

## ORIGINAL ARTICLE

# Incidence of Allergic Rhinitis and Meteorological Variables: Non-linear Correlation and Non-linear Regression Analysis Based on Yunqi Theory of Chinese Medicine\*

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**ABSTRACT** **Objective:** To analyze the correlations between the incidence of allergic rhinitis (AR) and meteorological variables of previous periods, so as to establish non-linear prediction equations of AR in Beijing area. **Methods:** AR patients (10,478 cases) collected from Beijing Tongren Hospital during 2007—2010 and meteorological data (including daily average temperature, daily maximum temperature, daily minimum temperature, daily relative humidity, daily average vapor pressure, daily dew point temperature, daily precipitation, daily average wind speed, sea level pressure, and degree of comfort) collected from Beijing Municipal Meteorological Observatory in the same periods were used for the analysis. Non-linear correlation and regression were adopted to analyze the relationship between AR incidence and meteorological variables of former six-qi stage which was defined according to Yunqi theory of Chinese medicine. Comprehensive meteorological parameter was introduced to establish the predictive model. **Results:** The high incidence of AR appeared in the 4th qi stage (from the Beginning of Autumn to Autumn Equinox), while the changes of meteorological variables appeared in the 3rd qi stage (from Grain in Beard to Greater Heat), which advanced one phase. The incidence of AR was closely associated with vapor pressure. The correlation coefficients of two predictive models were between 0.8931–0.9176 and all of them have passed significant statistical tests, which showed a satisfactory fitting effect. **Conclusion:** Comprehensive meteorological parameters can be used to forecast AR incidence, which is beneficial to AR prevention.

**KEYWORDS** allergic rhinitis, comprehensive meteorological parameter, non-linear correlation, forecast, Chinese medicine, five circuits and six qi, Yunqi

Allergic rhinitis (AR) is a multifactorial disease induced by interaction of genetic and environmental factors. In recent years, this disease has received increasing attention owing to the rising global morbidity.<sup>(1-3)</sup> However, AR has its own seasonal pattern, which can be easily affected by climatic changes. In Chinese medicine, the recognitions of seasonal patterns in disease occurrence dates back at least as far as the era of *Huangdi's Internal Classic* (Huang Di Nei Jing), particularly the theory of five circuits and six qi (abbreviation: Yunqi) in the *Plain Questions* (Su Wen) of the *Huangdi's Internal Classic*. The theory of Yunqi systematically discusses the law of climate changes and the impact of those changes on the incidence of diseases. In particular, 1 year can be divided into 6 phases (i.e. six qi) according to the Yunqi theory, which reflected the ancient Chinese idea of solar terms. Recently, the theory of Yunqi has gradually received increasing attention and there are many studies adopted 'six qi' perspective of time for data processing<sup>(4,5)</sup>

Accordingly, the research on the relationship between meteorological factors and AR morbidity in six qi, including adolescent, middle-aged and elderly patients with AR, was conducted based on the AR data collected from Beijing Tongren Hospital and meteorological data (2007–2010) from Beijing Municipal Meteorological Observatory.

## METHODS

### Study Area

The city of Beijing has a semi-humid continental monsoon climatic and includes four distinct seasons,

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which characterized as windy spring, hot and rainy summer, dry autumn and cold winter. Previous studies have indicated that the climate of Beijing area was applicable to the research of Yunqi theory.<sup>(6,7)</sup> Furthermore, according to the Yunqi theory, the climatic changes deduced by six qi mode (i.e. wind represents the 1st qi, warm represents the 2nd qi, fire and summer heat represents the 3rd qi, dampness represents the 4th qi, dryness represents the 5th qi as well as cold represents the 6th qi) are quite consistent with actual climatic changes in six phases of Beijing.<sup>(8)</sup>

### Case Data

AR patients (10,478 cases), including adolescent, middle-aged and elderly people, were collected from AR Treatment Center of Beijing Tongren Hospital from February 25, 2007 to December 31, 2010. Every patient had skin prick test (SPT)-positive test results and symptoms including sneezing, runny or stuffy nose, and had not taken any medicine which might affect the SPT result such as antihistamines and corticosteroids 1 week before the test. All above refers to AR diagnostic criteria.<sup>(9)</sup> The cases were collected in day units, and no patients were examined during weekends and statutory holidays.

### Meteorological Data

Data regarding 10 basic meteorological factors were collected from Beijing Municipal Meteorological Observatory during the same period, which included daily average temperature, daily maximum temperature, daily minimum temperature, daily average relative humidity, daily average vapor pressure, daily dew point temperature, daily precipitation, daily average wind speed, sea level pressure, and degree of comfort.<sup>(10)</sup>

### Data Processing

The AR patients were divided into two groups, which include adolescent group: aged  $\leq 35$  years, middle-aged and elderly group: aged  $\geq 36$  years.

The ancient Chinese divided each year equally into 24 periods in one type of traditional Chinese calendar. These periods are called the 24 solar terms. According to the Yunqi theory, starting from the Beginning of Spring (1st solar terms), each year can be divided into 6 equal periods that are called "six qi" phases.<sup>(11)</sup> Each phase includes 4 solar terms. Therefore, the

six qi phase are respectively called 1st qi (from the Beginning of Spring to Spring Equinox), 2nd qi (from the Pure Brightness to Lesser Fullness of Grain), 3rd qi (from Grain in Beard to Greater Heat), 4th qi (from the Beginning of Autumn to Autumn Equinox), 5th qi (from Cold Dew to Lesser Snow) and 6th qi (from Greater Snow to Greater Cold). Consequently, the number of "six qi" phases from 2007 to 2010 was 23, because the 6th qi of 2010 could not be calculated due to a lack of data about January 2011. Consequently, the average values of 10 meteorological factors and AR incidence in six qi were calculated to establish a database across the years of 2007–2010.

### Statistical Methods

First, single-factor correlation was adopted to investigate the association between the incidence of AR and meteorological factors in six qi phases, which aimed to identify the important meteorological variable related to the disease.  $r_{\alpha=0.001}=0.5963$  and  $F_{\alpha=0.001}=14.00$  were considered as the criterion for statistical significance. Second, comprehensive meteorological parameter was introduced to analyze the correlation between AR incidence and weather change in six qi phases. Non-linear correlation was used to determine the relations among them. Third, the predicted values and AR actual incidences in six qi phases was compared and the fitting of non-linear regression was evaluated. Model diagnosis and error analysis were also assessed.

### Correlation and Regression Analyses

The 10 meteorological factors were used to create a variety of mathematical combination expressions with weather effects. Moreover, correlation analysis between these mathematical formulae and AR patients (adolescent group and middle-aged and elderly group) were conducted, respectively. Based on these numerous experiments, comprehensive meteorological parametric equations, referred to comprehensive meteorological parameters, were established to summarize the complex effects of meteorological factors on AR incidence. The equation achieved an optimal correlation, meaning that when comprehensive meteorological parameter increases, AR incidence also increases. The following two comprehensive meteorological parametric equations were formed according to the empirical formulae.<sup>(12)</sup>

$$CS1_i = \frac{E_i V_i^2}{P_i} \quad (1)$$

$$CS2_i = \frac{E_i T D_i I_i T d_i}{P_i} \quad (2)$$

The first equation (CS1) relates to adolescent patients with AR and the second one (CS2) relates to middle-aged and elderly patients with AR. In the above equations, "E" represents average vapor pressure in one phase, "TD" means average minimum temperature in one phase, "P" indicates average sea level pressure in one phase, "V" means average wind speed in one phase, "I" denotes average comfort in one phase, "Td" means average dew point temperature in one phase, and "i" means 1, 2, 3...23 (23 solar terms in 4 years). "E/P" represents the relative vapor pressure of air (unit: %). When relative vapor pressure becomes smaller, the air is dry; while when it becomes greater, the weather is hot and humid. "V<sup>2</sup>" represents the degree of heating and cooling. The value of "V<sup>2</sup>" is relatively smaller in summer and relatively larger in spring and autumn. The product of "TD·I·Td" represents the intensity of integrated change of temperature, comfort degree and dew point temperature. When the value is greater, it indicates high humidity and temperature, but low wind speed, which is conducive to the breeding of various kinds of allergens, and vice versa.

Thus, the first equation (CS1) reflected the degree of change in atmospheric pressure, water vapor content and wind speed (unit: m<sup>2</sup>·s<sup>-2</sup>). The second equation (CS2) reflected the degree of change in atmospheric pressure, water vapor content, temperature and wind speed (unit: °C<sup>3</sup>). The statistical process was simplified through using comprehensive meteorological parameters, instead of a variety of single meteorological elements. Thus, the cumbersome calculation steps of multiple regression and other statistical methods are avoided.

In a summary, firstly, ordered by six phases or 24 solar terms, the average of minimum temperature, vapor pressure, wind speed, comfort, dew point temperature and sea level pressure in the former phase can be calculated according to the 1st day in a certain six qi phase. Secondly, the comprehensive meteorological parameters were obtained by inputting the above meteorological factors into equations. Thirdly, the numerical trend forecast of AR incidence (adolescents and middle-aged and elderly) in a certain

six qi phase can be calculated by substituting the two comprehensive meteorological parameters (CS1 and CS2) into non-linear correlation expressions, (3) and (4). That is, the incidence trends of AR in the next 2 months might be known according to the weather condition of the 1st day in a certain six qi phase.

$$Y_{\text{adolescent}} = 129837 \times HCS1^3 - 5819.2 \times CS1^2 + 16.864 \times CS1 + 22.350 \quad (3)$$

$$Y_{\text{middle-aged and elderly}} = 0.0000004 \times CS2^3 - 0.0002 \times CS2^2 + 0.0348 \times CS2 + 14.878 \quad (4)$$

## RESULTS

### Descriptive Statistics for Meteorological Variables and AR Incidence in Six Qi Phases

The peak onset of AR, including adolescent, middle-aged and elderly patients, appeared in the 4th qi (i.e. autumn to the autumn equinox). In comparison, the peak of 8 meteorological variables (including daily average temperature, daily maximum temperature, daily minimum temperature, daily relative humidity, daily vapor pressure, daily dew point temperature, daily precipitation and degree of comfort) appeared in the 3rd qi (i.e. Grain in Beard to Greater Heat). In addition, the valley of sea level pressure also appeared in the 3rd qi, and the peak in the 6th qi. But the peak of wind speed appeared in the 1st qi (i.e. the Beginning of Spring to Spring Equinox), and the valley appeared in the 4th qi. These data suggested that the high incidence of AR in the 4th qi was related to the changing trends of meteorological factors in previous phase of the 3rd qi. Consequently, the changing trends of meteorological factors during each six qi phase might be used to predict the incidence of AR in the next qi phase (Table 1).

### Correlation Analysis between AR Incidence and Meteorological Factors

The relationship between sea level pressure or wind speed and AR incidence showed a left anti-parabolic non-linear correlation (similar to negative correlation), meaning that the smaller the values of sea level pressure and wind speed, the more active a variety of allergens of AR, then the higher morbidity of AR. While the associations between other 8 meteorological factors and AR incidence presented a right anti-parabolic nonlinear correlation (equivalent to a positive correlation), indicating that the higher the values of temperature or vapor pressure appeared, the more quickly the allergens of AR breed and the AR incidence became higher.

**Table 1. Average Values of Meteorological Factors and AR Incidence in Six Qi Phases from 2007 to 2010**

| Meteorological factors                  | AR incidence |        |        |        |        |        |
|-----------------------------------------|--------------|--------|--------|--------|--------|--------|
|                                         | 1st qi       | 2nd qi | 3rd qi | 4th qi | 5th qi | 6th qi |
| Maximum temperature (°C)                | 10.0         | 24.8   | 31.3   | 27.8   | 13.4   | 2.3    |
| Minimum temperature (°C)                | -4.4         | 8.9    | 19.4   | 14.4   | -1.8   | -10.5  |
| Relative humidity (%)                   | 43.5         | 45.5   | 64.3   | 65.5   | 51.8   | 38.5   |
| Dew point temperature (°C)              | -8.9         | 4.6    | 18.3   | 15.1   | -3.2   | -16.7  |
| Sea level pressure (hPa)                | 1021.5       | 1010.4 | 1004.1 | 1011.9 | 1023.0 | 1027.6 |
| Degree of comfort (°C)                  | 35.1         | 61.0   | 76.2   | 69.4   | 41.4   | 22.0   |
| Precipitation (mm)                      | 6.8          | 22.1   | 51.4   | 47.2   | 7.1    | 1.2    |
| Vapor pressure (hPa)                    | 3.7          | 9.8    | 21.8   | 18.1   | 5.7    | 1.9    |
| Temperature (°C)                        | 4.7          | 19.2   | 27.2   | 23.3   | 7.9    | -2.7   |
| Wind speed (m/s)                        | 2.5          | 2.7    | 2.1    | 1.9    | 2.0    | 2.3    |
| Adolescent patients (Case)              | 21.4         | 26.7   | 45.5   | 83.0   | 26.1   | 19.5   |
| Middle-aged and elderly patients (Case) | 13.9         | 20.5   | 15.3   | 36.1   | 14.9   | 9.6    |

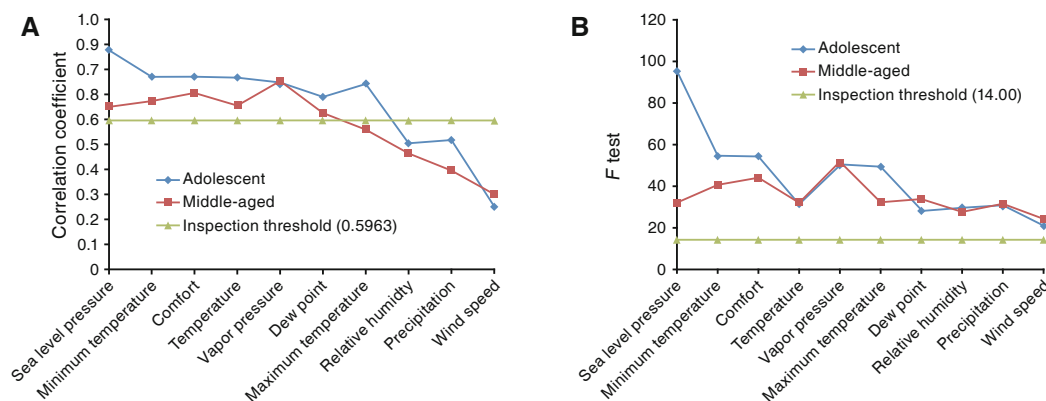
Twenty groups of correlation analyses indicated that the correlation coefficients of adolescent AR incidence and 7 meteorological factors have passed the tests, while relative humidity, precipitation and wind speed did not pass the tests ( $r_{\alpha=0.001}=0.5963$ ). Among them, the correlation coefficient of adolescent AR incidence and sea level pressure was the highest (0.8776) and the one of wind speed was the lowest (0.2508). By contract, the correlation coefficients of the middle-aged and elderly AR incidence and 6 meteorological factors have passed the tests, while maximum temperature, relative humidity, precipitation and wind speed did not ( $r_{\alpha=0.001}=0.5963$ ). Among them, the correlation coefficient of middle-aged and elderly AR incidence and vapor pressure was the highest (0.7540), and the one of wind speed was the lowest (0.2993; Figure 1A). Additionally, the  $F$  values in the correlation analysis between two groups of AR incidence and 10 meteorological factors have all passed the tests ( $F_{\alpha=0.001}=14.00$ ; Figure 1B).

### Correlation Analysis between AR Incidence and Comprehensive Meteorological Parametric

The following two nonlinear correlation prediction models obtained by using AR incidence (adolescents and middle-aged and elderly) and two comprehensive meteorological parameters (CS1 and CS2) were established successfully, which indicated that the AR incidence in two groups have increased as the risen of comprehensive meteorological parameters. It means that the climate condition of high temperature and water vapor pressure plus low atmospheric pressure could easily lead to the breeding of various kinds of allergens in later period. The correlation coefficient of adolescents group was higher than the middle-aged and elderly one and its fitting effect was also better (Figure 2).

### Regression Analysis of AR Incidence Trends

Predictive values of AR in each qi phase from 2007 to 2010 were calculated by substituting CS1

**Figure 1. Correlation Analysis between Ten Meteorological Factors and AR Incidence**

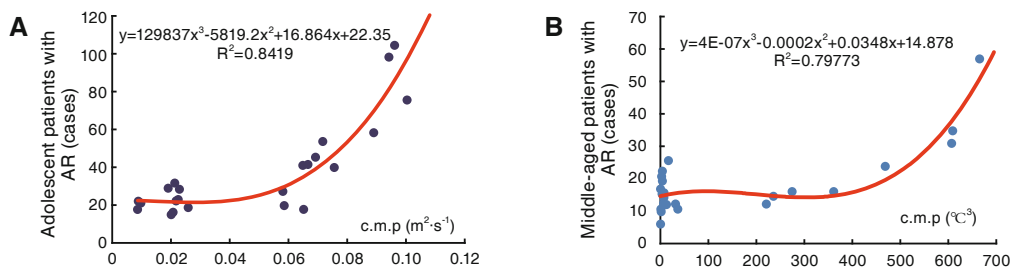


**Figure 2. Related Scatter Charts of Comprehensive Meteorological Parameter in Each Six Qi Phase and AR Incidence in the Next Adjacent Phase**

and CS2 to equations (3) and (4). The fitting of AR incidence trends in each six qi phase from 2007 to 2010 have passed significant statistical tests ( $r_{\alpha=0.001}=0.5974$ ,  $F_{\alpha=0.001}=14.2$ ,  $P<0.001$ ). Additionally, the two correlation coefficients of equations in (3) and (4) were 0.9176 and 0.8931, respectively.

The fitting effect of adolescent group was better than that of middle-aged and elderly group. The predictive value and actual AR incidence of adolescent group in the 4th qi appeared a good fitting in wave peak. It was glad to see that the incidence trends of adolescent patients with AR in the next six qi phase could be forecasted based on comprehensive meteorological parameters in previous six qi phase.

However, the middle-aged and elderly group did not have a good fitting in wave trough (Figure 3).

### Model Diagnosis and Error Analysis of AR Incidence

The AR cases (including adolescent group and middle-aged and elderly group) were divided into 5 grades to test the model diagnostic results of equation (3) and (4). The classification criteria were defined as follows: level I: AR cases  $\leq 15$ ; level II: AR cases = 16–30; level III: AR cases = 31–55; level IV: AR cases = 56–70; level V: AR cases  $\geq 71$ . According to the above standards, the diagnostic values of the model in six qi each year and the actual values of AR incidence in the same period were compared. An accurate prediction was considered as the same level of diagnostic value and AR case. On the contrary, if those two values are not in the same level, it is deemed to have errors.

Take the middle-aged and elderly group for example, in the 1st qi in 2007, the AR cases were 13 (level I) and the model diagnostic value was 15 (level I). Thus, it was considered as an accurate prediction. By contract, in the 3rd qi in 2010, the AR cases were 25 (level II) but the model diagnostic value was 15 (level I). So it was considered as have an error. Consequently, the conditions of accurate and error for each six qi period over the years from 2007 to 2010 were counted (a total of 23 six qi phases), respectively. Thus, accuracy and error rate could be calculated. As a result, the AR forecasting accuracy of middle-aged and elderly patients was 74%, while the error rate was 26%. The AR predicting accuracy of adolescent patients was 87%, while the error rate was 13%. It was obviously that the error rate of middle-aged and elderly group was higher than that of adolescent group.

### DISCUSSION

This study found that the AR incidence was

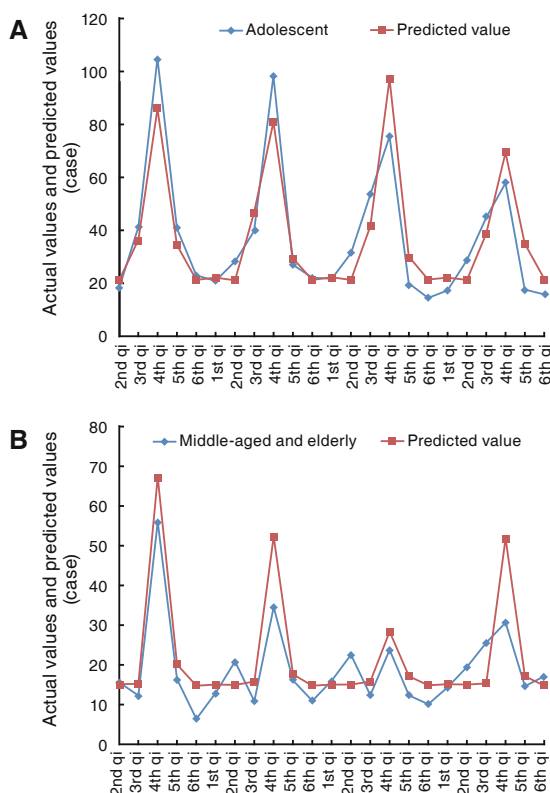


**Figure 3. Comparative Graph of Actual Cases and Predicted Values of AR from 2007 to 2010**

closely associated with vapor pressure. When the vapor pressure in the 3rd qi became higher, the morbidity of AR in the 4th qi would also increase, which means a positive correlation. By contrast, there was a negative linear correlation between the AR incidence and sea level pressure or wind speed, which represented the less incidence of AR might attributed to the great wind speed in spring and high sea level pressure in winter. The principle demonstrated that the high humidity weather in summer was conducive to the breeding of allergens in the air, but the weather condition of high atmospheric pressure and great wind speed was not conducive to the mite multiplication, pollen spreading and bacteria surviving. In a word, 8 meteorological factors and 2 kinds of AR patients in this study presented a positive correlation, only 2 meteorological factors and 2 kinds of AR patients in this study shown a negative correlation. Self-evidently the high temperature and humidity will lead to active allergens in the air.

A previous study found that the AR incidence and 5 kinds of allergens shown a positive linear correlation, and the relevance between them were sorted in descending order as the following: pollen allergy, animal hair allergies, dust mite allergy, mold allergy, and food allergy.<sup>(13)</sup> The pollen allergy has the best relevance with the adolescents and middle-aged and elderly patients with AR. In this study, AR appeared high prevalence in the 4th qi in Beijing. This period is also the pollen scattering peak of weed plants. This time coincidence from two studies indicated that a good correlation between the AR onset time and the scattering amount of pollen, owing to the fact that pollen of weed plants maybe the major source of allergens to the onset of hay fever in Beijing. Besides, the peak of vapor pressure, temperature, relative humidity and dew point temperature in the 3rd qi could also directly affected the pollen concentration in the next phase, i.e. the 4th qi.

Additionally, we found that the AR incidence of adolescents or middle-aged and elderly in the 4th qi was closely related to the peak of meteorological factors in the 3rd qi.<sup>(14)</sup> Their wave peak were entirely identical as shown in Figure 3 by two nonlinear correlation equations. The high incidence of AR was related to the comprehensive meteorological parameter in previous period of six qi stage and two nonlinear correlation prediction models were

obtained. The onset of AR in next adjacent phase could be estimated according to the comprehensive meteorological parameters in every six qi each year. The trend of AR incidence could be predicted in 59 days ahead, which play an important role in AR prevention and treatment.

The design of this research is different from previous studies.<sup>(15,16)</sup> The comprehensive meteorological parameters in previous qi phase were adopted to predict the AR incidence in the next qi phase. The comprehensive meteorological parameters reflect the complexity of climate change, which better than the use of single meteorological factor.

### Conflict of Interest

None to declare.

### Author Contributions

Zhang DS and Zhang X analyzed the data and wrote the manuscript. Ouyang YH and Zhang L collected and checked the data. Ma SL revised the manuscript. He J designed the experiments. All authors have read and approved the contents of the final version.

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