (a) Daily mean concentration (DailyPM$_{2.5}$mean), (b) Daily hourly peak concentration (DailyPM$_{2.5}$max), (c) Daily morning concentration (DailyPM$_{2.5}$mor), (d) Daily evening concentration (DailyPM$_{2.5}$eve) and (e) Daily excessive concentration hours (PM$_{2.5}$DECH). The PM$_{2.5}$DECH was defined as daily total concentration hours > 25 µg/m³. We collected daily records of COPD admission and hourly data on air pollutants and meteorological factors from Tianshui, China, 2018–2019. DailyPM$_{2.5}$mean, DailyPM$_{2.5}$max, DailyPM$_{2.5}$mor, DailyPM$_{2.5}$eve and PM$_{2.5}$DECH were used as the exposure variables. A generalized additive model (GAM) based Poisson-distribution combined with a distributed lag non-linear model (DLNM) was applied to quantify the association between five different exposure metrics of PM$_{2.5}$ and COPD admission. Stratified analyses were conducted to examine the effect modifications of gender, age, and season. The analysis revealed significant associations between five different exposure metrics of PM$_{2.5}$ and COPD admission. PM$_{2.5}$-related risks of COPD admission differed by five exposure metrics. An interquartile range (IQR) increment in DailyPM$_{2.5}$mean at lag06, DailyPM$_{2.5}$max at lag06, DailyPM$_{2.5}$mor at lag04, DailyPM$_{2.5}$eve at lag06 and PM$_{2.5}$DECH at lag07 was associated with a 21.64%(95%CI: 7.46%, 36.68%), 12.84%(95%CI: 1.47%, 24.58%), 16.47%(95%CI: 0.96%, 33.01%), 31.54%(95%CI: 16.49%, 47.58%), and 30.37%(95%CI: 13.91%, 46.88%) increase in Tianshui's COPD admissions, respectively. Associations of COPD admission with five different exposure metrics of PM$_{2.5}$ appeared to be stronger in the cold season and among the females, while we found significantly higher effects in the population < 65 years old. The five metrics of PM$_{2.5}$ exposure and COPD hospitalization show an exposure-response relationship that resembles a function curve that increases monotonically. This study added evidence for increased risk of admissions associated with exposure to the five metrics of ambient PM$_{2.5}$ in Tianshui City, China, and DailyPM$_{2.5}$eve or PM$_{2.5}$DECH may be a significant risk factor for the increased risk of COPD admission, indicating that we should focus more on the relationship between air pollution and related diseases during the evening peak hours.

Keywords Fine particulate matter, Air pollution, COPD, China

Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory airway illness that is characterized by ongoing airflow restriction. Due to the gradual and partially irreversible progression of this condition, COPD

[1]The 1st School of Clinical Medicine, Lanzhou University, Lanzhou 730000, China. [2]The Department of Respiratory and Critical Care Medicine, The First Hospital of Lanzhou University, Lanzhou 730000, China. [3]School of Public Health, Lanzhou University, Lanzhou 730000, China. ✉email: baohr9301@163.com

treatment is challenging and can place a substantial economic burden on patients[1]. As one of the most common respiratory diseases, the global prevalence of COPD reached 212 million in 2019[2]. In China, the number of COPD cases increased from 32.4 million in 1990 to 100 million in 2019[3].

COPD arises when the airways and the lungs become inflamed and damaged due to a variety of factors such as genetic background, smoking, air pollution, occupational dust exposure, biofuel smog, infections, and socioeconomic level[4,5]. Of these, smoking and ambient particulate matter are the primary risk factors. The former is the main contributor, while the latter accounts for 20.7% of COPD cases[3]. An increasing number of studies have indicated that short-term exposure to particulate matter is strongly associated with an increased risk of COPD morbidity[1,5,6]. Particulate matter pollutants are classified according to their aerodynamic diameter. Recent studies have asserted that fine ambient particulate matter with an aerodynamic diameter less than 2.5 μm ($PM_{2.5}$) is more toxic than larger particles due to its ability to infiltrate the lungs and access the pulmonary alveolar area[7–9]. Thus, it has been suggested that $PM_{2.5}$ exacerbates COPD symptoms and increases the risk of COPD[8,9]. Notably, previous studies have utilized the daily mean concentration as a measure to describe exposure levels. Nevertheless, the daily mean concentration does not accurately represent the actual exposure, since individuals are not exposed to outdoor air pollution continuously for 24 h. Besides, this approach ignores the substantial disparities at different time points within one day. Engaging in outdoor activities such as commuting or exercising may result in increased exposure to pollutants. Consequently, utilizing daily mean concentration may introduce possible exposure bias and erroneously assess the impact of air pollution on COPD morbidity. Therefore, it is reasonable to hypothesize that high levels of outdoor air pollution during peak hours have certain effects on COPD morbidity. To mitigate the significant variations in pollution concentration levels on an hourly basis within a given day, we adopted the daily mean concentration ($DailyPM_{2.5}mean$) as well as four other new indicators: (a) Daily hourly peak concentration ($DailyPM_{2.5}max$)[10,11], (b) Daily morning concentration ($DailyPM_{2.5}mor$)[12,13], (c) Daily evening concentration ($DailyPM_{2.5}eve$)[12,13], and (d) Daily excessive concentration hours ($PM_{2.5}DECH$)[14,15]. Subsequently, we quantified the associations between these five $PM_{2.5}$ metrics and the risk of COPD-related admissions.

There is ongoing research examining the associations between COPD hospitalizations and weather-related features such as temperature and humidity. These factors may also lead to an increased risk of respiratory infection and reduced lung function[16,17].

Firstly, we should note that most research regarding associations between COPD hospitalizations and $PM_{2.5}$ was conducted in cities in eastern China and other economically developed areas of China[1,5–9,18]. In contrast, little information is available for cities in the inland provinces of Northwest China. Besides, the documented correlations exhibit inconsistencies and diverge greatly among various geographical regions. These discrepancies are most likely due to disparities in environmental conditions, population demographics, or socioeconomic progress. For instance, some studies observed a significant positive association between $PM_{2.5}$ and COPD morbidity in Ganzhou[1], Beijing[7], and Ningbo[8]. However, no apparent associations were detected in two other studies in Jinan and Qingdao[5,6]. Moreover, very few studies have examined the association between pollution and COPD utilizing estimations of particulate matter levels using different exposure metrics. Gender and age may also influence the relationships between environmental factors and COPD, since they may impact the physiological parameters or health status of COPD patients. Hence, it is vital to examine the delayed associations between different $PM_{2.5}$ exposure metrics and COPD morbidity in cities in Northwest China, while considering the modified effects of gender and age.

Tianshui is a prefecture-level city in the inland province of Gansu in northwest China. It is surrounded by mountains and has a temperate monsoon climate. Due to its unique topographical features, the diffusion of local pollutants is often impeded, causing severe air pollution. Furthermore, the weather in winter is cold, with low humidity and low wind speeds. Because of its unique geography and climate, Tianshui is an excellent location for investigating the influence of different $PM_{2.5}$ exposure metrics on COPD.

In this study, we applied a generalized additive model (GAM) based Poisson distribution combined with a distributed lag non-linear model (DLNM) to quantify the association between five different $PM_{2.5}$ exposure metrics and COPD admission. Stratified analyses were conducted to examine the additional effects of gender, age, and season.

Methods

Hospital admission data

Daily data on hospital admissions for COPD from January 1st, 2018 to December 31st, 2019 were retrieved from all the tertiary and secondary hospitals in Tianshui City. The collecting information included gender, age, admission date, primary diagnosis, and International Classification of Diseases-10th Revision (ICD-10) discharge diagnosis codes. All individuals with a diagnosis of COPD and ICD-10 code J40-44 were included in the study, and patients living outside the urban areas of Tianshui City were excluded from our study.

Data on air pollutants and meteorological factors

The hourly concentration data of $PM_{2.5}$, PM_{10}, SO_2, NO_2 and CO for the same study period as morbidity data from a varying number of fixed air monitoring stations in Tianshui City. These stations were spaced at distances ranging from 1 km to 5 km. On average, each air monitoring station covered an area of approximately 5 km–30 km. Air samples were collected about 10–20 m above ground level and regularly operated according to the China National Quality Control ((HJ/T 193–2005) and (GB3095-2012))[1,5–9,18–20]. The methods based on Tapered Element Oscillating Microbalance (TEOM), chemiluminescence, ultraviolet fluorescence, and infrared absorption were used for the measurement of $PM_{2.5}$, PM_{10}, SO_2, NO_2, and CO. Daily average concentration of $PM_{2.5}$, PM_{10}, SO_2, NO_2, and CO were calculated as an arithmetic mean measure across all the monitoring stations from hourly values, as in most time-series studies[1,5–9,18–20].

To adjust for the effect of weather factors on COPD admissions, after referring to the relevant literature[1,5–9,18–20], we obtained daily meteorological data (daily mean temperature (°C) and relative humidity (%)) from Gansu Meteorological Bureau.

Exposure metrics

To investigate the short-term impact of $PM_{2.5}$ on daily COPD admissions, five different exposure metrics were established: (a) Daily mean concentration ($DailyPM_{2.5}mean$), (b) Daily hourly peak concentration ($DailyPM_{2.5}max$), (c) Daily morning concentration ($DailyPM_{2.5}mor$), (d) Daily evening concentration ($DailyPM_{2.5}eve$) and (e) Daily excessive concentration hours ($PM_{2.5}DECH$). The details of the calculating formulas and definitions of the five metrics were available here. As in the previous method of defining daily average concentrations for the other four air pollutants[1,5–9,18–20].

The daily average concentrations of $PM_{2.5}$ ($DailyPM_{2.5}mean$) defined as an arithmetic mean measure across all the monitoring stations from hourly values within a given day. The hourly peak concentrations of $PM_{2.5}$ ($DailyPM_{2.5}max$) were defined as the maximum concentration of 24-h $PM_{2.5}$ within a given day. Considering the habit of morning and evening exercise of people, and the time spending on the way from car parking or bus station to home among commuting people, we extended this time period; thus, 7:00 to 9:00 in the morning were defined as Daily morning concentration ($DailyPM_{2.5}mor$)[12,13] and 17:00 to 20:00 in the evening were defined as Daily evening concentration ($DailyPM_{2.5}eve$)[12,13]. $PM_{2.5}DECH$ is calculated by adding the concentration hours over the course of a day that exceed the reference concentration, which takes into account both large changes in atmospheric pollutants and excess concentrations over the course of a day. According to the WHO air quality guidelines and relevant studies[21–23] the concentration threshold of $PM_{2.5}$ in our study was also determined to be 25 μg/m³. Its calculation formula is as follows:

$$PM_{2.5}DECH = \sum_{i=0}^{23} \Delta Ci$$

$$\Delta Ci = \left\{ \begin{array}{ll} Ci - 25, & Ci \geq 25 \\ 0, & Ci < 25 \end{array} \right.$$

Where i is the hourly time of one day, Ci is the $PM_{2.5}$ concentration at a given hour time point, and ΔCi is the difference between Ci and the threshold concentration (25 μg/m³).

Statistical models

Since the daily number of admissions for COPD usually obeys Poisson distribution, and Quasi Poisson regression would be better than Poisson to deal with over-dispersion in the analysis. As the impact of air pollutants on COPD morbidity typically exhibits clear hysteresis[1,5,6–9,18–20], which signifies a delay in the detrimental consequences of air pollutants. Additionally, the maximal impact is often attained after a cumulative time of several days following the individual's exposure[1,5,6–9,18–20]. To mitigate the impact of the hysteresis effect in current study, we used the quasi-Poisson generalized additive model (GAM) combined with a distributed lag nonlinear model (DLNM) to illustrate the association between five different exposure metrics of $PM_{2.5}$ and daily hospitalization for COPD. According to the results of previous time-series studies[1,5,6–9,18–20], several confounding factors including seasonality and long-term trend, meteorological factors (temperature, relative humidity) were controlled by smoothing using natural cubic spline curves (ns). Moreover, two other confounding factors: day of the week effect, and holiday effects were also controlled. We categorize the virtual variable "holidays" and assign values to indicate whether a day is a holiday or not. Specifically, we use the value 1 to represent holidays and the value 0 to represent non-holidays. Akaike's quasi-Poisson information criterion, also known as Q-AIC, was utilized in order to ascertain the degrees of freedom for every variable that was included in the model. In all variable, we chose the df based on the minimum Q-AIC value, so the degree of freedom of the seasonality and long-term trend in the model is selected as 7 df/year, the temperature and relative humidity degrees were both set to 3. Finally, we got the following model:

$$\text{Log}(Y_t) = \alpha + \beta X_{t,l} + ns(Tem_t, df) + ns(rh_t, df) + ns(Time, df) + Dow + Holiday$$

where t is day of observation, Y_t is the number of daily COPD admissions on day t, α is the model intercept, $X_{t,l}$ is the cross-basis matrix obtained by applying the DLNM to each exposure metrics of $PM_{2.5}$, l is the lag days, β is the coefficient of the crossbasis matrix of each exposure metrics of $PM_{2.5}$ at day t with lag l produced by DLNM. ns is the natural cubic spline function, df denotes the degrees of freedom. Tem_t, and rh_t represents daily temperature and relative humidity on day t; $Time$ reflects a time variable that is used to control seasonality and long-term trend; Dow, and $Holiday$ represent indicator variables for day of the week, holidays, respectively.

Previous studies have found that harmful effects of related diseases may occur when someone has been exposure the air pollutants on the same day or over a period of several consecutive days[1,5,6–9,18–20], and all of the above studies showed little evidence of an association beyond a delay of 7 days[1,5,6–9,18–20], we incorporated with different lag structures, including single-day lag (from current day to 7days before: lag0 to lag7) and multiple-day lag (from lag01 to lag07). For example, in single-day lag structures, a lag of 0 day (lag0) corresponds to the current-day concentration of the different metrics of $PM_{2.5}$, and a lag of 1 day (lag1) refers to the previous-day of the different metrics of $PM_{2.5}$; in multi-day lag structures, lag01 corresponds to 2-day moving average of the different metrics of $PM_{2.5}$ concentration of the current and previous day, and lag07 corresponds to 8-day moving average of the different metrics of $PM_{2.5}$ concentration of the current and previous 7 days.

In line with a conventional methodology employed in three previous research[19-24] we chose a lag day with the highest the excess risk (ER) of daily admissions for COPD associated with an IQR increase in concentrations of different metrics of $PM_{2.5}$ as a priori in subsequent analysis, including stratification analyses, fitting exposure-response curve and sensitivity analyses. Stratified analyses were utilized in order to explore the effect modification that was caused by individual variables, the above analyses were stratified by gender (males and females), age (< 65 years and ≥ 65 years), season [the cold season (November to April) and warm season (May to October)]. The stratified analysis differences were tested using a Z-test by using the formula below[7,9]:

$$(\beta_1 - \beta_2)/\sqrt{SE_1^2 + SE_2^2}$$

where β_1 and β_2 represent the estimates for the two categories, and SE_1 and SE_2 represent their respective standard errors.

In addition, we conducted two other sensitivity studies to assess the stability of the results in the primary models. First, we built two-pollutant models which adjustment for gaseous pollutants (NO_2, SO_2, and CO). Second, we estimated associations between the different metrics of $PM_{2.5}$ concentration and admissions for COPD changing using the df for the calendar time (6–10 df/year) to verify how the different choices of the calendar time would influence the effect, according to prior research formula[21-23]. The model is considered robust if the associations remained unchanged in the main result after modifying df or adjusting for other gas pollutants.

Prior research has discovered non-linear relationships between meteorological factors and COPD morbidity, as well as the presence of hysteresis effects, and daily number of are classified as low-probability events. Therefore, we applied the DLNMs based on the quasi Poisson generalized additive model (GAM) to quantify the relationship between meteorological factors and COPD morbidity.

The basic model of the relationship between ambient temperature and daily COPD morbidity is as follows:

$$\text{Log}(Y_t) = \alpha + \beta \, Tem_{t,\,l} + ns\,(Pollutant_t,\, df) + ns\,(rh_t,\, df) + ns\,(Time,\, df) + Dow + Holiday$$

where t is day of observation, Y_t is the number of daily COPD admissions on day t, α is the model intercept, $Tem_{t,\,l}$ represent the matrices of temperature, β refer to the vector coefficients of the matrix; ns is the natural cubic spline function, df denotes the degrees of freedom. $Pollutant_t$ represents PM_{10}, SO_2, and NO_2 on day t, and rh_t represents daily relative humidity on day t; $Time$ reflects a time variable that is used to control seasonality and long-term trend; Dow, and $Holiday$ represent indicator variables for day of the week, holidays, respectively.

The model formula for the daily COPD morbidity with relative humidity is similar to the above formula, as shown below:

$$\text{Log}(Y_t) = \alpha + \beta \, RH_{t,\,l} + ns\,(Pollutant_t,\, df) + ns\,(Tem_t,\, df) + ns\,(Time,\, df) + Dow + Holiday$$

where t is day of observation, Y_t is the number of daily COPD admissions on day t, α is the model intercept, $RH_{t,\,l}$ represent the matrices of temperature, β refer to the vector coefficients of the matrix; ns is the natural cubic spline function, df denotes the degrees of freedom. $Pollutant_t$ represents PM_{10}, SO_2, and NO_2 on day t, and Tem_t represents daily relative humidity on day t; $Time$ reflects a time variable that is used to control seasonality and long-term trend; Dow, and $Holiday$ represent indicator variables for day of the week, holidays, respectively.

Akaike's quasi-Poisson information criterion, also known as Q-AIC were utilized to determine degree of freedom of all variables. According to the minimum Q-AIC, we applied a natural cubic spline curve of 3df for pollutants and meteorological factors, the df for time's natural spline was set to 7/year. According to previous time series studies on COPD[16] we used a lag of one week (lag = 7) based on the lowest AIC value to assess the association between meteorological parameters (temperature and relative humidity) and COPD morbidity. Finally, we analyzed and graphed the cumulative relative risks associated with meteorological factors during a 7-day lag period.

We used the "nlme", "mgcv", "dlnm", "splines" and "tsModel" packages for all statistical analysis in R version 4.3.1. Firstly, estimates were calculated as Relative risk (RR) and 95% confidence intervals (95% CIs) in relation to an interquartile range (IQR) increment in each metrics of $PM_{2.5}$ concentrations based on the following model[22,25-27]:

$$\text{RR} = \exp(\beta \times \Delta C)$$
$$Lower\ 95\%\ CI = \exp((\beta - 1.96 \times SE) \times \Delta C)$$
$$Upper\ 95\%\ CI = \exp((\beta + 1.96 \times SE) \times \Delta C)$$

Where β is the coefficient of the crossbasis matrix of each exposure metrics of $PM_{2.5}$ at day t with lag l produced by DLNM, and SE was the standard error for β, ΔC is per-unit change or an IQR increase of exposure to each exposure metrics of $PM_{2.5}$ at day.

Based on the relative risk (RR), we calculated the excess risks (ER, i.e. the percent increase of daily hospital admissions for COPD per interquartile range (IQR) concentration increase of each metrics of $PM_{2.5}$ concentrations according to following equaions[22,28-29]:

$$\text{ER} = (RR - 1) \times 100\%$$

Statistical significance was defined as a P-value less than 0.05 or the 95% confidence interval (CI) excluded 0.

Ethics approval and consent to participate Human experiments and human tissue samples were not involved in this study. All experimental protocols in the study were approved by the ethics committee of The First Hospital of Lanzhou University, all methods were carried out in accordance with relevant guidelines and regulations.

Consent to methods. I confirm that all methods and procedures were executed in strict accordance with the relevant guidelines and regulations.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Results

Statistical description of COPD hospitalization, air pollutants, and meteorological variables

Table 1 provides a concise overview of the descriptive data found in the investigation. From January 2018 to December 2019, a total of 3,038 COPD admissions living in Tianshui City were recorded, with an average of around four per day. The numbers of male and female patients were 1,924 and 1,114, respectively. Adult patients (<65 years) accounted for 70.8% of the total, while the remaining 28.2% were elderly patients (≥ 65 years). The average $DailyPM_{2.5}mean$ value was 32.6 μg/m³ (SD: 22.6), while the mean $DailyPM_{2.5}max$ level was 48.1 μg/m³ (SD: 33.9). The mean values of $DailyPM_{2.5}mor$, $DailyPM_{2.5}eve$, and $PM_{2.5}DECH$ were 31.9 μg/m³ (SD: 22.3), 30.6 μg/m³ (SD: 22.8), and 334.1 μg/m³ (SD: 232.5), respectively. Besides, the daily average concentrations of PM_{10}, SO_2, NO_2, and CO were 63.4 μg/m³, 13.7 μg/m³, 30.7 μg/m³, and 0.7 mg/m³, respectively. The daily average temperature was 11.9 °C and the relative humidity was 66.5%.

The correlation between different atmospheric pollutants and meteorological factors

The Spearman correlation coefficients between the air pollutants and meteorological factors are shown in Supplemental Materials Table S1. The $PM_{2.5}$ and PM_{10} values are strongly associated with each other, and these two particles also correlate with other air pollutants to varying degrees. There is a significant correlation between $PM_{2.5}$ and PM_{10} ($r=0.915$, $p<0.05$), and the Spearman correlation coefficient is greater than 0.8. There are moderate correlations between $PM_{2.5}$ and SO_2 ($r=0.661$, $p<0.05$), NO_2 ($r=0.667$, $p<0.05$), and CO ($r=0.748$, $p<0.05$), with Spearman correlation coefficients between 0.6 and 0.8. All air pollutants correlate negatively with temperature and relative humidity.

Associations between five exposure metrics of $PM_{2.5}$ and the risk of hospitalization for COPD

Figure 1 depicts the ER and 95% CIs of COPD hospitalization per IQR increase in the five $PM_{2.5}$ exposure metrics across different lagged days. Significant positive impacts of $PM_{2.5}$ on daily COPD morbidity were observed in all five metrics. Specifically, $DailyPM_{2.5}eve$ exhibits the greatest effect, followed by $PM_{2.5}DECH$ and $DailyPM_{2.5}mean$. Notably, the multiple-day lag effects of the five $PM_{2.5}$ exposure metrics exhibit higher estimates than those of single-day exposure, and we also observed more positive associations when using $DailyPM_{2.5}eve$. Among the five $PM_{2.5}$ exposure metrics, the highest risks of COPD hospitalization are associated with the IQR elevations of $DailyPM_{2.5}mean$ at lag06 (ER = 21.64%, 95% CI: 7.46%, 36.68%), $DailyPM_{2.5}max$ at

	Mean	SD	Min	Percentile			Max
				P_{25}	P_{50}	P_{75}	
Hospitalizations per day							
All	4	4	0	0	3	7	21
Male	3	3	0	0	2	4	15
Female	1	2	0	0	1	2	11
<65	3	3	0	0	2	5	16
≥ 65	1	2	0	0	1	2	9
Air pollution							
$DailyPM_{2.5}mean$ (μg/m³)	32.6	22.6	4.0	18.0	26.0	41.0	224.00
$DailyPM_{2.5}max$ (μg/m³)	48.1	33.9	6.0	26.0	39.3	59.8	399.7
$DailyPM_{2.5}mor$ (μg/m³)	31.9	22.3	4.1	17.3	26.8	40.8	268.5
$DailyPM_{2.5}eve$ (μg/m³)	30.6	22.8	4.0	15.8	24.6	37.2	258.3
$PM_{2.5}DECH$ (μg/m³)	334.1	232.5	0.0	42.0	163.2	480.9	4142.0
PM_{10} (μg/m³)	63.4	45.5	8.0	36.0	56.0	82.0	761.0
SO_2 (μg/m³)	13.7	8.5	5.0	8.0	10.0	17.0	56.0
NO_2 (μg/m³)	30.7	13.2	8.0	20.0	28.0	38.5	74.0
CO (mg/m³)	0.7	0.4	0.2	0.4	0.6	0.9	2.5
Meteorological variables							
Temperature, °C	11.9	9.1	− 8.9	3.8	13.1	19.8	27.8
Relative humidity, %	66.5	12.2	17.4	58.8	68.0	75.0	94.0

Table 1. Statistical description of hospitalization in patients with COPD, air pollutants, and meteorological variables. SD, standard deviation; DECH, daily excessive concentration hours.
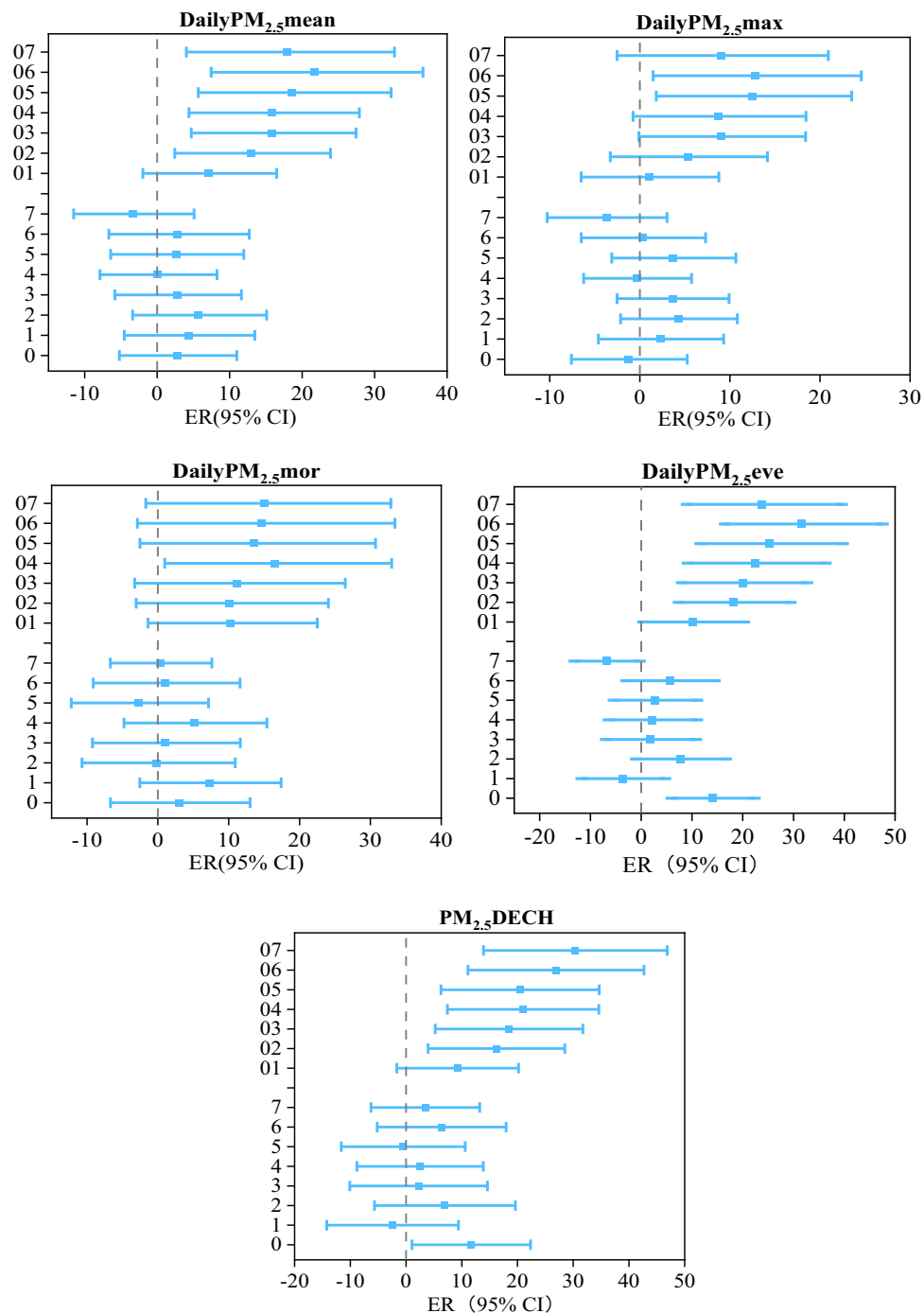
Fig. 1. The excess risk and 95% confidence intervals of the hospital admissions for COPD associated for per IQR increase in the five-exposure metrics of ambient $PM_{2.5}$ at different lag periods.

lag06 (ER = 12.84%, 95% CI: 1.47%, 24.58%), DailyPM$_{2.5}$mor at lag04 (ER = 16.47%, 95% CI: 0.96%, 33.01%), DailyPM$_{2.5}$eve at lag06 (ER = 31.54%, 95% CI: 16.49%, 47.58%), and PM$_{2.5}$DECH at lag07 (ER = 30.37%, 95% CI: 13.91%, 46.88%).

Table 2 displays the estimated ER with 95% CI of COPD hospitalizations stratified by gender, age, and season. We observed slightly larger estimates in females than in males, except for PM$_{2.5}$DECH, although the differences are not statistically significant. The differences between the age groups are insignificant, but we noticed that the ER of COPD hospitalizations associated with the five PM$_{2.5}$ exposure metrics is consistently higher among patients under 65 years than those aged 65 years and older. Stratification by season indicates that the associations are more prominent during the winter, but the difference is only statistically significant for different seasons concerning the effect of DailyPM$_{2.5}$mor on COPD.

Category	Groups	Exposure metrics				
		DailyPM$_{2.5}$mean	DailyPM$_{2.5}$max	DailyPM$_{2.5}$mor	DailyPM$_{2.5}$eve	PM$_{2.5}$DECH
Gender	Male	21.74(3.51,41.49)	9.43(− 4.36,23.80)	11.94(− 7.47,33.02)	21.74(3.51,41.49)	45.46(4.10,47.40)
	Female	45.82(22.49,71.45)	17.20(-0.88,36.30)	22.51(0.05,47.12)	45.82(22.49,71.45)	36.87(13.17,60.57)
	p-value	0.40	0.56	0.57	0.25	0.77
Age	< 65	33.92(15.45,53.86)	19.60(1.72,38.46)	16.83(− 2.33,37.58)	33.92(15.45,53.86)	32.92(13.17,52.23)
	≥ 65	27.67(3.79,54.16)	9.77(− 4.50,24.61)	14.15(− 9.73,40.54)	27.67(3.79,54.16)	26.33(− 0.88,53.98)
	p-value	0.60	0.47	0.90	0.77	0.76
Season	Warm	21.29(− 34.15,93.86)	16.93(− 0.51,35.29)	− 6.72(− 58.23,59.85)	21.29(− 34.15,93.86)	32.37(− 175.56,342.78)
	Cold	31.27(11.90,52.28)	25.35(1.96,50.36)	23.76(1.86,47.68)	31.27(11.90,52.28)	34.67(14.04,55.30)
	p-value	0.83	0.65	0.009	0.82	0.84

Table 2. Excess risk and 95% confidence intervals for COPD hospitalization per interquartile range increment for each metric in subgroups.

Figure 2 shows the exposure-response curve between the different PM$_{2.5}$ exposure metrics and hospital admissions for COPD. While not perfectly linear, the morbidity risk rises along with increases in the different PM$_{2.5}$ exposure metrics, with no obvious threshold.

Figure 3 depicts the cumulative exposure-response curve, which shows the relationship between daily mean temperature or relative humidity and the overall number of hospitalized patients with COPD. According to the figure, the cumulative RR increases as the temperature slightly drops, and the association is significant in the 10 ℃ to 12 ℃ temperature range. Additionally, an irregular M-shaped association exists for relative humidity. The cumulative RR increases as RH rises or falls from 65%, with significant associations in the 30–50% and 70–80% ranges.

Initially, we conducted a sensitivity analysis by employing a two-pollutant model (see Table S2 in Supplemental Materials). The results indicate that the associations between the different PM$_{2.5}$ exposure metrics and COPD admission are robust after adjustment for other pollutants (SO$_2$, NO$_2$, and CO). Additionally, a sensitivity analysis using various df values (6–10 df/year) of calendar time indicates that effect estimates of different PM$_{2.5}$ exposure metrics on COPD admission are also robust (see Table S3 in Supplemental Materials).

Discussion

Most existing studies examining the health impacts of PM$_{2.5}$ utilize the daily average PM$_{2.5}$ concentration as the exposure indicator. It is worth noting that the concentration of PM$_{2.5}$ pollution exhibits obvious variations throughout the day[12,13]. Individuals are not exposed to outdoor air pollution 24 h a day, and current research does not consider this. Consequently, we used DailyPM$_{2.5}$mean and four other novel PM$_{2.5}$ exposure metrics (DailyPM$_{2.5}$max, DailyPM$_{2.5}$mor, DailyPM$_{2.5}$eve, and PM$_{2.5}$DECH) to examine the association between short-term PM$_{2.5}$ exposure and COPD admissions in Lanzhou, China. The results of this study demonstrate that all five PM$_{2.5}$ metrics are significantly associated with increased COPD morbidity on different lag days. Particularly, DailyPM$_{2.5}$eve exhibits the largest ER, followed by PM$_{2.5}$DECH and DailyPM$_{2.5}$mean. The effects of the five PM$_{2.5}$ exposure metrics on COPD admission are more pronounced in females, the elderly, and during winter. However, the differences between the gender, age, and season subgroups are not statistically significant, except for DailyPM$_{2.5}$mor and season.

There are differences in the acute morbidity effects of three PM$_{2.5}$ exposure metrics on COPD admissions. Compared to PM$_{2.5}$DECH and DailyPM$_{2.5}$mean, DailyPM$_{2.5}$eve demonstrates the greatest impact. This may be due to differences in diurnal PM$_{2.5}$ variations, time activity patterns of residents, and meteorological conditions among the studied cities[21,23]. In Tianshui, the highest concentration of PM$_{2.5}$ usually occurs from 5:00 to 8:00 p.m. Additionally, the outdoor temperature is higher during this time of the day than between 7:00 and 9:00 a.m. Residents spend more time outdoors in the evening for reasons such as leaving work, exercising, and gathering for meals. During the evening peak hours when PM$_{2.5}$ concentrations are high, the residents may suffer greater exposure, thereby inhaling more particles. Some susceptible population groups do not cope well with peak PM$_{2.5}$ exposure during the evening and may therefore exhibit greater adverse health effects. In contrast to PM$_{2.5}$DECH and DailyPM$_{2.5}$mean, DailyPM$_{2.5}$eve considers the substantial variations in hourly concentrations within a day, and it fully addresses the health effects of high PM$_{2.5}$ concentrations above the WHO guidelines. Thus, instead of focusing only on the DailyPM$_{2.5}$mean, we suggest that future studies also consider peak concentrations of air pollution.

Although numerous studies have focused on the link between ambient PM$_{2.5}$ and the risk of COPD-related admissions, no research employs the metrics used in this paper. The results of our research indicate that PM$_{2.5}$DECH, a metric of the overall extent of excessive exposure to PM$_{2.5}$, shows a higher risk of COPD-related admissions. This observation aligns with findings from previous research, which indicated that PM$_{2.5}$ DECH has a larger impact than the daily mean[22,23].

The greater influence of PM$_{2.5}$DECH may be due to the PM$_{2.5}$ values collected at various times of the day. DECH is the cumulative total of all the excessive PM$_{2.5}$ values for each hour throughout the day. The hourly peak refers to the greatest concentration of a substance at a particular hour during the day. The daily mean, however, does not consider the reference standard. Furthermore, existing research indicates that PM$_{2.5}$DECH exhibits superior model fit performance, as assessed by the Akaike information criterion[21]. PM$_{2.5}$DECH can also be
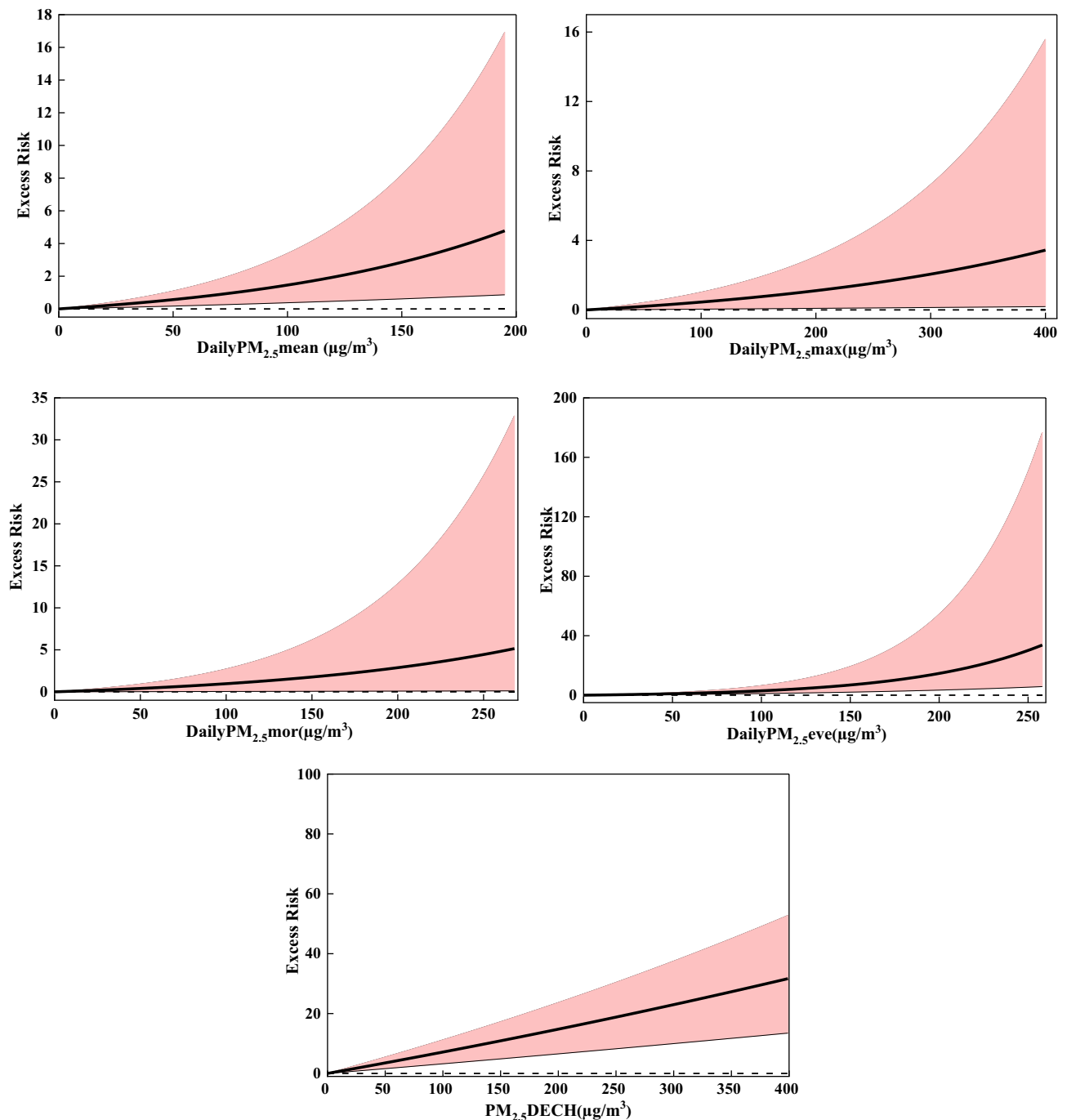
Fig. 2. The exposure-response curve between different $PM_{2.5}$ exposure metrics and hospital admissions for COPD.

easily adapted to different reference concentrations and may be calculated according to particular regional and national guideline concentrations. Given that there are several directives from various organizations that are not consistent with one another, such as the World Health Organization standard and the United States National Ambient Air Quality Standards, this is of great assistance. As a potential alternative to the daily mean, our findings indicate that $PM_{2.5}$DECH can be utilized as a measurement of the $PM_{2.5}$ concentration in the ambient environment. As other studies demonstrate, peak metric measurements do not account for the hours during which individuals are most susceptible to contaminated ambient air exposure[21]. Therefore, it is likely that the hourly peak measure has a weak correlation with the activity patterns of the population in our study. Considering the significant correlations between hourly peak $PM_{2.5}$ levels and health outcomes in certain studies, further research on this temporal measure is necessary.
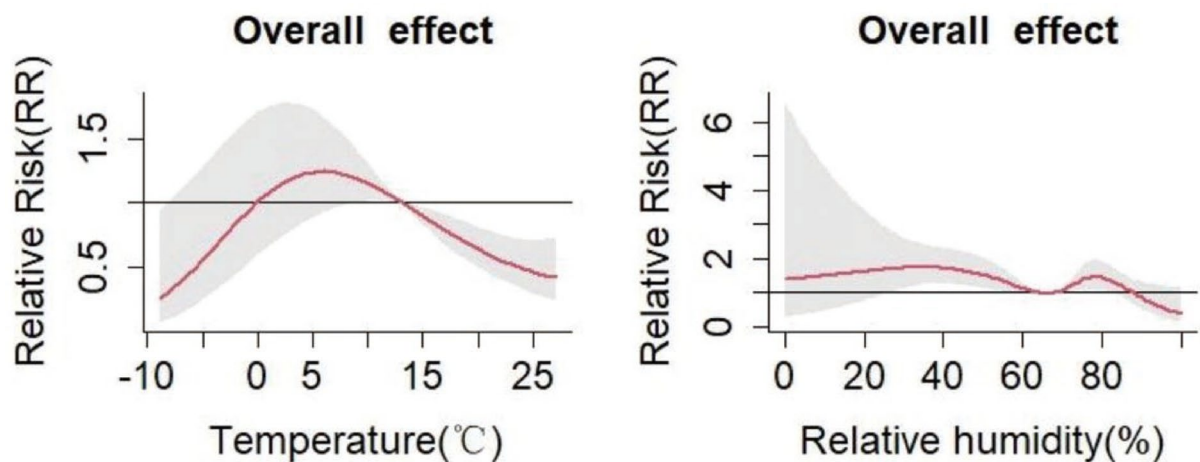
Fig. 3. Plots of cumulative RR for COPD hospitalizations of the overall population (Jan/2018–Dec/2019, Tianshui, China) against: temperature, relative humidity.

The findings of our study align with previous research on the relationship between daily $PM_{2.5}$ levels and COPD morbidity. For example, in Ningbo, an interquartile range increase in $PM_{2.5}$ concentration corresponded to a 7.3% increase in COPD morbidity[8]. Other local studies in Ganzhou, Jinan, and Qingdao, and a nationwide study in China, also found significant associations between $PM_{2.5}$ and COPD morbidity[1,5,6,9]. Furthermore, a recent study has also documented similar findings, which revealed a 1.60% increase in COPD morbidity for each 10 μg/m³ increase in daily mean $PM_{2.5}$ concentration[9].

Consistent with previous surveys[6,7], our study established that females have somewhat higher ER values for COPD than males when utilizing different $PM_{2.5}$ exposure metrics. Females are inherently more susceptible to air pollution due to several socio-economic, behavioral, and physiological reasons. For instance, females have smaller lungs and airway diameters as well as enhanced airway responsiveness and greater fine particle accumulation. Additionally, we discovered that $PM_{2.5}$ pollution is more harmful to elderly patients than to those aged under 65 years. However, young people, who are exposed to similar amounts of $PM_{2.5}$, are at a higher risk of respiratory disease onset due to their enhanced activity levels. Young people in China spend more time outdoors than older people for various reasons, including during times of severe air pollution.

We discovered that the associations between different $PM_{2.5}$ exposure metrics and COPD morbidity are considerably greater during colder months than warmer months. This discovery is consistent with comparable investigations in other regions of China[19,20]. The low temperatures in Tianshui City during the winter potentially amplify the negative influence of ambient air pollution through various mechanisms, such as reduced immune response in the respiratory tract, inadequate airflow, and sluggish air movement[19,20].

After assessing the consequences of cumulative $PM_{2.5}$ exposure, we observed positive and significant associations between the different exposure metrics of $PM_{2.5}$ and COPD morbidity with cumulative lags of 0–6 and 0–7 days. The cumulative effect estimates for all exposure metrics of $PM_{2.5}$ with lags of 0–6 and 0–7 days were far greater than those estimated by single-day and two-day moving average lag structures. Similar results were reported in previous single-city studies conducted in Beijing, Dingxi, and Jiuquan[7,19,20], where significantly stronger relationships were observed with longer average exposure periods. Variations in cumulative lag periods and effect estimates may be attributed to the distinct physicochemical characteristics of the pollutants and the underlying biological pathways implicated[30,31]. Existing evidence indicates that exposure to particulate matter induces airway hyperresponsiveness, inflammatory reactions, and malfunction in macrophages and epithelial cells, which in turn exacerbates pre-existing respiratory inflammation in COPD patients[30,31]. These processes require time to develop and for the cumulative effects to be subsequently generated. Collectively, the heterogeneity and underlying mechanisms linking particulate matter to COPD require further validation through comprehensive experimental and epidemiological investigations.

Our time-series investigation revealed a significant association between temperature and COPD admission, with a statistically significant risk effect between 10 ℃ and 12 ℃, which corresponds closely with the results of recent studies conducted under various climatic conditions[16,17]. For example, one study in Panzhihua in southwest China that used DLNM models also determined that the increased risk of acute exacerbation of chronic obstructive pulmonary disease (AECOPD) admission was significant between 4.2 ℃ and 21.7 ℃[16]. A similar study in Ganzhou, China[17] found that the relationship between hospitalizations for AECOPD and ambient temperature was significant when the ambient temperature was between 1 ℃ and 18 ℃. These results may be explained by the different climatic characteristics of each region. The whole city of Tianshui has a temperate continental climate, with a temperate semi-humid climate near the urban area. The number of days with an average daily temperature below 0 °C in the urban area of Tianshui is relatively limited, typically occurring between late December and mid-January each year. Following the cooling period from October to November, residents gradually adapt to the cold weather. From late December to mid-January, residents generally spend minimal time outdoors, except when required by work or daily life. This tendency is even more pronounced

among those with chronic obstructive pulmonary disease (COPD), who spend even less time outdoors during this period. Consequently, when the average daily temperature in Tianshui falls below 0 ℃, low temperatures may exert a certain protective effect on COPD patients.

Regarding relative humidity, we observed an irregular M-shaped association. Unlike several previous studies, which regarded RH as a confounding variable, we considered its nonlinear and delayed impact using a cross-basis function. The findings of this study are in line with those of existing research. For instance, a study in Chengdu also showed that lower humidity was linked to an increase in COPD hospitalizations[17]. The combination of low temperature and low humidity may cause bronchoconstriction, which in turn causes the mucosal membrane lining the airway to become dry. Consequently, the airway becomes more susceptible to bacterial and viral infections[17], which together increase the risk of COPD hospitalizations. An increased relative risk of COPD hospitalizations is also associated with a high RH, which often leads to elevated levels of airborne pollutants, including dust mites, bacteria, and viruses. As a result, there is an increase in the likelihood of triggers caused by pollutants that exacerbate the symptoms of COPD[17].

There are some limitations to this study. First, time-series research that utilizes daily hospitalization counts can be regarded as inherently aggregated ecological research, making it susceptible to ecological fallacy. Besides, due to the unavailability of patient addresses, we could only estimate the exposure to $PM_{2.5}$ at the city level rather than the individual level. This approach may have led to misclassifications of exposure, since it did not account for variations in ambient air pollution at various locations. Finally, because we utilized the secondary administrative database of the hospital, certain important variables were missing from the analyses, such as indoor air pollution, smoking, diet, economic status, and insurance.

Conclusions
In summary, there is a significant association between different $PM_{2.5}$ exposure metrics and COPD morbidity. More meaningful results were observed using DailyPM$_{2.5}$eve and PM$_{2.5}$DECH, suggesting that DailyPM$_{2.5}$eve serves as a useful cumulative indicator for evaluating air pollution exposure. The effects of different exposure metrics of $PM_{2.5}$ are stronger among females, patients aged under 65, and during the winter.

Data availability
The datasets generated and/or analyzed during the current study are not publicly availa-ble due to confidentiality agreements but are available from the corresponding author on reasonable request.

References
1. Zhou, X. et al. Ambient air pollutants relate to hospital admissions for chronic obstructive pulmonary disease in Ganzhou, China. *Rev. Saude Publica.* **56**, 46. https://doi.org/10.11606/s1518-8787.2022056004324 (2022).
2. Safiri, S. et al. Burden of chronic obstructive pulmonary disease and its attributable risk factors in 204 countries and territories, 1990–2019: results from the global burden of disease study 2019. *BMJ* **378**, e069679. https://doi.org/10.1136/bmj-2021-069679 (2022).
3. Hou, S. S. et al. Disease burden of chronic obstructive pulmonary diseases in China from 1990 to 2019. *Chin. J. Epidemiol.* **43** (10), 1554–1561. https://doi.org/10.3760/cma.j.cn112338-20211009-00773 (2022).
4. Delavar, M. A. et al. Relationship between Fne particulate matter ($PM_{2.5}$) concentration and risk of hospitalization due to chronic obstructive pulmonary disease:a systematic review and meta-analysis. *BMC Public. Health.* **23** (1), 2229. https://doi.org/10.1186/s12889-023-17093-6 (2023).
5. Cheng, C. et al. Associations between air pollutants and hospital admissions for chronic obstructive pulmonary disease in Jinan: potential benefits from air quality improvements. *Environ. Sci. Pollut Res. Int.* **30**, 46435–46445. https://doi.org/10.1007/s11356-023-25567-8 (2023).
6. Yang, J. et al. Investigating the impact of air pollution on AMI and COPD hospital admissions in the coastal City of Qingdao, China. *Front. Env Sci. Eng.* **16**, 1–13. https://doi.org/10.1007/s11783-021-1490-7 (2022).
7. Tian, Y. et al. Short-term effects of ambient fine particulate matter pollution on hospital visits for chronic obstructive pulmonary disease in Beijing, China. *Environ. Health.* **17**, 1–8. https://doi.org/10.1186/s12940-018-0369-y (2018).
8. Lin, C. Y. et al. Short-term associations between ambient fine particulate matter pollution and hospital visits for chronic obstructive pulmonary disease in Yinzhou district, China. *Environ. Sci. Pollut Res. Int.* **27**, 21647–21653. https://doi.org/10.1007/s11356-020-08448-2 (2020).
9. Jin, J. Q. et al. Individual exposure to ambient PM$_{(2.5)}$ and hospital admissions for COPD in 110 hospitals: a case-crossover study in Guangzhou, China. *Environ. Sci. Pollut Res. Int.* **29**, 11699–11706. https://doi.org/10.1007/s11356-021-16539-x (2022).
10. Lin, H. et al. Hourly peak PM$_{(2.5)}$ concentration associated with increased cardiovascular mortality in Guangzhou, China. *J. Expo Sci. Environ. Epidemiol.* **27**, 333–338. https://doi.org/10.1038/jes.2016.63 (2017).
11. Lin, H. et al. Daily exceedance concentration hours: A novel indicator to measure acute cardiovascular effects of PM$_{(2.5)}$ in six Chinese subtropical cities. *Environ. Int.* **111**, 117–123. https://doi.org/10.1016/j.envint.2017.11.022 (2018).
12. Guo, B. et al. Using rush hour and daytime exposure indicators to estimate the short-term mortality effects of air pollution: A case study in the Sichuan basin, China. *Environ. Pollut.* **242**, 1291–1298. https://doi.org/10.1016/j.envpol.2018.08.028 (2018).
13. Zhao, Z. et al. Acute effect of air pollutants' peak-hour concentrations on ischemic stroke hospital admissions among hypertension patients in Beijing, China, from 2014 to 2018. *Environ. Sci. Pollut. Res. Int.* **29**, 41617–41627. https://doi.org/10.1007/s11356-021-18208-5 (2022).
14. Lin, H. et al. Using daily excessive concentration hours to explore the short-term mortality effects of ambient PM$_{(2.5)}$ in Hong Kong. *Environ. Pollut.* **229**, 896–901. https://doi.org/10.1016/j.envpol.2017.07.060 (2017).
15. Lin, H. et al. Hourly peak concentration measuring the $PM_{2.5}$-mortality association: results from six cities in the Pearl river Delta study. *Atmospheric Environ.* **161**, 27–33. https://doi.org/10.1016/j.atmosenv.2017.04.015 (2017).
16. Yang, Y. et al. Assessing the impact of temperature on acute exacerbation of chronic obstructive pulmonary disease hospitalizations in residents of Panzhihua city: a multi-districts study using a distributed lag non-linear model. *BMC Public. Health.* **24**, 2151. https://doi.org/10.1186/s12889-024-19677-2 (2024).

17. Shi, C. Y. et al. Time series analysis of the interaction between ambient temperature and air pollution on hospitalizations for AECOPD in Ganzhou, China. *Scientifc Rep.* **14**, 17106. https://doi.org/10.1038/s41598-024-67617-2 (2024).
18. Xia, X. L. et al. A Comparison Analysis of Causative Impact of PM$_{2.5}$ on Acute Exacerbation of Chronic Obstructive Pulmonary Disease (COPD) in Two Typical Cities in China. *Atmosphere.* **12**, 970–970.https://doi.org/10.3390/ATMOS12080970 (2021).
19. Wang, H. et al. Association between air pollution and hospital admissions for chronic obstructive pulmonary disease: a time series analysis in Dingxi, China, 2018–2020. *Air Qual. Atmos. Health.* **18**, 865–876. https://doi.org/10.1007/S11869-023-01486-Y (2024).
20. Bao, H. et al. Short-Term effects of ambient air pollution on chronic obstructive pulmonary disease admissions in Jiuquan, China. *Toxics* **12**, 364. https://doi.org/10.3390/TOXICS12050364 (2024).
21. Jiao, A. et al. Short-term impacts of ambient fine particulate matter on emergency department visits: comparative analysis of three exposure metrics. *Chemosphere* **241**, 125012. https://doi.org/10.1016/j.chemosphere.2019.125012 (2020).
22. Liang, Z. et al. Three exposure metrics of size-specific particulate matter associated with acute lower respiratory infection hospitalization in children: A multi-city time-series analysis in China. *Sci. Total Environ.* **816**, 151636. https://doi.org/10.1016/j.scitotenv.2021.151636 (2022).
23. Xiao, D. et al. Three exposure metrics for fine particulate matter associated with outpatient visits for acute lower respiratory infection among children in Guangzhou, China. *Front. Public. Health.* **10**, 876496. https://doi.org/10.3389/fpubh.2022.876496 (2022).
24. Hua, Y. et al. Association between air pollution and hospital admissions for chronic respiratory disease in people aged over 65 years: a time series analysis in Ningbo, China, 2015–2017. *Int. Arch. Occup. Environ. Health.* **95**, 1293–1304. https://doi.org/10.1007/s00420-022-01887-z (2022).
25. Lin, X. The short-term association of ambient fine particulate air pollution with hypertension clinic visits: A multi-community study in Guangzhou, China. *Sci. Total Environ.* **774**, 145707. https://doi.org/10.1016/j.scitotenv.2021.145707 (2021).
26. Zhang, X. L. et al. Independent risk evaluation associated with short-term black carbon exposure on mortality in two megacities of Yangtze river delta, China. *Sci. Total Environ.* **880**, 163273. https://doi.org/10.1016/j.scitotenv.2023.163273 (2023).
27. Luo, H. H. et al. Ambient air pollution and hospitalization for type 2 diabetes in china: A nationwide, individual-level case-crossover study. *Environ. Res.* **216**, 114596. https://doi.org/10.1016/j.envres.2022.114596 (2023).
28. Wei, F. et al. Association between short-term exposure to ambient air pollution and hospital visits for depression in China. *Sci. Total Environ.* **724**, 138207. https://doi.org/10.1016/j.scitotenv.2020.138207 (2020).
29. Tang, M. L. et al. The association of short-term effects of air pollution and sleep disorders among elderly residents in China. *Sci. Total Environ.* **708**, 134846. https://doi.org/10.1016/j.scitotenv.2019.134846 (2020).
30. Gao, N. N. et al. Short-term effects of ambient air pollution on chronic obstructive pulmonary disease admissions in Beijing, China (2013–2017). *Int. J. COPD.* **14**, 297–309. https://doi.org/10.1016/j.scitotenv.2019.134846 (2019).
31. Yang, J. L. Study on the effect of air pollution on the hospitalization of respiratory and cardiovascular system disease in Jinan. Dissertation, Shandong University (in Chinese) *PLoS. One.* 8(8): e71414. (2018). https://doi.org/10.1371/journal.pone.0071414 (2013).

Author contributions
J.Y. Dong contributed to the conception or design of the work. D.S. Li, X.J. Liu, J. Shu and L.S. Zhu contributed to the acquisition, analysis, or interpretation of data for the work. D.S. Li drafted the manuscript. H.R. Bao critically revised the manuscript. All authors final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Funding
This study was supported by Gansu's key research and development program under Grant No. 23YFFA0033.

Declarations

Competing interests
The authors declare no competing interests.

Additional information
Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-025-10116-9.

Correspondence and requests for materials should be addressed to H.B.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.