Association of meteorological factors with paediatric intussusception in Hangzhou: an 8-year retrospective cohort study

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ABSTRACT

Objectives This study aimed to investigate the seasonality of paediatric intussusception and the associations between meteorological factors and paediatric intussusception in Hangzhou, as well as aimed to compare the variance in sex and disease type.

Design An 8-year retrospective study was conducted from January 2014 to December 2021 in the Children’s Hospital of Zhejiang University, Hangzhou, China.

Setting This was a single-centre retrospective study review of intussusception cases in a large Children’s Hospital in Hangzhou.

Participants There were 17674 patients with intussusception in this study.

Methods A Spearman correlation analysis and Poisson regression analysis were used to determine the association between weekly intussusception cases and meteorological factors. The seasonality of paediatric intussusception was demonstrated via the t-test and visualised.

Result In January, May and December, there were relatively more intussusception patients. In February, there was a trough in the number of intussusception patients. Both the Spearman correlation analysis and Poisson regression analysis proved that weekly intussusception cases had significant associations with temperature ($\lambda=-0.205$, $p<0.01$; $\beta=-0.080$, $p<0.01$), feels-like temperature ($\lambda=-0.214$, $p<0.01$; $\beta=-0.012$, $p<0.01$), dew ($\lambda=-0.249$, $p<0.01$; $\beta=0.095$, $p<0.01$), humidity ($\lambda=-0.230$, $p<0.01$; $\beta=-0.037$, $p<0.01$), precipitation ($\lambda=-0.148$, $p<0.01$; $\beta=-0.001$, $p<0.01$), windspeed ($\lambda=-0.135$, $p<0.01$; $\beta=0.005$, $p<0.01$), visibility ($\lambda=-0.206$, $p<0.01$; $\beta=-0.066$, $p<0.01$), sea level pressure ($\lambda=0.171$, $p<0.01$; $\beta=-0.004$, $p<0.01$) and a total of 20 of 25 dynamic meteorological factors ($p<0.05$). These associations reflected gender differences but showed stronger associations in groups that were prone to recurrence.

Conclusions Paediatric intussusception in Hangzhou showed a seasonal tendency. Additionally, intussusception was significantly associated with certain meteorological factors in all of the cases. These findings suggest that parents and paediatricians should be more vigilant about the occurrence of intussusception in children regarding seasonal change times and climate change times.

INTRODUCTION

Intussusception is the insertion of a section of the intestine and its mesentery into the connected intestine.1 It is one of the most common abdominal emergencies that occur among infants (afflicting more than 50% of all patients under 1 year of age).2 Although paediatric intussusception may be accompanied by the classic triad (ie, red jelly stool, paroxysmal abdominal pain and a palpable abdominal mass) and obvious symptoms, including children crying, vomiting and lethargy (which will prompt parents to quickly seek medical attention), only one-third of patients exhibits these typical symptoms.1 3 This indicates that the remaining patients who lack these typical symptoms are at risk for delayed treatment. However, untreated paediatric intussusception is a potentially deadly disease that affects the blood supply to the intestine, thus leading to intestinal ischaemia and even perforation.4

Currently, the cause of most cases of intussusception in children is unknown. However, in the experiences of some paediatric clinicians, emergency cases of intussusception are usually more frequent when climate changes quickly and drastically. Therefore,
ongoing studies are attempting to understand the association between intussusception and environmental (especially seasonal) climatic factors. To date, there have been controversies about the seasonality of paediatric intussusception worldwide, as reported by different studies. For example, Das et al noted that the number of paediatric intussusception cases in India had a distinct seasonality, with a peak number observed in the summer and a minimum number observed in the autumn. The results of Chen et al also demonstrated a seasonal pattern in the prevalence of paediatric intussusception in Taiwan. Nevertheless, a retrospective study of children aged under 2 years in Pakistan reported that paediatric intussusception did not exhibit any seasonality. Greenberg et al also demonstrated no significant seasonality in the prevalence of intussusception in children in southern Israel. Moreover, Tang et al observed that more paediatric intussusception patients were diagnosed in the summer (from May to July), and the incidence rate was positively correlated with the temperature in Shenyang, China. The study from Guo et al showed that the number of paediatric intussusception cases in Suzhou had positive correlations with monthly average temperature, sunshine and precipitation. One drawback of these studies is that intussusception (as an acute onset disease) may need to be analysed over a specific time period (eg, weekly). In addition, meteorological factors change dynamically from time to time; therefore, more dynamic features need to be incorporated (in addition to the conventional mean values) to obtain more information in complex correlations.

When considering the limitations of these studies, this study aimed to analyse the seasonality of paediatric intussusception and to explore correlations between weekly meteorological factors, including dynamic features and the number of paediatric intussusception visits.

METHODS

Patient data collection
In this study, the patient data were obtained from the database which is generated by the Hospital Information System of the Children’s Hospital Affiliated to Zhejiang University School of Medicine. Given its status as the centre of children’s healthcare in Zhejiang Province and the National Clinical Research Center for children’s health and diseases in China. There were more than 3 million outpatient visits and 70,000 inpatient admissions per year for paediatrics to the hospital. Due to the fact that patients do not require a referral to visit children’s hospitals as outpatients in China, the disease spectrum of outpatients is an adequate reflection of the disease spectrum of the population of children in this area. The database recorded outpatient/emergency visit information such as patient ID, sex, age, visit date, visit department, diagnosis result and ICD-10 (International Classification of Diseases, Tenth Revision) code. We selected intussusception patients’ records based on ICD-10 code as K56.1 and visiting this hospital during January 2014 to December 2021 as patient data. In total 17675 selected cases, only 1 case missed sex and age information. Therefore, we removed this record and analysed the remaining 17674 records in the study. All the intussusception diagnosis were confirmed by imaging (usually ultrasonography) examinations.

Meteorological data collection
This study was conducted in Hangzhou, which is a city located in southern-east China in the subtropical monsoon zone, with four distinct seasons (detailed climate data are shown in online supplemental table S1 and online supplemental figure S1). In this study, basic daily meteorological data (temperature, feels-like temperature, dew, humidity, precipitation, windspeed, visibility and sea level pressure) from January 2014 to December 2021 were obtained from the National Center for Environmental Information (https://www.ncei.noaa.gov), which is an agency of the US government and manages one of the world’s largest archives of atmospheric data. The climate data used in this study is complete and reliability as it is vetted using standards established by the National Research Council.

Statistical analysis
There were 17675 patient records with a diagnosis of intussusception, and 17674 of these records were included in this study (one record was removed due to a lack of detailed information). In this study, Microsoft Excel 2016 was used for preliminary data processing and descriptive statistical analyses. R V.4.0.2 was used to visualise the seasonality of the patient population by ggplot2 package. R was used to check the differences in the monthly number of patients by t-test. In the association analysis, a total of 17674 cases of intussusception from 2014 to 2021 were divided into 2 groups according to sex and type of disease (recurrent or not). The meteorological factors that were associated with weekly intussusception cases were explored via a Spearman correlation analysis (in Hmisc package) and Poisson regression analysis (by building generalised linear models) with R. Static and dynamic weekly meteorological factors were generated from basic meteorological factors that contained daily temperature (°C, maximum, minimum and average values), feels-like temperature (°C and average values), dew (°C), humidity (g/m3), precipitation (mm), wind-speed (m/s), visibility (m) and sea level pressure (hPa). There were eight static meteorological factors and 25 dynamic meteorological factors grouped into four types used in this study. The definitions of these factors were shown in table 1. In brief, type I is the weekly average of the difference between the meteorological factors of the 2 adjacent days; type II is the weekly maximum of the difference between the meteorological factors of the 2 adjacent days; type III is the maximum difference between the meteorological factors of the 7 days of the week; type IV is only applied for temperature to reflect the reflects the maximum difference in temperature.
Of these cases, 10 from January 2014 to December 2021 was 17 total number of records of intussusception patient cases. As shown in table 1, the majority of patients under 2 years and cases below 3 years accounted for approximately two-thirds of the total number of cases. The majority of these cases (15,318 cases, 86.67%) occurred only once during this study period, but some of the children had recurrent intussusception. From 2014 to 2021, the annual number of cases continued to decline and became the lowest in 2020 (1263 cases). In the following year, the number of cases increased to 1913 (10.82%).

### Patient and public involvement

No patient involved.

### RESULTS

#### Overview of intussusception cases

As shown in table 2 and online supplemental figure S2, the total number of records of intussusception patient cases from January 2014 to December 2021 was 17,674 records. Of these cases, 10,893 cases (61.63%) were boys, and 6,781 cases (38.37%) were girls, with a clear predominance of boys. Approximately half (46.55%) of the patients under 2 years and cases below 3 years accounted for approximately two-thirds of the total number of cases. The majority of these cases (15,318 cases, 86.67%) occurred only once during this study period, but some of the children had recurrent intussusception. From 2014 to 2021, the annual number of cases continued to decline and became the lowest in 2020 (1263 cases). In the following year, the number of cases increased to 1913 (10.82%).

#### Seasonality of intussusception

Figure 1 shows the distribution of monthly meteorological factors and the number of monthly intussusception cases in this study. According to figure 1, there was a seasonality for intussusception. The results of the t-test showed that there were significant differences in the

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**Table 1 Meteorological factors in the study**

| Factors                  | Type                          | Formulas                                      | Calculation steps                                                                 |
|--------------------------|-------------------------------|-----------------------------------------------|-----------------------------------------------------------------------------------|
| Static factors           | Weekly average of eight basic meteorological factors between 2 days. | $\bar{D}_n = \frac{1}{8} (\bar{D}_1 + \bar{D}_2 + \cdots + \bar{D}_8)$ | We get the gap ($\bar{D}$) of the climate between neighbouring 2 days at first. |
| Dynamic factors I        | Weekly average of the difference in eight basic meteorological factors between 2 days. | $\bar{D}_n = temp_n - temp_{n-1}$ | We get the gap ($\bar{D}$) of the climate between neighbouring 2 days at first. |
|                          | $\bar{D}_n = \frac{1}{8} (\bar{D}_1 + \bar{D}_2 + \cdots + \bar{D}_8)$ | $\bar{D}_n$ is the difference of the mean temperature between day $n$ and day $n-1$. | Then, we divide these $\bar{D}_n$ into several groups and each group has seven $D$.
|                          | $\bar{D}_n = \frac{1}{8} (\bar{D}_1 + \bar{D}_2 + \cdots + \bar{D}_8)$ | $\bar{D}_n$ is the difference of the mean temperature between day $n$ and day $n-1$. | Finally, we calculate the average of $\bar{D}_n$ in each group and type I dynamic factor is made up of these averages. |
| Dynamic factors II       | The maximum of the difference in eight basic meteorological factors between 2 days in a week. | $\bar{D}_n = temp_n - temp_{n-1}$ | We get the gap ($\bar{D}$) of the climate between neighbouring 2 days at first. |
|                          | $\bar{D}_n = \frac{1}{8} (\bar{D}_1 + \bar{D}_2 + \cdots + \bar{D}_8)$ | $\bar{D}_n$ is the difference of the mean temperature between day $n$ and day $n-1$. | Then, we divide these $\bar{D}_n$ into several groups and each group has seven $D$.
|                          | $\bar{D}_n = \frac{1}{8} (\bar{D}_1 + \bar{D}_2 + \cdots + \bar{D}_8)$ | $\bar{D}_n$ is the difference of the mean temperature between day $n$ and day $n-1$. | Finally, we select the maximum of $\bar{D}_n$ in each group and type II dynamic factor is made up of these maximums. |
| Dynamic factors III      | Weekly range of eight basic meteorological factors. | $\bar{D}_n = \min (temp_n) - \min (temp_{n-1})$ | At first, we divide climate data into several groups and each group have 7-day data. |
|                          | $\bar{D}_n = \frac{1}{8} (\bar{D}_1 + \bar{D}_2 + \cdots + \bar{D}_8)$ | $\bar{D}_n$ is the difference of the mean temperature between day $n$ and day $n-1$. | Then we find the maximum and minimum of the factor in each group. |
|                          | $\bar{D}_n = \frac{1}{8} (\bar{D}_1 + \bar{D}_2 + \cdots + \bar{D}_8)$ | $\bar{D}_n$ is the difference of the mean temperature between day $n$ and day $n-1$. | Finally, we use maximum minus minimum in each group and these gap values are made up type III dynamic factor. |
| Dynamic factors IV       | Daily range of temperature. | $\bar{D}_n = \bar{T}_{\max} - \bar{T}_{\min}$ | It is the value calculate by maximum minus minimum of climate factor in a day. |
|                          | $\bar{D}_n = \frac{1}{8} (\bar{D}_1 + \bar{D}_2 + \cdots + \bar{D}_8)$ | $\bar{D}_n$ is the difference of the mean temperature between day $n$ and day $n-1$. | Then, we divide these $\bar{D}_n$ into several groups and each group have 7-day data. |
|                          | $\bar{D}_n = \frac{1}{8} (\bar{D}_1 + \bar{D}_2 + \cdots + \bar{D}_8)$ | $\bar{D}_n$ is the difference of the mean temperature between day $n$ and day $n-1$. | Finally, we select the maximum of $\bar{D}_n$ in each group and type II dynamic factor is made up of these maximums. |

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monthly cases of intussusception (p<0.01). Compared with other months, there were relatively more intussusception cases diagnosed in January, May and December. May is the month when Hangzhou begins to continuously exhibit temperature increases during progression into hot summers, whereas December and January are the time periods when Hangzhou continues to cool down into the winter season.

Correlation between weekly intussusception cases and static meteorological factors

As shown in table 3, the Spearman correlation analysis results revealed that weekly intussusception cases were significantly associated with temperature ($\lambda=-0.205$, p<0.01), feels-like temperature ($\lambda=-0.214$, p<0.01), dew ($\lambda=-0.249$, p<0.01), humidity ($\lambda=-0.230$, p<0.01), precipitation ($\lambda=-0.148$, p<0.01), windspeed ($\lambda=-0.135$, p<0.01), visibility ($\lambda=-0.206$, p<0.01) and sea level pressure ($\lambda=0.171$, p<0.01). However, most of the correlations were weak ($|\lambda|<0.4$).

Interestingly, although the prevalence of intussusception was lower in girls, it showed a higher correlation with meteorological factors. Surprisingly, a large number of meteorological associations were not statistically significant in male children, and only humidity and visibility retained significant associations for boys. In the recurrent subgroups, temperature, feels-like temperature, dew and sea level pressure had even stronger significant associations with weekly intussusception cases. However, the other meteorological factors lost the statistical significance of the association.

As shown in online supplemental table S2, the Poisson regression analysis results also revealed that there were significant associations between weekly intussusception cases and temperature, feels-like temperature, dew, humidity, precipitation, windspeed, visibility and sea level pressure.

In different gender groups, temperature, dew, humidity and sea level pressure were significantly associated with both male and female cases. However, there were no significant gender differences. Temperature, dew, humidity and visibility were significantly associated with weekly intussusception cases, regardless of whether the cases were recurrent or not. However, the analysis also showed that the recurrent cases were more strongly associated with meteorological factors.

According to the results of the Spearman correlation analysis and Poisson regression analysis (table 3 and online supplemental table S2), for all of the cases, eight static meteorological factors (temperature, feels-like temperature, dew, humidity, precipitation, windspeed, visibility and sea level pressure) were all significantly associated with weekly intussusception cases. In gender
groups, humidity and visibility had statistically significant associations with both male and female cases. Moreover, in the recurrent and non-recurrent groups, temperature and dew had significant associations with both recurrent and non-recurrent cases.

**Correlation between weekly intussusception cases and dynamic meteorological factors**

There were four types of dynamic meteorological factors that were defined in this study. All eight meteorological factors only contained dynamic factors I, II and III, and only temperature contained dynamic factor IV. Table 4 shows the Spearman correlation analysis results between weekly intussusception cases and 25 dynamic meteorological factors. Most of the dynamic meteorological factors had significant associations with weekly intussusception cases (p<0.05). However, most of the dynamic factors lost their significance in the subgroups when stratified by sex and recurrence type. Dew dynamic factor II had significant associations with both male and female cases (p<0.05). Additionally, dew dynamic factor II, dew dynamic factor III and humidity dynamic factor III had significant associations with weekly intussusception cases, regardless of whether the cases were recurrent or not (p<0.05).

For all of the temperature dynamic factors, type III, which indicates the maximum temperature difference of a week, showed stronger correlations. In addition, dew dynamic factor II, which indicates the maximum daily dew point difference in a week, is the only factor that showed significant associations with all of the subgroups.

Online supplemental table S3 shows the results of the Poisson regression analysis between weekly intussusception cases and 25 dynamic meteorological factors. A total of 21 of 25 dynamic meteorological factors, except for precipitation dynamic factor III, windspeed dynamic factor II, pressure dynamic factor I and pressure dynamic factor III, had significant associations with weekly intussusception cases (p<0.01).

The Poisson regression analysis revealed that temperature dynamic factor III, feels-like temperature dynamic factor III and humidity dynamic factor III had significant associations with both male and female cases (p<0.05). For the recurrent and non-recurrent groups, humidity dynamic factor III was significantly associated with weekly intussusception cases, regardless of whether the cases were recurrent or not (p<0.05).

When combining the results of the Spearman correlation analysis and Poisson regression analysis (online supplemental table S2) and online supplemental table S3), a total of 20 of the 25 dynamic meteorological factors (temperature dynamic factors I, II, III and IV; feels-like temperature dynamic factors I, II and III; dew dynamic factors I, II and III; humidity dynamic factors I, II and III; precipitation dynamic factors I and II; windspeed dynamic factors I and II; visibility dynamic factors I and II; and sea level pressure dynamic factor II) were significantly associated with weekly intussusception cases. In the recurrent and non-recurrent groups, maximum humidity difference in a week (type III) had significant associations with weekly intussusception cases, regardless of whether the cases were recurrent or not (p<0.05).

**DISCUSSION**

Paediatric intussusception is one of the most common abdominal emergencies in infants and children, and many previous studies have explored the epidemiological characteristics and influencing factors of paediatric intussusception. However, previous studies have demonstrated inconsistent seasonal results for paediatric intussusception and limited explorations of the association between the number of cases and meteorological factors. These inconsistent results are possibly influenced by the sample size and the time granularity. Previous study with no significance finding, such as the study in Pakistan with only 158 cases and study in Israel with only 316
patients, is significantly limited by the sample size. This is the first study that investigated the association between multiple static and dynamic climate factors and weekly paediatric intussusception cases using a large dataset.

In this study, there was a minimum number of intussusception patients each February, which is consistent with the conclusions of studies in East Asia that have demonstrated the seasonality of paediatric intussusception.\(^6\)\(^,\)\(^9\)\(^,\)\(^13\) However, the results for the peak number of paediatric intussusception cases were inconsistent in these studies. The results of this study showed a high incidence of disease in January, May and December, which are the times of transition to summer and winter seasons, respectively. The peak of this disease occurred from May to October in Taiwan.\(^6\) The epidemiological study of intussusception performed in Korea by Jo et al found that the maximum number of intussusception patients occurred in September, followed by July.\(^13\) Additionally, Tang et
al showed that May to July was the peak of paediatric intussusception in Shenyang, China, and June had the maximum number of patients. Both Korea and Shenyang are located to the north of Hangzhou, and their summer usually begins later than in Hangzhou. When considering this effect, the results of these studies more consistently highlight the idea of a high incidence of intussusception at the beginning of the summer. Sáez-Llorens et al proved that different geographical locations affect the seasonality of paediatric intussusception. In addition to geographical location, these different results may be related to differences in climate type, food culture and medical level in different regions. However, it is certain that the months with a high incidence of intussusception in these different regions occur at the point of seasonal change, with most of the studies confirming a sustained warming period before the summer and some studies confirming a sustained cooling period at the beginning of the winter. Due to this possible asymmetric U-shaped correlation, only relatively weak quantitative values of correlations were obtained for the overall correlations of both various static and dynamic indicators.

In studies conducted in China, Tang et al demonstrated a correlation between monthly mean temperature and the number of paediatric intussusception patients via the Pearson correlation analysis (p<0.01). Additionally, Guo et al found that monthly paediatric intussusception patients were significantly associated with monthly average increased temperature (p=0.0001), monthly summed amount of sunshine (p<0.0001) and monthly precipitation (p<0.0001), and these cases were marginally associated with monthly average increased windspeed (p=0.0709), with these data being analysed via the Poisson regression analysis. We also provide monthly correlation analysis in online supplemental tables S4–S7. The occurrence of intussusception in children is usually an acute episode, so its short-term association is more relevant. The results of this study also showed that the number of weekly paediatric intussusception patients was significantly associated with temperature, feels-like temperature, dew, humidity, precipitation, windspeed, visibility, sea level pressure and most of their weekly fluctuation factors. Although there were many meteorological factors influencing the number of intussusception patients per week, the correlation coefficients of all of the meteorological factors were low, thus suggesting that they may only play a secondary role in promoting or inducing the development of the disease. Interestingly, visibility shows rather higher ultimate correlation due to the joint influence of several other meteorological factors. In addition to associated meteorological factors, it was proven that virus infection, maternal smoking, child age, ethnicity and other factors were important influencing factors. The COVID-19 pandemic and associated measures, such as home quarantine and more frequent hand washing (which significantly reduced other infectious diseases). The daily intussusception visits during the lockdown period are only half of that before pandemic in the same period in this hospital (1.439 vs 2.875) may also contribute to the lower prevalence of intussusception in 2020. However, analysis of the association between the number of local rotavirus enteritis and the number of intussusceptions showed no significant association (r=0.252, p=0.088), with viral infections showing a more seasonal and infectious character. Although some monthly forecasting model have been reported, the climate factors were not included in the relevant model. Therefore, better parental awareness and protection during seasonal changes may further reduce the incidence of intussusception, and paediatric emergency departments need to be better resourced to cope with short-term peaks in visits during specific seasons.

More detailed results of the association analysis by age group are presented in online supplemental tables S8–S11. In brief, patients below 1 year are more affected by static meteorological factors. A large number of existing studies on paediatric intussusception have found that boys develop intussusception more often than girls (the ratio is about 2:1 or 3:2) for unknown reason. In our study, in addition to finding that the number of boys is much larger than that of girls, we also found that the correlation between female patients and the climate is higher. However, the methods we used can only show this phenomenon, there is no evidence to explain the mechanism of it. In any case, the results suggest that female patients have unique characteristics when exposed to external influences. This will inspire future studies on paediatric intussusception and gender.

There were also some limitations in this study. First, the data were not normalised over different years, which means that fluctuations in the number of annual patients may influence the results. Second, compared with a multicentre study or prospective study, this study was a single-centre retrospective study with a potential bias. Therefore, one important future direction of this study is the establishment of an appropriate model to quantitatively analyse the relationship between meteorological factors and the number of patients, as well as to predict the number of patients in the future after standardising the data.

CONCLUSION

In conclusion, in the time periods of seasonal changes, there were more intussusception cases in Hangzhou. The associations between the number of weekly intussusception cases and temperature, feels-like temperature, dew, humidity, precipitation, windspeed, visibility, sea level pressure and most of their weekly fluctuations were statistically significant, although most of these correlations were weak. These findings suggest that parents and paediatricians should be more vigilant about the occurrence of intussusception in children during seasonal and climate change periods.
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