



Research article

Heat and outpatient visits of skin diseases – A multisite analysis in China, 2014–2018

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ABSTRACT

Background: Many studies have shown that various kinds of diseases were associated with the variation of ambient temperature. However, there's only a scrap of evidence paying attention to the link between temperature and skin diseases, and no relevant national research was performed in China.

Objective: This study aimed to quantify the effect of heat on skin diseases and identify the vulnerable populations and areas in China.

Methods: Daily meteorological data, air pollutant data and outpatient data were collected from in 18 sites of China during 2014–2018. A time-series study with distributed lag nonlinear model and multivariate meta-analysis was applied to analyze the site-specific and pooled associations between daily mean temperature and daily outpatient visits of skin diseases by using the data of warm season (from June to September). Stratified analysis by age, sex and climate zones and subtypes of skin diseases were also conducted.

Results: We found a positive linear relationship between the ambient temperature and risk of skin diseases, with a 1.25% (95%CI: 0.34%, 2.16%) increase of risk of outpatient visits for each 1 °C increase in daily mean temperature during the warm season. In general, groups aged 18–44 years, males and people living in temperate climate regions were more susceptible to high temperature. Immune dysfunction including dermatitis and eczema were heat-sensitive skin diseases.

Conclusions: Our findings suggested that people should take notice of heat-related skin diseases and also provided some references about related health burden for strategy-makers. Targeted measures for vulnerable populations need to be taken to reduce disease burden, including monitoring and early warning systems, and sun-protection measures.

1. Introduction

Over past few decades, rising temperatures and global warming have become an issue of worldwide public concern. Extensive epidemiological and experimental literatures have verified that a variety of illnesses were associated with the increasing ambient temperature, especially cardiovascular and respiratory diseases [1, 2]. Recently, a growing number of researchers tend to assess the risk of high temperature on skin diseases, which can help calculate the excess burden of skin diseases caused by climate change. Several studies found that atopic dermatitis, measles and eczema were connected to ambient temperature [3, 4]. Besides,

infectious skin diseases and skin cancers were also related to ambient temperature [5, 6].

However, the results of different studies regarding the association between temperature and incidence of skin diseases were not consistent, and most researches only concerned about a single type of skin disease [7, 8, 9, 10]. Li and colleagues in Shanghai [8] discovered a positive correlation between high temperature and eczema prevalence through a time series study, while Ma and colleagues in Lanzhou [7] obtained an opposite conclusion. Additionally, a cohort study in the United States showed that high temperature was related to poorly controlled atopic dermatitis [10], however, an epidemiological survey of children

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indicated that atopic dermatitis reduced with high temperature increasing [9]. Therefore, whether rising temperatures will increase the risk of skin diseases remains an unsolved question.

Meanwhile, now most of existing studies were just conducted in a single city or district, so their results were inconsistent partly due to regional differences [8, 11]. Figuring out the discrepancy among various areas is essential to provide targeted guidance. Whereas, no such multisite analyses on heat and skin disease incidence were conducted in China, a country covering a vast territory with a great population. Multisite analysis can pool the site-specific RRs and estimate the combined values, and by this way, the relationship between heat and skin disease incidence could be observed at the national level.

Therefore, the purpose of our study is to explore the association between ambient temperature and the risk of skin diseases, and to identify the vulnerable populations and areas, and sensitive diseases in 18 sites in China from 2014 to 2018, providing practical preventive suggestions for the public.

2. Materials and methods

2.1. Study sites

This study is performed based on the national project called Scientific Investigation on Regional Climate-sensitive Diseases in China, which is supported by the National Ministry of Science and Technology. In this project, two or three sites were selected in each meteorological geographic region in China. According to China Meteorological Administration, there are 11 meteorological geographic regions in China. So, there are a total of 24 sites that were selected in this project. In each site, one or two general

hospitals capable of providing medical services to almost all disease types were selected. These selected hospitals were required to have at least 200 daily outpatient visits from each local sites. Due to the lack of hospital admission data in Wuxi, Ningbo, Wuhan, Shenzhen, Lhasa, and Nyingchi, we selected 18 sites which covered four climate zones including plateau mountain climate, subtropical monsoon climate, temperate continental climate and temperate monsoon climate in this study (Figure 1).

2.2. Data collection

2.2.1. Outpatient data for skin diseases

For each site, one or two comprehensive hospitals were selected to collect outpatient counts from 2014 to 2018, including the date of hospital visiting, age, sex and diagnose. Various skin diseases were classified in accordance with the 10th Revision of the International Statistical Classification of Disease (ICD-10). We emphatically analyzed all-cause skin diseases and specific diseases of high incidence or great hazard: all-cause skin disease (L00-L99), infections of the skin and underlying tissues (L00-L08), dermatitis and eczema (L20-L30) and skin diseases related to immune dysfunction (L20-L54). The data was also separated according to different age (0–6, 7–17, 18–44, 45–59, 60–74, ≥75 years) [12], sex (male and female) and climate regions (plateau mountain climate, temperate continental climate, temperate monsoon climate and subtropical monsoon climate).

2.2.2. Daily meteorological and air pollution data

Daily meteorological data was acquired from China Meteorological Administration, including daily maximum temperature (°C), daily mean temperature (°C), daily minimum temperature (°C), daily mean relative

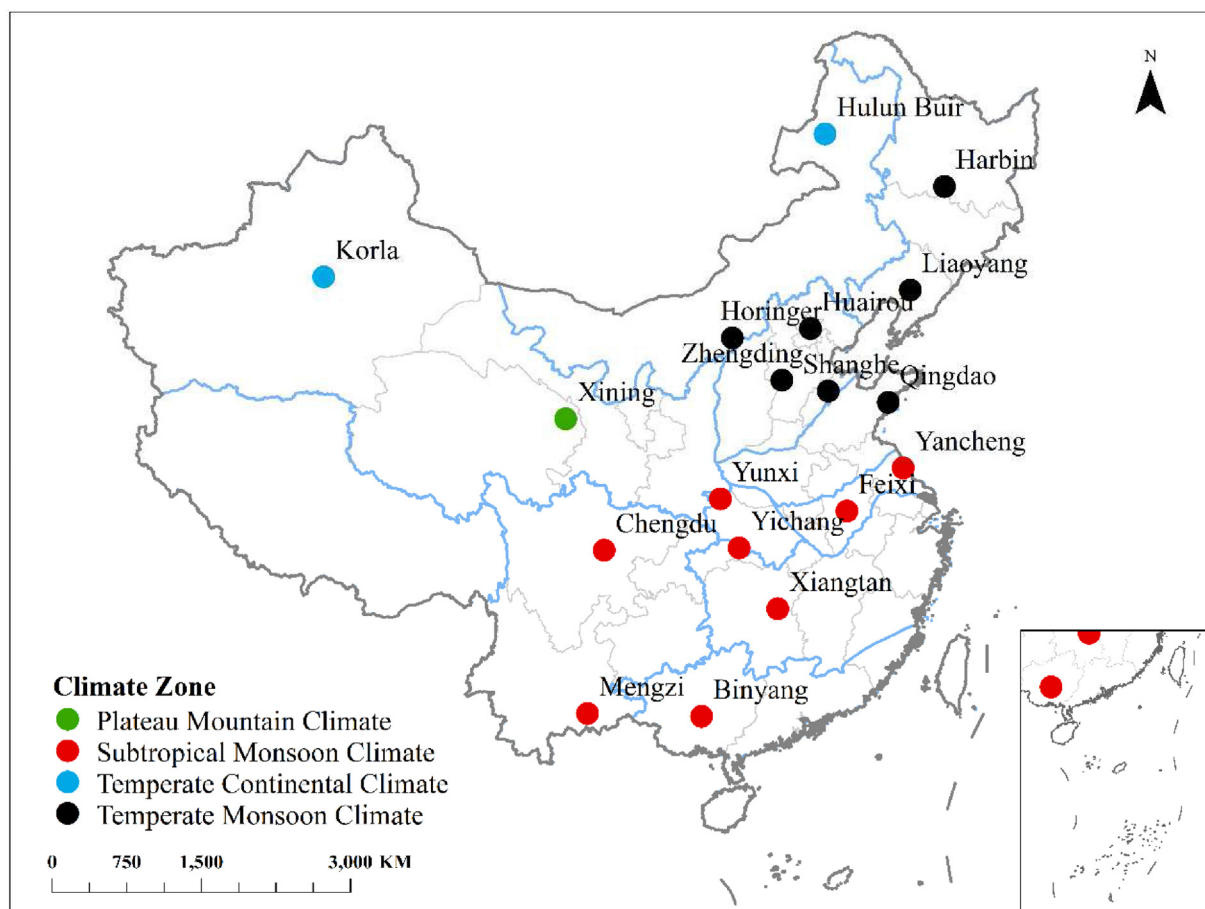


Figure 1. Geographical location of 18 study sites.

humidity (RH, %), 24-hour precipitation (PRCP, mm) and daily mean station pressure (P, hPa).

Daily air pollution data was collected from local Ecology and Environment Bureau including ozone (O₃, 8 h, 8-hour moving average maximum, μg/m³), PM₁₀ (μg/m³) and PM_{2.5} (μg/m³).

2.3. Statistical analysis

In the first stage, we used the warm-season data (from June to September) [13] and a distributed lag nonlinear model (DLNM) combined with a linear regression model to fit the site-specific association between daily mean temperature and daily outpatient visits of skin disease. We assumed that the risk of skin diseases was positively linear associated with high temperature exposure during the warm season as previous study suggested [14], and we set the lag day up to 5 days to entirely explore the delayed effect and accumulative effect of temperature and fitted the lag-response relationship using a natural cubic spline (*ns*) with 3 degrees of freedom (*df*) [14, 15]. The confounding effects of relative humidity, 24-hour precipitation, PM_{2.5} and ozone were controlled for using *ns* with 3 *df*, and station pressure with 5 *df* [16]. The DLNM model was indicated as equation (1):

$$\text{Log}[E(Y_t)] = \alpha + cb(temp) + ns(RH, 3) + ns(PRCP, 3) + ns(P, 5) + ns(PM_{2.5}, 3) + ns(O_{3,8h}, 3) + ns(time, 6^*2) + DOW + Holiday(1)$$

where Y_t is daily outpatient counts on day t ; α is the intercept; cb is the cross-basis function to capture exposure-response relationship and lag-response relationship of daily mean temperature ($temp$); ns is the natural cubic spline function for long-term trend ($time$) with 2 df for each warm season [15]; DOW is the day of week, $Holiday$ is the binary variable indicating public holidays in China.

In the second stage, we pooled overall results using multivariate meta-analysis with a random effects model. Stratified analysis by age, sex and cause of disease was also conducted by using the same method. Additionally, given the reliability of results, when performing the analysis in different climate regions, we excluded the data of plateau mountain climate and temperate continental climate zones due to the small sample size.

2.4. Sensitivity analysis

Sensitivity analyses were examined to confirm the stability of results as well, and the process was as follows: (1) Substituting the PM₁₀ for PM_{2.5} in the model; (2) Adjusting the df of RH, PRCP from 4 to 6; (3) Replacing the lag days of $temp$ with 4 and 6. Furthermore, health risks were assessed by percentage increases and confidence intervals. Difference test was used to verify the stability of the model using equation (2):

$$(\hat{Q}_1 - \hat{Q}_2) \pm 1.96\sqrt{SE_1^2 + SE_2^2} \tag{2}$$

where \hat{Q}_1 and \hat{Q}_2 are the effect estimates of two groups; and SE_1 and SE_2 are the standard errors of their estimates.

Data analysis was performed using R software (version 4.0.3, Free Software Foundation) with packages “dlnm” and “mvmeta”.

3. Results

3.1. Descriptive results

Table 1 manifested the descriptive results. Overall, 171, 741 outpatient visits were recorded during the warm season in 18 sites from 2014

Table 1. Descriptive statistics of daily meteorological data, air pollution data and outpatient visit data for skin system diseases from June to September in 18 regions, 2014–2018.

Variable	Mean ± SD	min	P ₂₅	P ₅₀	P ₇₅	max
Meteorological data						
Average temperature (°C)	13.8 ± 11.7	-38.8	6.4	16	23.1	35.9
Maximum temperature (°C)	19.3 ± 11.7	-34.1	11.5	21.6	28.5	51.7
Minimum temperature (°C)	9.6 ± 12.1	-42.4	2.0	11.7	19.3	30.9
RH (%)	67.3 ± 18.6	7	55	70	81	100
P (hPa)	968.7 ± 62.5	759.4	942.9	995.8	1009.6	1042.4
PRCP (mm)	3.2 ± 38.0	0	0	0	0.3	3276.6
Air pollution data						
O ₃ ,8h (μg/m ³)	87 ± 43	0	57	82.8	112	327
PM _{2.5} (μg/m ³)	53.4 ± 46.6	0	25	40.7	66	653
PM ₁₀ (μg/m ³)	94.1 ± 81.7	0	49	72	114	2659
Outpatient visit data						
Total	19 ± 26	0	4	11	21	204
Sex						
Male	9 ± 13	0	1	5	10	107
Female	10 ± 14	0	1	5	11	104
Age						
0–6	4 ± 10	0	0	2	4	174
7–17	2 ± 4	0	0	1	3	36
18–44	8 ± 12	0	1	4	9	101
45–59	3 ± 4	0	0	1	3	44
60–74	1 ± 2	0	0	1	2	22
≥75	0 ± 1	0	0	0	1	13
Type						
Infection	2 ± 3	0	0	1	2	27
Dermatitis and Eczema	11 ± 16	0	2	6	14	136
Immune Dysfunction	14 ± 20	0	2	8	16	158

Note. SD: Standard deviation; min: minimum; P25: the 25th percentile; P50: the 50th percentile; P75: the 75th percentile; max: maximum; RH: the relative humidity; P: daily mean station pressure; PRCP: 24-hour precipitation.

to 2018 in China. The daily average temperature was 24.1 °C (range: -0.6 °C–35.9 °C). The average relative humidity, average station pressure and 24-hour precipitation was 72.0%, 962 h Pa and 5.6 mm, respectively. The concentration of O₃, 8 h, PM_{2.5}, PM₁₀ was 106.4 µg/m³, 34.1 µg/m³ and 64.3 µg/m³, respectively. On average, approximately 21 visits went to hospital each day for skin disorders and 2 for infections of the skin and subcutaneous tissues, 12 for dermatitis and eczema, 15 for immune dysfunction.

After excluding the plateau mountain climate zone (3245 cases) and temperate continental climate zone (6316 cases), there were 64,337 cases in temperate monsoon climate zone and 97,843 cases in subtropical monsoon climate zone (Table 2).

3.2. Association between temperature and skin diseases

Figure 2 demonstrated a linear pattern of the association between temperature and outpatients of skin disease during the warm seasons.

Figure 3 showed the associations between daily mean temperature and outpatient of skin diseases among different subgroups nationwide and in different climate regions.

Overall, a 1 °C increase of daily mean temperature during the warm season was associated with 1.25% (95% confidence interval, 95%CI: 0.34%, 2.16%) increase of risk in skin disease. A 1 °C increase of temperature led to 1.67% (95%CI: 0.68%, 2.67%) and 1.42% (95%CI: 0.45%, 2.40%) increase of risk in patients with dermatitis and eczema and immune dysfunction. Besides, people aged 0–6 years [2.08%, (95% CI: 0.20%, 3.96%)], 18–44 years [1.373% (95%CI: 0.24%, 2.50%)] and males [1.22% (95%CI: 0.36%, 2.08%)] were more susceptible to ambient high temperature.

In temperate monsoon climate region, the risk of skin diseases-related outpatients was increased by 1.48% (95%CI: 0.58%, 2.37%) with each 1 °C increase of ambient temperature. A 1 °C increase in temperature resulted in 1.67% (95%CI: 0.68%, 2.67%) increase of risk in patients with dermatitis and eczema, and 1.42% (95%CI: 0.45%, 2.40%) risk in immune dysfunction. For different age group, only groups aged 18–44 years were at risk [2.07% (95%CI: 0.54%, 3.60%)]. And both males [1.52% (95%CI: 0.13%, 2.91%)] and females [1.23% (95%CI: 0.03%, 2.43%)] were susceptible to higher temperature. However, no

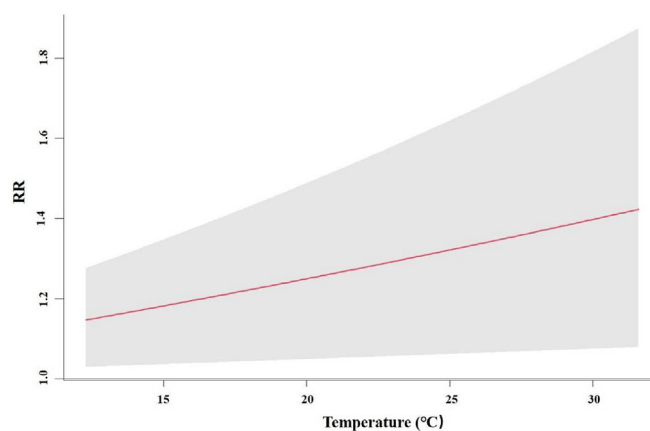


Figure 2. The relationship between temperature and outpatients of skin disease during the warm season in 18 study sites.

statistically significant results were obtained in subtropical monsoon climate region.

3.3. Sensitivity analysis

Table 3 showed that the association between temperature and outpatient visit counts was robust. Replacing PM₁₀ with PM_{2.5} in the model did not change the effect estimates. The results of varying the *df* of RH, PRCP were the same as main outcomes. And the significant result was stable when changing the lag days of temperature.

4. Discussion

For all we know, this is the first national study to estimate the association between ambient temperature and outpatient visits of skin diseases in China. Our results showed that the prevalence of skin diseases, especially immune dysfunction including dermatitis and eczema, was positively associated with high temperature. Groups aged 0–6 years and 18–44 years, males, and people living in temperate monsoon climate

Table 2. Characteristics of study periods, daily mean temperature and outpatient visits in 18 study sites in China from June to September, 2014–2018.

Sites	Study periods	Daily mean temperature (°C)				Total	Outpatient visits (cases)			
		Mean ± SD	Min	Median	Max		Mean ± SD	Min	Median	Max
Xining	2016–2018	15.1 ± 3.6	5.5	15.2	25.6	3245	9 ± 5	0	9	27
Korla	2015–2018	24.0 ± 4.4	10.3	24.2	35.9	1540	3 ± 2	0	3	11
Huairou	2016–2018	23.7 ± 3.8	9.9	24.2	32.2	5002	14 ± 5	3	13	35
Zhengding	2014–2018	25.7 ± 3.7	9.5	26.1	33.6	10,353	17 ± 7	1	17	38
Horinger	2014–2016	19.6 ± 4.3	4.8	20.1	31.0	358	1 ± 1	0	1	5
Hulun Buir	2014–2016	16.6 ± 5.5	0.2	17.3	28.6	4776	13 ± 6	0	13	34
Liaoyang	2014–2018	22.8 ± 4.2	7.7	23.2	32.6	3711	6 ± 8	0	1	33
Harbin	2016–2018	19.8 ± 5.0	4.7	20.6	30.8	6124	17 ± 17	0	10	83
Shanghe	2014–2016	24.3 ± 3.9	11.3	24.6	33.0	2214	6 ± 4	0	5	26
Qingdao	2015–2017	22.7 ± 3.7	12.4	23.2	30.6	36,575	100 ± 28	38	99	189
Yancheng	2015–2016	24.4 ± 3.8	14.5	24.3	34.2	28,134	115 ± 24	54	114	204
Feixi	2014–2017	25.5 ± 3.7	15.1	25.3	35.8	13,065	27 ± 9	5	26	57
Xiangtan	2014–2017	26.3 ± 3.7	15.3	26.3	34.2	2767	6 ± 7	0	2	27
Yunxi	2015–2018	24.5 ± 3.8	13.5	24.8	33.4	8046	17 ± 10	0	17	45
Yichang	2014–2017	24.6 ± 3.6	14.0	24.7	40.5	11,288	19 ± 8	4	17	41
Binyang	2014–2018	27.7 ± 2.1	18.8	28.0	32.1	6304	10 ± 7	0	9	29
Chengdu	2015–2018	23.3 ± 2.9	14.4	23.5	29.8	5451	11 ± 5	0	11	26
Mengzi	2014–2017	23.5 ± 1.9	14.7	23.4	28.9	22,788	47 ± 13	10	47	78
Total	/	23.2 ± 5.0	0.2	23.8	40.5	171,741	21 ± 28	0	13	204

Note: SD, standard deviation; Min, minimum values; Max, maximum values.

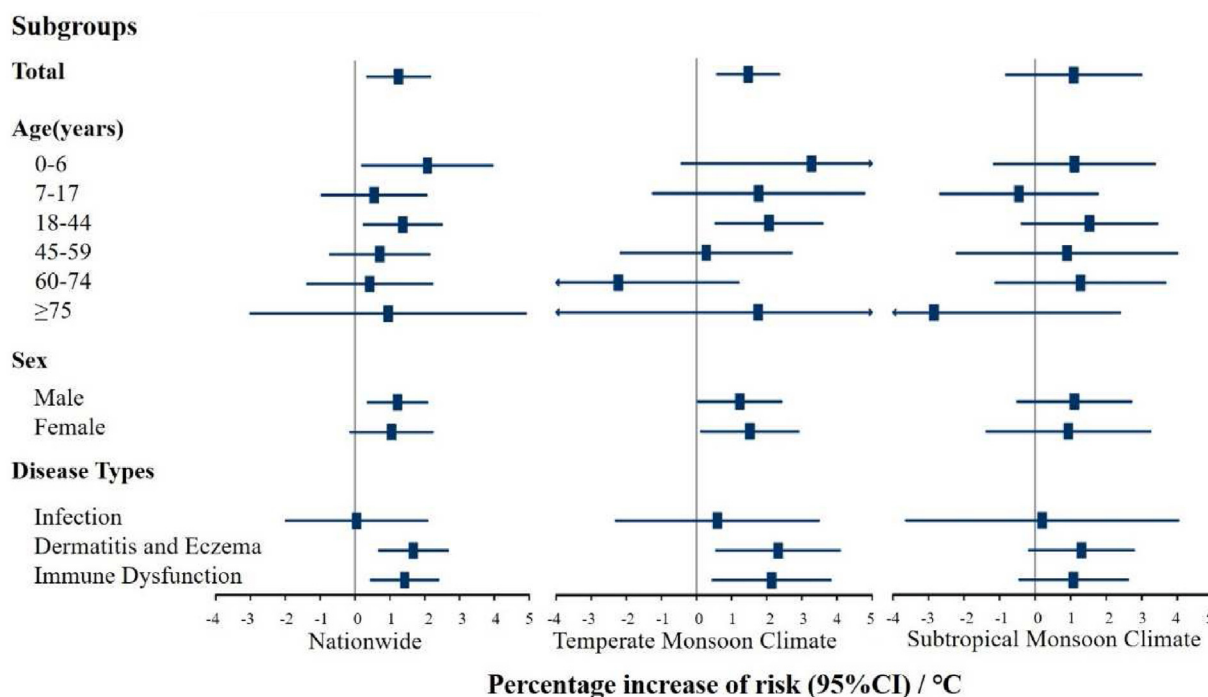


Figure 3. Subgroup associations between daily mean temperature and outpatients of skin disease nationwide and in different climate zones during the warm season.

Table 3. Sensitivity analysis results.

Parameter	Reset	AIC	Excess Risk/% (95% confidence interval)	Confidence interval [#]
Main model	/	-73.982	1.258 (0.339, 2.162)	Ref
PM ₁₀ - PM _{2.5}	/	-74.104	1.272 (0.355, 2.174)	(-0.0126, 0.0129)
df of RH	4	-74.474	1.249 (0.349, 2.132)	(-0.0125, 0.0127)
	5	-74.089	1.240 (0.325, 2.140)	(-0.0126, 0.0129)
	6	-74.595	1.254 (0.351, 2.142)	(-0.0127, 0.0128)
df of PRCP	4	-74.178	1.272 (0.360, 2.167)	(-0.0126, 0.0129)
	5	-74.258	1.272 (0.360, 2.168)	(-0.0129, 0.0126)
	6	-74.325	1.268 (0.359, 2.162)	(-0.0126, 0.0129)
lag of temperature	4	-76.623	1.174 (0.322, 2.012)	(-0.0115, 0.0132)
	6	-74.832	1.241 (0.356, 2.111)	(-0.0124, 0.0128)
	7	-74.997	1.121 (0.242, 1.987)	(-0.0112, 0.0140)

Note: RH: the relative humidity; PRCP: 24-hour precipitation; Excess Risk: (RR-1) × 100%.

[#] Confidence interval for the difference from the reference group, if including 0, then no statistical significance; if not including 0, then statistical significance; Ref, reference group.

zone were the most vulnerable populations. It suggested that specific preventive measures should be taken because of the increasing threats to skin diseases from high temperature in the context of global warming.

We found that high temperature would increase the prevalence of skin diseases. Consistently, a study in China showed a positive linear relationship between temperature (>10 °C) and daily outpatient visits [14]. It's partly because that the elevated temperatures may lead to increased ultraviolet (UV) damage from the same UV dose [17]. As several experimental and epidemiological studies suggested, the synergistic effect of UV radiation and heat were reinforced on carcinogenesis by the production of heat shock proteins in response to heat stress which would inhibit the cell-death signaling pathways, and lead to greater survival rate of DNA-damaged cells [18, 19]. And another reason may be that high temperature had an indirect impact on

skin-disease incidence by changing people's behavior. People tend to wear less clothing to dissipate heat, which result in their more UV exposure [20].

For disease types, high temperature has been found to increase the risk of skin immune diseases, especially atopic dermatitis and eczema, our finding was in line with some precious researches [9, 11, 21]. A time-series study in Lanzhou indicated that both extreme high temperature and moderate high temperature would increase the prevalence of atopic dermatitis, with RR of 1.85% (95%CI: 1.61%, 2.11%) and 1.45 (95%CI: 1.30%, 1.61%), respectively [11]. A questionnaire survey in China showed that high temperature was related with eczema with odds ratio of 1.09 [21]. Firstly, one reason may be that in high temperature atmosphere, too much sweat collects on the surface of skin would cause itching, producing irritation to the skin. Secondly, heat-causing sweating and fluid-electrolyte imbalance may be also an inducement. Too much transepidermal water loss will disrupt the function of cutaneous barrier through a variety of mechanisms, so skin will be more sensitive to physical and chemical stimulants in hot circumstances [22]. Thirdly, it may be partly because that wearing lighter clothing in warm seasons would make more areas of skin directly exposed to ultraviolet radiation, air pollutants and detrimental microorganism, leading to immune and infectious diseases, even skin cancers [23, 24, 25]. Ultraviolet B is a mutagen which can disrupt the DNA-repair mechanism, thus becoming a risk factor for skin diseases [26]. Air pollutants, especially polyaromatic hydrocarbons and ozone, may activate the process of cell metabolism and inflammation [27]. These combined causes contribute to the skin's vulnerability to high temperature.

In addition, amongst different age groups, people aged 18–44 years are the most vulnerable group both nationwide and in temperate monsoon climate. One reason may be that people aged 18–44 years, the largest proportion of labor force, are more likely to engage in outdoor work and be expose to heat. Moreover, our results also showed that children aged 0–6 years were at greater risk. These results were agreed by several other studies [11, 21]. It is probably because children's immune system is yet immature and their skin are tender to any ambient hazards, therefore they are susceptible to high temperature.

In terms of sex differences, male had a greater risk of developing skin diseases than female nationally. One reason may be that men were more likely to work outdoor. The another is that testosterone could be a heat stress susceptibility factor, making the skin more sensitive to ambient environment temperature [28]. While in temperate monsoon climate, both male and female were affected by high temperature, and female were at higher risk. Sex hormones and fragile skin barrier may play an important role [11]. As were shown in our study and previous studies, there is no unified conclusion, so more researches are needed to take this matter further.

In different climate zones, we found that the inhabitants in temperate monsoon climate were more vulnerable to high temperature than residents in subtropical monsoon climate regions. This discrepancy may be due to various living conditions. Same results were supported by other studies, which concluding that low-temperature, low-humidity, and low-ultraviolet exposure areas could affect the skin metabolism and genetic expression, causing higher incidence of skin diseases [29, 30]. Moreover, a larger number of pollution industries tend to locate in provinces with lax environmental regulation in temperate monsoon climate zones [31], so it can produce more pollutants which may lead to higher incidence of skin diseases.

We also have several limitations. First, the meteorological and air pollution data were collected from fixed monitoring sites, rather than individual exposure, so the link of temperature and skin diseases might be underestimated. Second, the statistical analysis only included temperate monsoon climate and subtropical monsoon climate, which can only be a rough reference for the whole country. This inadequacy should be addressed by expanding the scope of data collection in further study. Third, The outpatient data were collected from one or two general hospitals in each study sites, rather than all the hospitals, so the “missing outpatient visits” may lead to underestimation of the association between heat and incidence of skin diseases.

5. Conclusion

In conclusion, we found a positive linear correlation between ambient temperature and skin diseases in warm season. Overall, groups aged 0–6 years and 18–44 years, males and people living in temperate climate regions were more susceptible to high temperature. Immune dysfunction, especially dermatitis and eczema, were heat-sensitive skin diseases. Preventive measures for vulnerable populations should be taken to reduce the risk of skin diseases, including monitoring and early warning systems to forecast the risk of incidence of skin diseases, using hats and sunscreen, wearing proper clothes to reduce the damage from sun exposure on hot days, decreasing outdoor time when the sunlight is strong, and so on.

Declarations

Author contribution statement

Yushu Huang: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Hejia Song: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data.

Zixian Wang, Xinhang Zhang, Bo Sun, Yibin Cheng, Yue Liu, Shuxin Hao, Na Li, Yu Wang and Yan Wang: Contributed reagents, materials, analysis tools or data.

Yonghong Li and Xiaoyuan Yao: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

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Data availability statement

Data will be made available on request.

Declaration of interest's statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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