

Association of Exposure to Humidex with Schizophrenia Admissions in Qingdao, China: A Time-Series Study

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Purpose: This study aimed to quantify the effects of humidex (a composite index of temperature and relative humidity) on schizophrenia admissions.

Methods: The exposure-lag-response relationship between humidex and schizophrenia admissions was explored via a distributed lag nonlinear model (DLNM). The modification effects of sex and age were also investigated. We further calculated the attributable fraction (AF) and number (AN) due to humidex.

Results: During the study period, the median humidex in Qingdao was 15.22, and the low humidex (−7, 2.5th percentile) and high humidex (40, 97.5th percentile) were −7 and 40, respectively. The significant adverse effects of low humidex on schizophrenia admissions persisted from lag 2 [Relative risk (RR)=1.060, 95% CI (confidence interval): 1.006–1.117] to lag 5 (1.063, 1.008–1.122) and reached its maximum at lag 4 (1.078, 1.008–1.152). Females and young individuals are susceptible to low humidex. In addition, the AFs and ANs of schizophrenia admissions due to low humidex were 7.2% and 407, respectively.

Conclusion: Schizophrenia admission was associated with only low humidex. Humidex may serve as an early warning indicator of schizophrenia.

Keywords: distributed lag nonlinear mode, relative risk, humidex, attributable fraction

Introduction

Schizophrenia is a severe mental illness with an unknown etiology and complex symptoms, usually with a slow or subacute onset in young adulthood.¹ According to Simeone et al's statistics on the global prevalence of schizophrenia, the global prevalence of schizophrenia is approximately 0.48%.² In China, the prevalence of schizophrenia has reached 0.54%.³ According to World Health Organization (WHO) estimates, the burden of mental disorders will account for 25% of the total burden of disease in China.⁴ Therefore, identifying potential risk factors in time is of great significance for the prevention and control of schizophrenia.

Meteorological factors are very important factors affecting human life and health. In recent years, the influences of meteorological factors on mental disorders have attracted considerable attention. Roni Shiloh et al reported a strong correlation between the onset of schizophrenia and the maximum monthly temperature.⁵ In a 2014 study by Wang et al in Toronto, Canada, it was found that the risk of schizophrenia increased simultaneously with increasing temperature and that the effect was present on the same day, with the largest effect size (RR=1.10, 95% CI: 1.03–1.17), and that the harmful effect could persist until day 4 after exposure.⁶ However, through correlation analysis, Karasch et al reported that temperature was not related to the onset of schizophrenia.⁷ Notably, current studies on meteorological factors and schizophrenia admissions have focused mostly on one of these factors, such as average temperature, and have ignored the comprehensive impact of multiple indicators. Humidex is a composite index proposed by Canadian meteorologists Masterton and Richardson to reflect

the thermal comfort of the human body in hot or humid weather.^{8,9} At present, some scholars have used the humidex to investigate the associations with tuberculosis,¹⁰ hip fracture,¹¹ allergic conjunctivitis,¹² cardiovascular mortality¹³ and bacillary dysentery.¹⁴ However, no studies have used this indicator in relation to schizophrenia. To the best of our knowledge, this may be the first study to investigate the association between the two.

Therefore, we first performed a descriptive analysis of the characteristics of patients admitted to hospitals with schizophrenia in Qingdao, Shandong Province, then used a DLNM to investigate the associations between humidex and schizophrenia admissions, further identified vulnerable populations, and finally quantified the attributable disease burden due to humidex.

Materials and Methods

Study Site

Qingdao is located on the southeast coast of the Shandong Peninsula, east of the Jiaodong Peninsula, near the Yellow Sea, and across the sea from the Korean Peninsula. It is an important coastal central city, an open coastal city, an economic central city, a national historical and cultural city, an international port city, and a coastal resort and tourism city in Shandong Province, China. By 2023, the city has jurisdiction over 7 districts and 3 county-level cities, with a permanent population of 10,371,500. Qingdao is located in the northern temperate monsoon zone and has a temperate monsoon climate.

Data Collection

Daily schizophrenia admission data, including admission date, age and sex, from January 1, 2016, to December 31, 2020, were obtained from the hospital information system (HIS) of Qingdao Mental Health Center. Cases meeting the following requirements were included in the study: (a) people with schizophrenia according to the 10th edition of the International Classification of Diseases codes F20-F20.9¹⁵ and (b) registered residence in Qingdao. Patients whose information was incomplete (eg, lack of sex or age) or who were readmitted within 30 days were excluded.¹⁶

The daily average temperature (TEM), relative humidity (RH), sunshine duration, rainfall, atmospheric pressure and wind speed, were obtained from the National Meteorological Science Data Center (<http://data.cma.cn/metadata/#/layerType>). Air pollution data during the study period were obtained from the real-time air quality monitoring platform (<https://www.aqistudy.cn/historydata/>). Humidex is a new comprehensive indicator that combines daily relative humidity (RH) and average temperature (TEM) and is calculated via the following formula (Eq. A.1):^{12,13,17}

$$\text{Humidex} = \text{TEM} + 5 \times \left[6.112 \times 10^{7.5 \times \text{TEM} / (237.7 + \text{TEM})} \times (\text{RH} / 100) - 100 \right] / 9$$

Statistical Analysis

In this study, a generalized linear model combined with a DLNM was used to investigate the association between Humidex and schizophrenia admissions. [Table S1](#) shows the Spearman correlation coefficients between environmental factors from 2016–2020 in Qingdao. Humidex was highly correlated with atmospheric pressure ($r_s = -0.85$, $P < 0.05$) and daily average temperature ($r_s = 0.99$, $P < 0.05$). For air pollutants, PM_{2.5} was highly positively correlated with PM₁₀ ($r_s = 0.92$, $P < 0.05$), SO₂ ($r_s = 0.62$, $P < 0.05$), NO₂ ($r_s = 0.65$, $P < 0.05$) and CO ($r_s = 0.86$, $P < 0.05$). Humidex is calculated from daily relative humidity and mean temperature, to avoid multicollinearity, the following variables (atmospheric pressure, relative humidity, daily mean temperature, PM₁₀, SO₂, NO₂ and CO) are not included in the final model.

The constructed formula is as follows (Eq. A.2):

$$Y_t \sim \text{quasi-Poisson}(\mu_t)$$

$$\begin{aligned} \text{Log}[E(Y_t)] = & \alpha + \beta \text{Hum}_{t,l} + 3 + \text{ns}(\text{PM}_{2.5}, 3) + \text{ns}(\text{O}_3, 3) + \text{ns}(\text{Time}, 7 \times 5) + \text{ns}(\text{RF}, 3) + \text{ns}(\text{SD}, 3) \\ & + \text{ns}(\text{WS}, 3) + \text{DOW} + \text{Holiday} \end{aligned}$$

In the above formula:

ns (): natural cubic spline;

β : the matrix coefficient;

$\text{Hum}_{t,t}$: the cross-basis of Humidex;

E (Yt): the expected number on day t;

On the basis of the minimum quasi-Poisson Akaike information criterion (QAIC), 3 degrees of freedom (dfs) are determined to adjust for environmental factors and 7 df are adjusted for seasonal trends.¹¹ Three df were used for the exposure-response and lag-response dimensions of the humidex.¹¹ In addition, according to the minimum principle of the QAIC, 7 days was selected as the maximum lag day (Table S2).

Stratified analysis was performed by sex and age (0–44 years and ≥ 45 years).¹⁸ The Z-test was used to compare the two estimates derived from each sub-group.¹⁹ We defined the 2.5 and 97.5 percentiles of humidex as low and high humidex, respectively.

Consistent with many previously published studies,^{14,17,20} the attributable burden due to low humidex was calculated via the following formula (Eq. A.3):

$$AF_t = (RR_t - 1)/RR_t \quad AN_t = AF_t \times N_t$$

N_t : The number of schizophrenia admissions on day t;

AN_t : The number of schizophrenia admissions attributed to low humidex on day t;

AN: The total number of schizophrenia admissions attributed to low humidex

AF_t : The ratio of AN to the total number of schizophrenia admissions (N).

The model in this study was fitted by using the “dlnm” and “splines” software packages. Two-sided variables with $P < 0.05$ were considered significantly different.

Sensitivity Analysis

We first test the robustness of the model by changing the df of the time trend (6–9) and the environment variables (3–5). The cut-off point of the 2.5th percentile low humidex is then replaced with the 1st or 5th percentile.¹¹

Results

Descriptive Analysis

The characteristics of daily schizophrenia admissions in Qingdao, China, from 2016 to 2020 are shown in Table 1. There were 5630 hospital admissions for schizophrenia, with an average of 3.1 admissions per day. More females than males were admitted to the hospital for schizophrenia, with a ratio of approximately 2:1 (3747 vs 1883). In terms of age groups, 58.5% (3294 cases) were in the 0–44 years age group. Table 2 shows the basic statistics of the environmental factors in Qingdao. During the study period, the daily relative humidity, mean temperature, sunshine duration, wind speed, rainfall and atmospheric pressure were 68.6%, 13.9°C, 6.0 h, 0.6 m/s, 1.5 mm and 1.1008.1 hPa, respectively. The daily average concentrations of PM_{2.5}, PM₁₀, SO₂, NO₂, CO and the maximum 8-hour average concentrations of O₃ were 41.4 µg/m³, 82.5 µg/m³, 16.2 µg/m³, 34.5 µg/m³, 0.8 mg/m³ and 96.6 µg/m³, respectively. Humidex ranged from –16.4 to 44.1, with an average of 15.8.

Table 1 Characteristics of Daily Schizophrenia Admissions in Qingdao, China, from 2016–2020

Variables	Sum	Mean (SD)	Frequency Distribution				
			P(0)	P25	P50	P75	P(100)
Total	5630	3.1 (1.6)	0	2	3	4	13
Male	1883	1.0 (0.9)	0	0	1	2	9
Female	3747	2.0 (1.1)	0	2	2	2	4
0–44 years	3294	1.8 (1.3)	0	1	2	3	10
≥ 45 years	2336	1.3 (1.1)	0	0	1	3	3

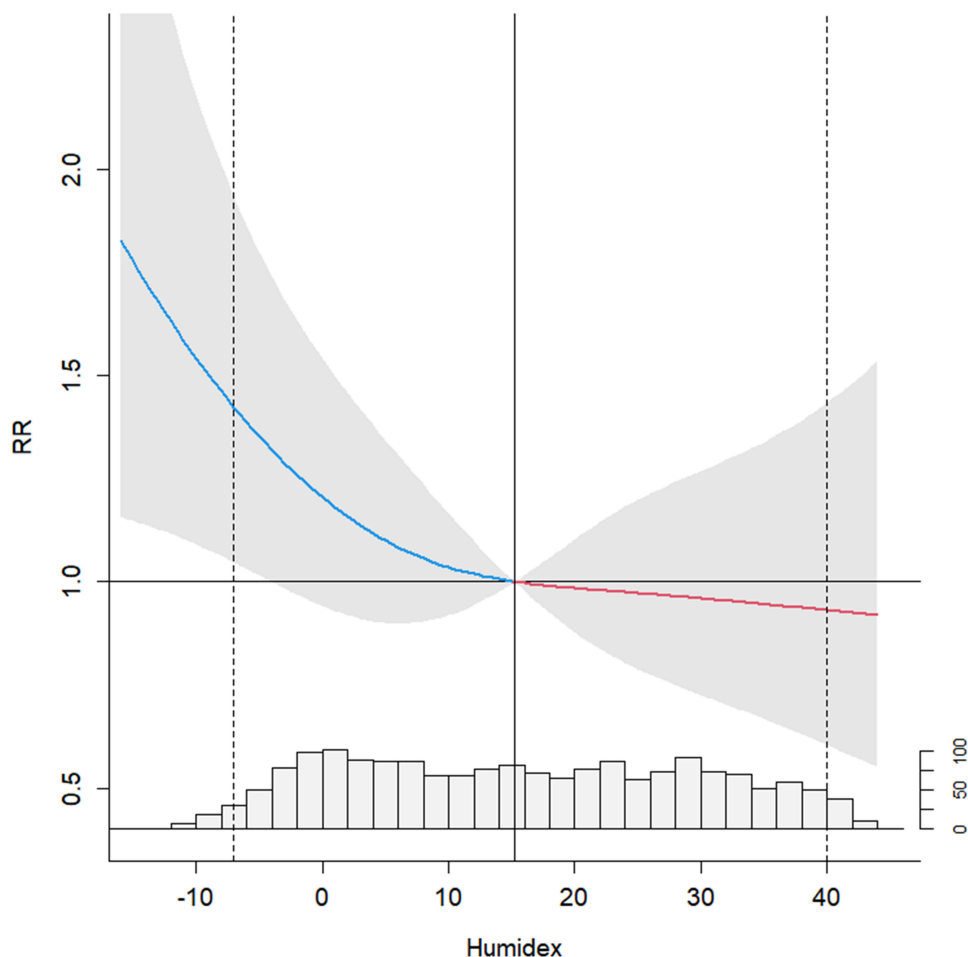
Table 2 Descriptive Statistics of Meteorological Variables and Air Pollutants in Qingdao

Group	Mean (SD)	Minimum	P(25)	P(50)	P(75)	Maximum
Humidex	15.8 (13.9)	−16.4	3.5	15.2	27.8	44.1
Mean temperature (°C)	13.9 (9.3)	−11.5	5.7	14.7	22.2	30.6
Relative humidity (%)	68.6 (16.5)	16.0	56.0	70.0	83.0	100
Wind speed (m/s)	0.6 (1.4)	0.0	0.0	0.0	0.0	8.5
Sunshine duration (h)	6.0 (3.9)	0.0	2.6	6.8	8.9	13.0
Atmospheric pressure (hPa)	1008.1 (9.2)	979.3	1000.4	1008.2	1015.4	1032.3
Rainfall (mm)	1.5 (6.7)	0.0	0.0	0.0	0.0	104.6
PM _{2.5} (μg/m ³)	41.4 (33.2)	4	20	31	53	304
PM ₁₀ (μg/m ³)	82.5 (49.9)	13	48	70	102	455
SO ₂ (μg/m ³)	16.2 (12.6)	2	7	13	21	130
NO ₂ (μg/m ³)	34.5 (16.9)	3	22	32	44	111
CO (mg/m ³)	0.8 (0.4)	0.2	0.5	0.7	0.9	3.4
O ₃ (μg/m ³)	96.6 (40.2)	10	65	94	120	254

Abbreviations: SD, standard deviation; PM_{2.5}, particulate matter with an aerodynamic diameter less than 2.5 μm; PM₁₀, particulate matter with an aerodynamic diameter less than 10 μm; SO₂, sulfur dioxide; NO₂, nitrogen dioxide; O₃, ozone; CO, carbon monoxide.

Association Between Humidex and Schizophrenia Admissions

Figure 1 shows the overall exposure-response association between Humidex and schizophrenia admissions in Qingdao, 2016–2020. A nonlinear statistical association between schizophrenia admissions and humidex was found.

**Figure 1** Exposure-response associations between Humidex and schizophrenia admissions in Qingdao, 2016–2020.

[Table S3](#) displays the RRs and 95% CIs of high humidex on schizophrenia admissions at various lag days (P 97.5 vs median). Thus, we could conclude that daily schizophrenia admissions were not associated with high humidex but were associated with low humidex. Therefore, our study focused mainly on the association between low humidex (2.5th percentile) and daily schizophrenia admissions.

[Tables 3](#) and [S4](#) show the lag effects of schizophrenia admissions associated with the 2.5th percentile of humidex in Qingdao, 2016–2020. A significant positive association between low humidex and hospital admission for schizophrenia has been reported. The significant single-day lag effects began at lag 2 (1.060, 1.006–1.117), reached a maximum at lag 4 (1.078, 1.008–1.152) and continued until lag 5 (1.063, 1.008–1.122). In addition, the significant cumulative lag effects continued from lag 0–4 (1.276, 1.003–1.622) to lag 0–7 (1.423, 1.048–1.934).

[Figure 2](#) shows the lag effects of low humidex on various subgroups of schizophrenia admissions. Significant adverse effects were found only in the female group and in the 0–44 year-old group, indicating that these two groups are more susceptible to low humidex. In the female group, the significant single-day lag effects persisted from lag 2 (1.066, 1.009–1.126) to lag 5 (1.079, 1.020–1.142), and reached their maximum at lag 4 (1.093, 1.018–1.172). The cumulative lag effects were significant from lag 0–4 (1.302, 1.012–1.677) to lag 0–7 (1.515, 1.098–1.991). For the 0–44 age group, the significant single-day lag effects were significant from lag 2 (1.080, 95% CI: 1.009–1.157) to lag 5 (RR = 1.084, 95% CI: 1.011–1.163), and the cumulative lag effects persisted from lag 0–5 (RR = 1.473, 95% CI: 1.059–1.887) to lag 0–7 (RR = 1.500, 95% CI: 1.048–1.949).

Calculation of Attributable Risk

[Table 4](#) displays the attributable fractions (AFs) and numbers (ANs) of low humidex on schizophrenia admissions for the total and different subgroups. Consistent with several previously published studies,^{11,21} we calculated the AF and AN above by selecting the maximum single-day lag effects for each group. The AF and AN of low humidex on schizophrenia admissions were 7.2% and 407, respectively. The AF and AN of females were 8.5% (95% CI: 1.8–14.7%) and 319, respectively. In terms of the age group, the AFs and ANs of the 0–44 years old age group were 9.6% (95% CI: 1.2–17.2%) and 316, respectively. Moreover, the effects in the male group and in the ≥45 years age group were not statistically significant.

Sensitivity Analysis

[Figures S1–S3](#) show the results of the effects of low humidex on schizophrenia admissions when the *df* varies with respect to time trend (6–9), meteorological factors (3–5) and air pollutants (3–5). We found no significant change in the results. We further varied the cut-off points (1st and 5th percentiles) of low humidex in the model, and found that the results did not change significantly ([Figure S4](#)). These sensitivity results indicate that our results are robust.

Table 3 The Relative Risk of Schizophrenia Admissions Associated with 2.5th Percentile of Humidex in Qingdao, 2016–2020

Lag	Single Lagged Effects (P _{2.5} vs Median)				
	Total	Male	Female	0–44 years	≥45 years
0	1.003 (0.887–1.135)	1.021 (0.823–1.267)	0.995 (0.874–1.132)	0.998 (0.846–1.176)	0.998 (0.812–1.225)
1	1.034 (0.964–1.109)	1.037 (0.918–1.172)	1.033 (0.960–1.111)	1.042 (0.949–1.143)	1.013 (0.901–1.139)
2	1.060 (1.006–1.117)*	1.049 (0.959–1.148)	1.066 (1.009–1.126)*	1.080 (1.009–1.157)*	1.026 (0.940–1.121)
3	1.077 (1.009–1.149)*	1.054 (0.941–1.181)	1.088 (1.016–1.166)*	1.104 (1.013–1.204)*	1.035 (0.927–1.156)
4	1.078 (1.008–1.152)*	1.048 (0.933–1.178)	1.093 (1.018–1.172)*	1.106 (1.012–1.208)*	1.038 (0.927–1.162)
5	1.063 (1.008–1.122)*	1.032 (0.940–1.132)	1.079 (1.020–1.142)*	1.084 (1.011–1.163)*	1.034 (0.943–1.133)
6	1.039 (0.976–1.105)	1.009 (0.905–1.124)	1.054 (0.987–1.125)	1.048 (0.966–1.138)	1.025 (0.923–1.138)
7	1.010 (0.907–1.124)	0.982 (0.815–1.185)	1.023 (0.914–1.145)	1.006 (0.872–1.162)	1.014 (0.848–1.212)

Notes: *P < 0.05. The median of the humidex (15.22) was used as the reference value.

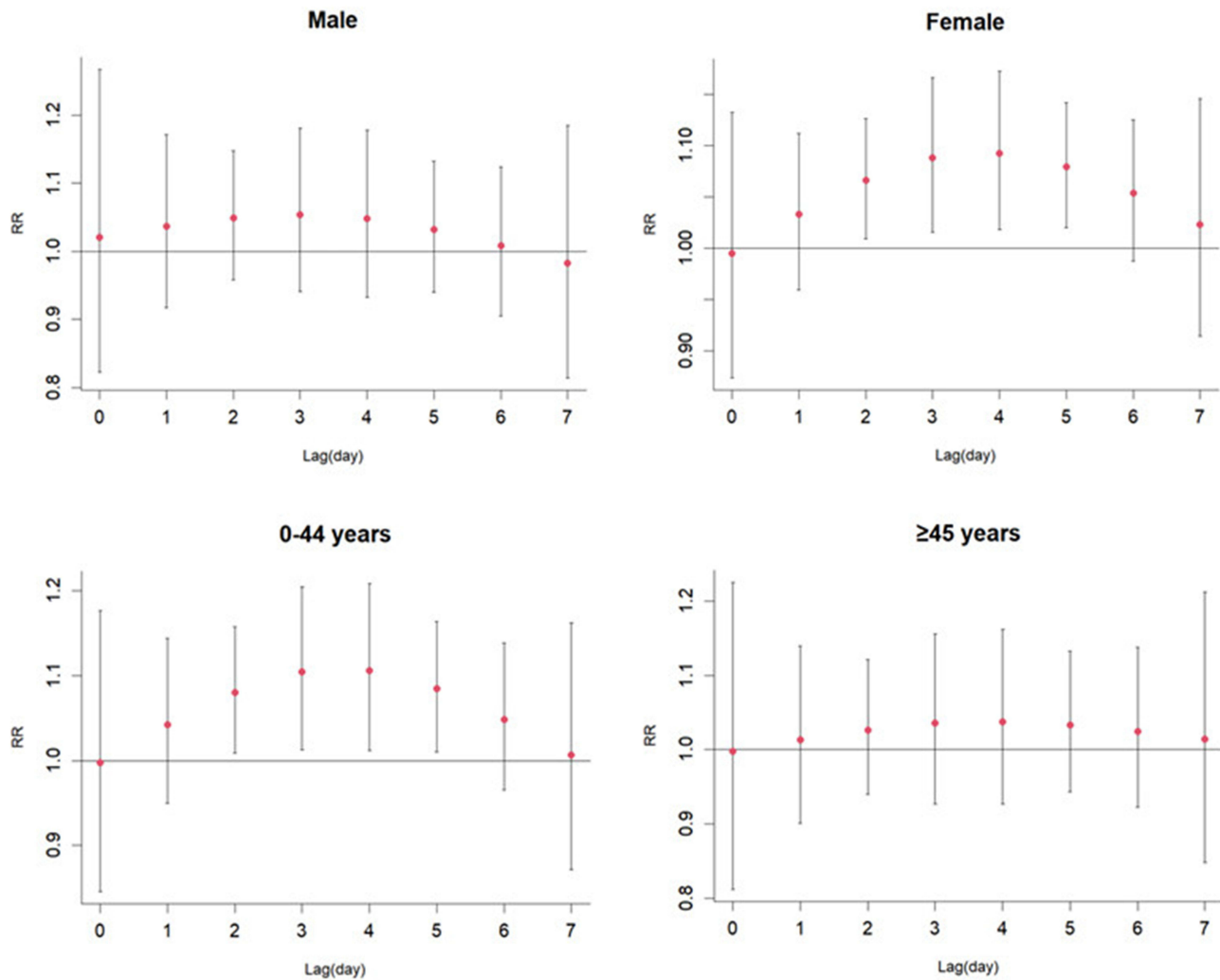


Figure 2 The lag-effects of specific humidex (P2.5) on various subgroups of schizophrenia admissions.

Discussion

In the context of climate change, there is growing concern about the impact of meteorological factors on adverse mental health outcomes. However, previous studies have focused on the effects of a single level of meteorological factors, which may underestimate or overestimate the effects on outcomes. To the best of our knowledge, this study is currently the first to evaluate the effects of humidex on schizophrenia admissions with a time series study design. A total of 5630 schizophrenia admissions were included during the study period, and after adjusting for other confounding factors,

Table 4 Attributable Fractions (AF) and Numbers (AN) of Schizophrenia Admissions for the Total and Different Subgroups

Group	AN	AF	95% CI	
Total	407 (45, 743)	7.2%	0.8%	13.2%
Male	96 (–118, 289)	5.1%	–6.3%	15.3%
Female	319 (66, 550)	8.5%	1.8%	14.7%
0–44 years	316 (39, 567)	9.6%	1.2%	17.2%
≥45 years	86 (–184, 326)	3.7%	–7.9%	13.9%

such as sunshine duration, wind speed, rainfall, PM_{2.5}, and O₃, we found that low humidex had a statistically significant effect on schizophrenia admissions. 7.2% (407 patients) of schizophrenia admissions were attributed to low humidex. Moreover, females and young individuals (<45 years) are susceptible to low humidex.

Humidex is a comprehensive index that combines average daily temperature and relative humidity to reflect the actual perceived temperature. Previously published studies have shown that low humidex is associated with a series of adverse health outcomes. For example, in a time series study of four cities in Southwest China, an inverted J-shaped relationship was found between humidex and cardiovascular disease mortality.²² The cumulative RRs of high and low humidex were 1.19 (95% CI: 0.98–1.44) and 2.52 (95% CI: 1.88–3.38), respectively, and 20.6% of cardiovascular mortality was due to low humidex.¹³ Another time series study investigated the association between tuberculosis (849,676 cases) and humidex in 22 cities in China and reported a conspicuous J-shaped relationship between the two.¹⁰ Low humidex significantly increased the risk of tuberculosis incidence, with a maximum relative risk of 1.40 (95% CI: 1.11–1.76). In Shantou, low humidex significantly increased the risk of hip fracture admission in middle-aged and older adults, and the cumulative lag effects of low humidex (13, 2.5th) lasted from lag 0–0 (1.145, 1.041–1.259) to lag 0–6 (1.258, 1.010–1.567) and reached a maximum at lag 0–3 (1.330, 1.113–1.590).¹¹ Low humidex is also associated with an increased risk of asthma in children in Hefei.²¹ Studies have also revealed that high humidex are harmful to humans. For example, in Shanghai, China, a study investigated the association between exposure to humidex and allergic conjunctivitis in children and adolescents. Humidex exposure significantly increased the risk of allergic conjunctivitis, especially in highly high humidex, and the cumulative RRs ranged from lag 0–0 (1.08, 1.05–1.11) to lag 0–14 (1.21, 1.13–1.28).¹² A study in the hot and humid city of Chongqing, China, reported that high humidex (≥ 40) was significantly associated with depression visits, with 1.1% (1709 cases) of depression visits being due to high humidex.¹⁷ Overall, there are few studies on humidex and mental health, and this study is the first to investigate the associations between humidex and schizophrenia admissions.

The biological mechanism is currently unknown, but it may be related to low temperature. Ambient temperature regulates related biochemicals such as serotonin production and plasma tryptophan, whereas low temperatures stimulate the sympathetic nerves and increase blood levels of catecholamines.²² The dopamine receptor hypothesis in schizophrenia has been widely recognized, and many studies have shown that the dopamine 2 receptor in the brains of patients with schizophrenia is significantly higher than that in the brains of normal people and that impaired dopamine participation in thermoregulation can easily lead to thermoregulatory dysfunction in patients, who are more sensitive to temperature changes than normal people, are, have difficulty adapting to low temperature environments, and experience the onset of schizophrenia.²³ Moreover, patients with schizophrenia have cognitive impairment to a certain extent, so their cognition of the surrounding environment is low, they are unable to be aware of themselves when exposed to low temperatures, and they cannot actively take interventions and protective measures to aggravate their condition.^{24,25}

In this study, females were more susceptible to low humidex than males, and the attributable burden was greater in females than in males. The physical fitness of females is weaker than that of males, and their ability to regulate body temperature is relatively weak. When they encounter low humidex, physical function may slow, resulting in poor blood circulation, which affects the oxygen supply to the brain and aggravates tension and anxiety.^{26–28} In addition, low humidex can stimulate the sympathetic nervous system, further exacerbating the onset of schizophrenia.^{29,30} Most cases of schizophrenia occur during childhood, adolescence, or early adulthood, but the prevalence of schizophrenia in middle-aged individuals has also increased in recent years.³¹ The results suggest that young individuals (0–44 years) are more susceptible to low humidex, possibly because young individuals face more study pressure, occupational pressure, and family responsibilities,³² which leads to an increased incidence of schizophrenia admissions. On the other hand, young individuals had more opportunities to go outside and were exposed to more low-humidex.

This study has the following advantages. First, this may be the first study to explore the association of humidex with schizophrenia admissions. Compared with previous studies that investigated the average daily temperature or relative humidity alone, the introduction of Humidex, a comprehensive indicator that combines the two, may have more pronounced effects on human health. Second, we further calculated the AF and AN of schizophrenia admissions due to low humidex, providing more information about the adverse effects, which is important for people to better understand the harms of low humidex and take further preventive measures.

However, this study has several limitations. First, this study was conducted in only one city, Qingdao, which may represent the characteristics of coastal cities, but the results should be promoted with caution. Second, exposure measurement bias was inevitable. We used average data from monitoring stations and did not have individual exposure data, which may underestimate the effects of humidex on schizophrenia. Third, we collected only basic information from schizophrenia patients, and more detailed personal information, such as disease history, lifestyle, outdoor exercise time, socioeconomic status, comorbid conditions, or medication use, may also affect the results, which needs further detailed analysis. In conclusion, more studies are needed to validate our conclusions, especially multicenter and studies based on precise individual exposures.

Conclusion

In the coastal Chinese city of Qingdao, low humidex was associated with schizophrenia admissions. These results remind us to strengthen the protection of vulnerable groups (females and young individuals). In addition, this study not only complements the current evidence on the association between humidex and schizophrenia, but also provides a reference for the rational allocation of medical care in the medical sector and the formulation of targeted policies by the government.

Ethics Approval and Informed Consent

This research was approved by the Ethics Committee of Qingdao Mental Health Center. Patient privacy in this study will be respected at all times. During the stable period of the patient's condition, the nurse will seek the patient's informed consent. All study procedures were conducted in accordance with the guidelines of the Declaration of Helsinki.

Author Contributions

All the authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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