**Association between Ambient Temperature, Particulate Air Pollution and Emergency Room Visits for Conjunctivitis**

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# ABSTRACT

**Background**: Numerous studies have confirmed the association of ambient temperature and air pollution with a higher risk of morbidities, yet few have addressed their effect on the ocular system. The purpose of the study is to determine the association between temperature, air pollution and emergency room visits for conjunctivitis.

**Methods:** In this case-crossover study, the records of all emergency room visits to Soroka University Medical Center (SUMC) from 2009 to 2014 were reviewed for patients with conjunctivitis. Exposure to fine and coarse particulate matter and temperature were determined by a hybrid model involving daily satellite sensors.

**Results:** 6001 patients were diagnosed with conjunctivitis in the SUMC emergency room. We discovered a positive association between temperature increments and incidence of conjunctivitis. The strongest effect was found during summer and autumn, where the incidence increased 8.1% for each 1oC rise in temperature between 24 and 28oC in the summer and 7.2% for each 1oC rise in temperature between 13 and 23oC in the autumn. There was no statistically significant association between fine and coarse particulate matter and incidence of conjunctivitis.

**Conclusion:** Temperature increases during summer and autumn are significantly associated with an increased risk of conjunctivitis. Conjunctivitis is not associated with non-anthropogenic air pollution. These findings may help community clinics and hospital emergency rooms better predict conjunctivitis cases and hopefully lead to improved prevention efforts to lower the financial burden on both the individual and public.

**Keywords:** conjunctivitis, temperature, weather, air pollution, ocular disease

**1. BACKGROUND**

Conjunctivitis is an inflammation of the conjunctiva characterized by swelling, redness, discharge and discomfort. It is a common diagnosis in the general population (Azari et al., 2013), and the most common ocular condition diagnosed in United States’ emergency rooms where it accounts for almost one-third of all eye-related visits (Channa et al. 2016). Conjunctivitis can be infectious (generally caused by adenovirus) or noninfectious (autoimmune, hypersensitivity…etc).

Conjunctivitis significantly impacts health care systems; outbreaks can cause significant morbidity, high health care costs and loss of workdays, which eventually result in financial burdens on both individuals and the public worldwide. (Azari et al., 2013; Channa, et al., 2016; Schneider et al.,2014). In the United States, 4–6 million conjunctivitis visits annually have entailed nearly 800 million dollars in treatment costs (Schneider, 2014). The direct effects of the condition on patients’ quality of life can vary, ranging from lost school/work to irreversible eye and vision damage. With the financial and quality life impacts, more information about environmental risk factors are crucial to develop measures to reduce incidence and burden on public health (Chen et al., 2019).

Ambient temperature and air pollution are known to be associated with a variety of health problems and disorders that affect multiple body systems, such as respiratory, cardiovascular, and neurological systems (Maayan et al., 2015; Gerber et al., 2006; Anderson et al., 2013; Eccles et al. 2002; Alina et al., 2015; Aditi et al., 2016; Vencloviene et al., 2015; Vodonos et al., 2015; Yang et al., 2011). In severe cases, temperature and air pollution can be fatal to individuals (Jhun, et al., 2017; Lilieveld, et al., 2015; Aditi, et al., 2016; Jun, et al., 2016). Several studies reveal meteorological changes on the ocular system (Bourcier et al., 2003; Hu et al., 2007; Stein et al., 2011; Christoph et al., 2016; Matthew et al., 2016; Setten et al., 2016; Augera et al., 2017),but few studies agree on the relationship of meteorological changes with conjunctivitis (Andre et al., 2011; Chia-Jan et al., 2012; Chiang et al., 2012; Hong et al., 2016; Szyszkowicz et al., 2016).

Chia-Jan et al. (2012) reported a higher number of outpatient visits for conjunctivitis in winter than in summer; however, Chiang et al. (2012) reported that the average daily visits for acute conjunctivitis peaked in the summer. According to Szyszkowicz et al. (2016), the number of visits was higher in the warm season than the cold season. Azari et al. (2013) reported a greater incidence of viral conjunctivitis in summer and bacterial conjunctivitis from December through April. In addition to the varying results, these studies evaluated the incidence of conjunctivitis by seasons rather than by the temperature.

The present study was undertaken to evaluate the association between air pollution, ambient temperature and emergency room visits for conjunctivitis in the Negev Desert of southern Israel. This 13,000 km² semi-arid region lies between the Saharan and Arabian deserts and the three together constitute the world’s largest dust belt. In light of climate change and desertification, the Negev can be considered a predictor of future climate change in many regions of Europe.

# 2. METHOD

**2.1. Study Population**

The study enrolled all patients who arrived at the Soroka University Medical Center (SUMC) Emergency room during the years 2009-2014 who were diagnosed with conjunctivitis. Patients with other eye disorders were used to determine incidence of conjunctivitis compared to other eye complaints. SUMC is a tertiary 1000-bed hospital in the southern Negev Desert of Israel, and the only medical center in the region for a population of 700,000 inhabitants. The Center is owned by the largest health maintenance organization HMO in Israel, the Clalit Health Services. Only residents of the southern Negev were enrolled. Demographic and clinical data obtained from the electronic database of Clalit Health Services, included date of birth, gender, age, place of residence, eye diseases and comorbidities.

### **2.2 Air pollution and meteorology data measurement**

We used a hybrid method for assessing spatiotemporal resolved PM2.5 and PM10 exposures (Nordio et al., 2013; Kloog et al., 2014; Kloog et al., 2015; Shtein et al., 2018), and a satellite-based method for monitoring temperature in the Negev recently installed by the Israel Meteorological Service. Seasons were defined according to Alpert et al.,(2004); winter (December 7-March 30), summer (May 31-September 22) each last about 4 months (3 months and 23 days), autumn (September 23-December 6) and spring (March 31-May 30) each lasts only 2 months (75 days and 61 days, respectively).

**2.2.1. Air pollution**

There are two main source of air pollution: naturally occurring non-anthropogenic pollutants (such as volcanic eruptions, forest fires and dust); and anthropogenic air pollutants created by human activity (such as O3, NO2, NOX and SO2) (Popescu et al., 2010).

Daily average concentrations of PM10 (particulate matter 10 micrometers or less in diameter) and PM2.5 (particulate matter 2.5 micrometers or less in diameter) were estimated using a hybrid satellite-based model that provides daily satellite remote sensing data at 1×1 km spatial resolution (Kloog et al., 2015; Shtein et al., 2018) according to the residential address of each patient. Briefly, using an algorithm developed by NASA - MAIAC (Multi-Angle Implementation to Atmospheric Correction) (Lyapustin et al., 2011) that provides aerosol optic depth (AOD) data in high resolution, we applied mixed models to regress daily PM10 and PM2.5: AOD, traditional land use regression, and temporal and spatial predictors. When AOD was not available, we fitted a generalized additive model with a thin plate spline term of latitude and longitude to interpolate PM estimates. Good model performance was achieved, with out-of-sample cross validation R2 values of 0.92 and 0.87 for PM10 and PM2.5, respectively. Model predictions had little bias, with cross-validated slopes (predicted vs. observed) of close to 1 for both models. Exposure estimates were assigned for each patient based on his/her geocoded home address.

**2.2.1. Meteorological data**

Daily data on mean air temperature obtained by satellite-based model that provides daily satellite remote sensing data at 1×1 km spatial resolution for each patient. Mean relative humidity was obtained from the Ministry of Environmental Protection Meteorological monitoring station located in Beer-Sheva, the location of SUMC and the largest city in southern Israel.

## 3. STATISTICAL ANALYSIS

The association between air pollution, ambient temperature and emergency room visits for conjunctivitis was examined by a case-crossover design (Maclure et al., 1991; Navidi et al., 1998; Vodonos et al., 2015; Mieczysław et al., 2016; Yitshak-Sade et al., 2015).

This design samples only cases and compares each case’s exposure to temperature and particulate air pollution during a time period just before the case-defining event (hazard period) with the subject’s own exposure in other reference periods (control periods). Because each subject serves as his or her own control, there is perfect matching on all measured or unmeasured subject characteristics that do not vary over time. We used a symmetric bidirectional case-crossover design. In this design, reference periods are symmetrically spaced in time, both before and after the hazard period, which minimizes potential time-varying confounding by season or time trends. In this study, the hazard period was defined as the day of day of admission and temperature and particulate air pollution exposure was modeled as the exposure on the day of admission and a mean exposure seven days prior to admission. Matched strata were constructed for each subject (that is, admission day), consisting of the event day (day of admission) and six matched control days. These days were chosen to be the 7, 14, 21,28 days before the event, and 7, 14, 21,28 days after the event.

Next we performed a conditional logistic regression (Bateson et al., 1999) to calculate odds ratios (OR) and 95% confidence intervals (CI) for lag0 to lag 6, a total of 7 days for our main exposure as most the incubation period for conjunctivitis is up to 5-6 days, daily mean temperature adjusted to PM10 and relative humidity. To allow a non-linear effect we also used penalized splines with 5 degrees of freedom for temperature. Our last step included the same model only this time we tested each season separately.

The estimates provided for PM10 are per 10 μg/m3 changes in air pollution. Separate analysis was performed for each subgroup such as seasons (fall, winter, spring, summer), gender (female, male), age (0-18 years old, 18-65 years old, and above 65). Statistical analysis was performed with the IBM SPSS Statistics software package (version 23.0, IBM, Armonk, NY) and R statistical software.

The study was conducted according to the Declaration of Helsinki and approved by the Medical Helsinki Committee of the Soroka University Medical Center, Ben-Gurion University of the Negev.

**4. RESULTS**

**4.1. Population**

Of the 19,264 visits to the ophthalmology SUMC emergency room between 2009 and 2014, 6001 (31.1%) were diagnosed with conjunctivitis (Table 1 in the Appendix). Mean age of patients was 34.6 years, range 0.5-96 years and 54.4% were males (Table 1). The majority of cases, 4063 patients (67.7%), were between 16 and 65 years of age.

**4.2 Pollution and Meteorology**

The average daily levels of meteorological and air pollution variables by seasons are presented in Table 2. The interquartile range (IQR) of PM2.5 ranged between 17.2 and 24.82 μg/m3, reaching a maximum value of 53 μg/m3, with no significant differences between seasons. The IQR of PM10 ranged between 38.44 and 56.66.3 μg/m3, reaching a maximum value of 193 μg/m3, slightly higher during the winter. The climate in the study region is relatively hot and dry, with average daily IQR temperatures of 11.86 - 15.65oC in winter, 18.64- 20.95oC in spring, 25.06 - 27.32oC in summer, and 17.02 - 23.39oC in autumn. The overall IQR relative humidity range was 57.00-75.00%, with no difference between seasons.

**4.3. Effect of air pollution on the incidence of conjunctivitis**

Odds ratios and 95% confidence intervals were estimated from conditional logistic regression analysis of association between PM2.5, PM10 (separately), temperature and emergency room visits due to conjunctivitis where models were adjusted for humidity. There was no statistically significant correlation between levels of PM2.5, PM10 and the incidence of conjunctivitis (Table 2 in the Appendix).

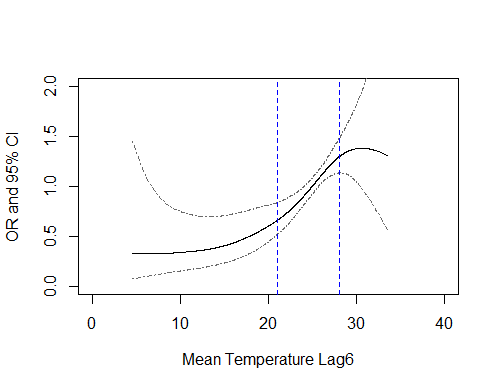
**4.4. Effect of temperature on the incidence of conjunctivitis**

A subgroup analysis by season was conducted to assess the seasonal relationship between temperature and conjunctivitis. The number of emergency room visits for conjunctivitis was higher in summer (36.4%, p<0.001) than in winter (26%, p<0.001), autumn (22.1%, P=0.773) and spring (15.4%, p=0.135), with the highest rates recorded in July and August (Figure 1) (Table 1 in the Appendix). When the incidence of conjunctivitis was compared with other ophthalmological disorders by seasons (Table 1 Appendix), it was significantly higher in summer (36.4% and 32.8%, respectively, P<0.001), and significantly lower in winter (26% and 28.6%, respectively, p<0.001).

The same results were obtained when the data was stratified by age, with summer leading in each age group (P<0.001). When analyzed by month, July and August had the highest incidence for each age group (Fig. 1 and Table 3 in the Appendix). In multivariable analysis there is no association between the incidence of conjunctivitis and age.

Females were found to have a significant association between temperature and conjunctivitis in all 7 days lags and males were found to have a significant association on lags 0 and 6 (Table X Appendix).

There is an overall non-linear association between temperature and conjunctivitis. But for certain temperature ranges at summer and autumn where considered the relevant temperature range for each season; we noticed a form of linear positive association between temperature increments and incidence of conjunctivitis (Fig. 2). For summer at temperatures between 24 and 28oC the incidence increased 8.1% for each rise of 1 degree Celsius, and for autumn at temperatures between 13 and 23 oC the incidence increased 7.2% for each rise of 1 degree Celsius. This association remained after taking into account a 6-day lag between exposures and developing conjunctivitis for both autumn and summer. There was no association between temperature and conjunctivitis during spring and winter (Fig. 2).



**5. DISCUSSION**

The main result of our study is the significant association between temperature and the incidence of conjunctivitis during a relevant range of temperature for summer and autumn. No association found between air pollution (PM2.5, PM10) and the incidence of conjunctivitis

Meteorological changes and air pollution have been a public health concern for the last several decades due to accelerated global warming and desertification. Contemporary studies document the effect of temperature and air pollution on human morbidities, especially cardiovascular, respiratory and neurological systems, as well as on human mortality, even within the normal range of temperatures (Aditi et al., 2016).

Several studies had investigated the association between Meteorological changes and ocular diseases. Hu et al. (2007) found that primary angle closure glaucoma admission rates were significantly higher with increased relative humidity, but with no correlation to temperature. Matthew et al. (2016) reported a higher frequency of infectious keratitis during the higher temperatures and humidity levels of summer. Even increased risk of traction retinal detachment had been linked elevated outdoor temperatures by Augera et al. (2017).. Furthermore Christoph et al. (2016)supported a correlation between higher weekly average temperature and increased ophthalmology emergency room visits.

Few studies have investigated the effect of temperature on conjunctivitis. Of the studies examining conjunctivitis and seasons, they negate to account for isolated and direct effect of temperature on the conjunctivitis incidence (Chiang et a., 2012; Hong et al., 2016; Szyszkkowicz et al., 2016).

The pathophysiological mechanisms of air pollution and metrological changes on conjunctiva remain to be characterized. Some studies (Li et al., 2017; Gao et al., 2016) have speculated that PM2.5 and PM10 particles cause intraocular epidermal cells to lose their ability to adapt, leading to cell death and inflammation. Krishna et al. (1996) pointed to the strong oxidative stress effect of NO2 and O3 that may stimulate conjunctival cell inflammation. While various authors have related subtypes of conjunctivitis to specific seasons – viral conjunctivitis common in summer, bacterial in winter, allergic in spring – there is no consensus among them on the exact mechanism (Azari 2013; Chiang et a., 2012; Hong et al., 2016; Szyszkkowicz et al., 2016 ).

In this study there is no association between air pollution (PM2.5, PM10) and the incidence of conjunctivitis

In the Negev Desert, there was low level of anthropogenic (chemical) pollution, supporting the result of our study that non-anthropogenic air pollution is not related to conjunctivitis without the confounding effect of anthropogenic pollution. However, other studies may have had chemical pollution confound the effect of PM on the incidence of conjunctivitis.

Our findings of seasonal differences in the incidence of conjunctivitis agree with Hong and co-workers (2016) where higher levels of temperature and lower humidity lead to increased outpatient visits for allergic conjunctivitis, potentially the result of pollen production in warmer temperatures. In our study, we investigated the meteorological effect on non-specific conjunctivitis while this study targeted allergic conjunctivitis. Furthermore, our study measured exact temperatures in relation to each patient’s condition while Hong et al. grouped patients by season. Chiang et al. (2012) found a peak incidence of chronic conjunctivitis in summer, mainly in rural areas and less prominent in urban areas, a difference they attributed to factors such as socioeconomic status, income and occupation. Szyszkowicz et al. (2016) found the number of visits to the emergency room due to conjunctivitis was higher in warm seasons (58%) compared to cold seasons (42%), as seen in our study with the incidence of conjunctivitis in the summer (36.4%) (P<0.001) and winter (26%) (P<0.001). Of note, these authors studied the effect by season and not, as we did, by the effect of temperature.

The statistically significant higher incidence of conjunctivitis in summer and lower incidence in winter suggests that higher temperatures are risk for conjunctivitis and lower temperatures are protective against conjunctivitis. We determined that certain temperature ranges are associated with incidence of conjunctivitis in summer and autumn. However, the lack of association between temperature and conjunctivitis in spring (moderate climate), and winter (cold climate) indicates a multifactorial relationship with other factors involved in conjunctivitis. Further research is needed to understand more of these factors.

**6. LIMITATIONS**

**Our study investigates a specific region with specific climate conditions considered as a dry, hot semi-desert climate with a limited population; however, our hospital is a tertiary hospital, and the only hospital in the region and the whole population concentrated on this hospital. Furthermore, we took the entire population sample in our study without selection.**

**7. CONCLUSION**

Temperature is significantly associated with conjunctivitis in southern Israel during summer and autumn. Incidence of conjunctivitis is significantly higher than other eye disorders in summer and lower in winter. There is no association between non-anthropogenic air pollution and conjunctivitis. These findings can help community clinics and hospital emergency rooms prepare for the upticks in conjunctivitis during certain seasons and acute rises in temperatures.

**Abbreviations**:

AOD – aerosol optic depth

PM – particulate matter

IQR – interquartile range

O3 – trioxygen

NO2 – nitrogen dioxide

NOX – nitric oxide

SO2 – sulfur-dioxide

**8. DECLARATIONS**

**- Ethics approval and consent to participate:**   The study was conducted according to the Declaration of Helsinki and approved by the Medical Helsinki Committee of the Soroka University Medical Center, Ben-Gurion University of the Negev.

Permission to access data was obtained by the Medical Helsinki Committee of the Soroka University Medical Center, Ben-Gurion University of the Negev.

- **Consent to publish**: Not applicable

**- Availability of data and materials:** All data generated or analysed during this study are included in this published article

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**- Authors' Contributions:**

All authors have read and approved the manuscript.

* SK: Conception or design of the work; data collection; data analysis and interpretation; drafting the article.
* TC: Data collection.
* AV: Critical revision of the article.
* IK: Data analysis and interpretation.
* AS: Data analysis and interpretation.
* LC: Revision of the article
* VN: Critical revision of the article.
* ET: Conception or design of the work; Critical revision of the article.

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**10.** **FIGURE LEGENDS**

**Figure 1:** Rate of conjunctivitis by a. season and b. month

**Figure 2:** Association between increase in temperature and visits to the emergency room for conjunctivitis, by season. The solid lines are the odds ratios (ORs) and the dotted lines are 95% confidence intervals. Models were adjusted for humidity and PM10.