Clinical and Epidemiologic Research

Intraocular Pressure and Its Relation to Climate Parameters—Results From the Gutenberg Health Study

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Purpose. To investigate the association between intraocular pressure (IOP) and climate parameters.

Methods. The Gutenberg Health Study (GHS) is a population-based cohort study in Mainz, Germany. Participants underwent two comprehensive ophthalmologic examinations (baseline visit and five-year follow up) including non-contact tonometry, objective refraction, pachymetry, perimetry, and fundus imaging in the time frame of 2007 to 2017. The respective climate parameters were assessed at the University Mainz including temperature, air humidity, and air pressure. Associations of IOP and climatic parameters were computed using component models and cross-correlation plots. Multivariable regression analysis was performed to adjust for age, sex, body mass index, diabetes, central corneal thickness, and systolic blood pressure. To further explore the link between systolic blood pressure, temperature, and IOP, an effect mediation analysis was conducted.

Results. A total of 14,632 participants (age 55 ± 11 years at baseline, 49.1% female) were included in this analysis. Mean IOP was 14.24 ± 2.8 mm Hg at baseline. There was a similar periodic change in IOP and in temperature, as shown in the component models. IOP was not associated with air humidity. In univariable and multivariable regression analyses we found a significant association between lower IOP during the summer months with higher air temperature (B = −0.011, $P < 0.001$). This could be partially explained in mediation analysis by lower systolic blood pressure at higher air temperature. Furthermore, IOP was associated with air pressure in univariable (B = 0.005, $P = 0.04$.) and multivariable models (B = 0.006, $P = 0.03$).

Conclusions. There is a periodic annual change of IOP with higher values in winter and lower values in summer supporting the hypothesis of an impact of environmental temperature on IOP, which is partly mediated by lower systolic blood pressure in summer.

Keywords: intraocular pressure, environmental factors, seasonality, time series analysis

The major modifiable risk factor for development and progression of open-angle glaucoma is elevated intraocular pressure (IOP).[1] Knowledge of IOP, its distribution in the general population over different time courses, and influencing factors play an important role in the diagnosis and treatment of glaucoma.[2]

Several studies analyzed time-of-day and yearly fluctuations.[3–7] It has already been proven that patients with

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glaucoma have high IOP fluctuations. Few studies have investigated daily IOP variations in healthy subjects. Fluctuations were also seen in these patients, but these were smaller compared to in glaucoma patients.[8,9] Larger fluctuations occur at night because of the lying sleeping position.[10] Studies that attempted to characterize a daily IOP pattern concluded that there is no uniform pattern in healthy subjects.[11–13]

Furthermore, little is known about possible environmental factors influencing IOP on large studies or on population-based level. A former study from the 1980s found an association between IOP and air pressure: increased air pressure led to lower IOP.[14] However, a multiple regression analysis taking into account interindividual variations showed only a negligible influence of atmospheric pressure on IOP.[14] An experimental study in healthy volunteers showed that an air pressure increase to two bars over 40 minutes led to a significant decrease of IOP from 11.8 mm Hg to 10.7 mm Hg.[15] A possible association between IOP and air humidity is barely investigated and showed no significant correlation.[14]

With respect to air temperature, a study of healthy Chinese showed an IOP change over the time course of one year, indicated that IOP is higher on cold days and lower on warm days.[12] Also, other studies showed differences of IOP in winter and summer.[4,12,16–21]

The Gutenberg Health Study (GHS) offers the opportunity to gain new insights into potential environmental factors influencing IOP. The study population is one of the largest population-based samples, in which IOP, climate parameters and anthropometric parameters are observed over a period of 10 years.

Methods

Procedure and Study Sample

The GHS is a population-based, prospective, observational single-center cohort study in the Rhine-Main Region in Germany. The sample was equally stratified for sex, residence (urban or rural), and for age-decade. At baseline, 15,010 individuals were included (2007–2012), and 12,423 were re-examined after five years (2012–2017).

Ophthalmic Parameters

IOP was measured with a noncontact tonometry and automatic air-puff control (NT 2000; Nidek, Inc., San Jose, CA, USA), the mean of three measurements within a 3 mm Hg range was obtained for each eye. The date and time of the measurement was recorded. IOP measurements were mainly performed between 11:00 and 18:00 hours. First, the right eye was measured three times followed by the left eye. If there was a difference of more than 3 mm Hg between the three measurements, the measurement was immediately repeated. For further calculations, the mean IOP value of the right and left eye was used. Further information on the lens status were determined with slit-lamp examination at baseline examination[22] and Scheimpflug imaging at follow-up examination.[23] Pachymetry was measured with Pachycam (Oculus, Wetzlar, Germany) at baseline and Pentacam HR (Oculus) at follow-up examination. Glaucoma status was determined on optic disc photographs and using frequency doubling technology perimetry according to a modified definition of the Glaucoma classification according to International Society of Geographical and Epidemiological Ophthalmology (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1771026/).[24]

Climate Parameters

Climate parameters were provided by the "Institute for Atmospheric Physics (Johannes Gutenberg University)." Air pressure, humidity, and temperature were continuously measured, and daily mean, minimum, and maximum values were provided. In addition, the GHS also provided data on measured temperature inside and outside the study center.

General Parameters

Characteristics of the study population including age, sex, height, weight, and body mass index (BMI) were surveyed. Diabetes mellitus was defined as an established diagnosis, use of anti-diabetics, or HbA1c $\geq$ 6.5%, arterial hypertension as use of antihypertensive medication, systolic blood pressure >140 mm Hg, diastolic blood pressure >90 mm Hg, or an established diagnosis. Further information, such as the HbA1c-level, were determined by using standardized measurement procedures.

Statistical Analysis

Descriptive analysis was conducted for primary and secondary variables. For categorical parameters, absolute and relative frequencies were computed. For continuous variables, mean and standard deviation were calculated for approximately normal-distributed data, otherwise median and interquartile range were calculated.

For IOP analysis, the mean value from both eyes was used, if available. Population-based IOP distribution within the day, daily IOP averages, and the IOP distribution over the year with monthly averages were computed.

To analyze the association of IOP and climate parameters, time series diagrams (the component models) were created that highlight the seasonal component, as well as the trend. The component model is subject to the assumption that not all time series are stationary. They are therefore subject to a trend, seasonality and thus variance, which is not constant. To analyze the nonstationary time series in more detail, it is decomposed into several components.[25] In the analysis, the time series was decomposed into the following four components: observed values, trend, seasonal component, and random data. Time series were then adjusted for trend and tested for a significant relationship using a cross-correlation function. One function of time series is to be able to recognize possible correlations in successive temporal intervals. This is illustrated by the autocorrelation, which shows possible correlation between the temperature and the subsequent values of the IOP in the following correlation plot.[25,26] The lags in the correlation plot establish periods of time between the two time series. The observations in one time series are tested against lagged values in the other time series.[25] An association between IOP and the temporal component was additionally examined using cosinor analysis ("cosinor package" in R).[27]

Univariable and multivariable linear regression analyses were conducted to analyze the association between IOP and climate parameters (air temperature, air humidity, air pressure) on individual participant level (repeated measures were modeled with generalized estimating equations). Analyses were adjusted for potential confounding factors (age, sex, diabetes, BMI), and in addition an effect mediation for systolic blood pressure was conducted. The mediation analysis helps to speculate why an independent variable is possibly associated with another variable. We looked at an intervening variable (mediator = systolic blood pressure) that could possibly be the reason for the present association. The percentage of the mediator causing the association is calculated.[28]

As sensitivity analyses, glaucoma patients, those with a prescription of IOP lowering therapy were excluded and only participants with phakic lens status were included. The study population was stratified by sex, and stratified on age decades. Data were processed with the statistical program R (version: 4.0.3 (2020-10-10)).

Results

Overall, 14.632 study participants were included. The mean age of the study population was 55 ± 11.11 years, and 49.5% were female. Table 1 shows the participants' characteristics at baseline. The mean IOP was 14.11 ± 2.69 mm Hg in women and 14.37 ± 2.87 mm Hg in men.

Table 1. Participants' Characteristics (*N* = 14,632, Baseline Examination) and Climatic Parameter in the Gutenberg Health Study

	Overall	Men	Women
Anthropometric data	14,632	7390	7242
Age (y), mean (SD)	55 (11.1)	55.22 (11.1)	54.77 (11.1)
Weight (kg), mean (SD)	79.72 (16.58)	87.28 (14.36)	72.01 (15.08)
Height (cm), mean (SD)	170.44 (9.5)	176.98 (7.08)	163.79 (6.61)
BMI, mean (SD)	27.38 (5.02)	27.86 (4.29)	26.88 (5.62)
Medical history			
Systolic blood pressure (mm Hg), mean (SD)	131.30 (17.42)	133.86 (16.22)	128.69 (18.20)
Arterial hypertension	7261 (49.7%)	4026 (54.5%)	3235 (44.7%)
Diabetes	1364 (9.3%)	841 (11.4%)	523 (7.2%)
Ophthalmic parameters			
IOP (mm Hg), mean (SD)	14.24 (2.79)	14.37 (2.87)	14.11 (2.69)
Glaucoma (ISGEO)	128 (1.1%)	63 (1.0%)	65 (1.1%)
Central corneal thickness (µm)	553.76 (35.28)	556.19 (35.1)	551.30 (35.29)
Spherical equivalent (diopters), mean (SD)	−0.42 (2.44)	−0.44 (2.36)	−0.40 (2.51)
Lens status (phakic)	14,055 (96.1%)	7106 (96.2%)	6936 (95.8%)
Local eye medication			
Sympathomimetics	37 (0.3%)	20 (0.3%)	17 (0.2%)
Parasympathomimetics	8 (0.1%)	2 (0.0%)	6 (0.1%)
Carbonic anhydrase inhibitors	46 (0.3%)	20 (0.3%)	26 (0.4%)
Beta blocking agents	202 (1.4%)	103 (1.4%)	99 (1.4%)
Prostaglandin analogues	95 (0.7%)	48 (0.7%)	47 (0.7%)
Climatic parameters			
Temperature in F° and C° , mean	50.34°F/10.19°C		
Air humidity, mean	80%		
Air pressure (mB), mean	1000.3		

SD, Standard deviation; ISGEO, Glaucoma classification according to International Society of Geographical and Epidemiological Ophthalmology (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1771026/).

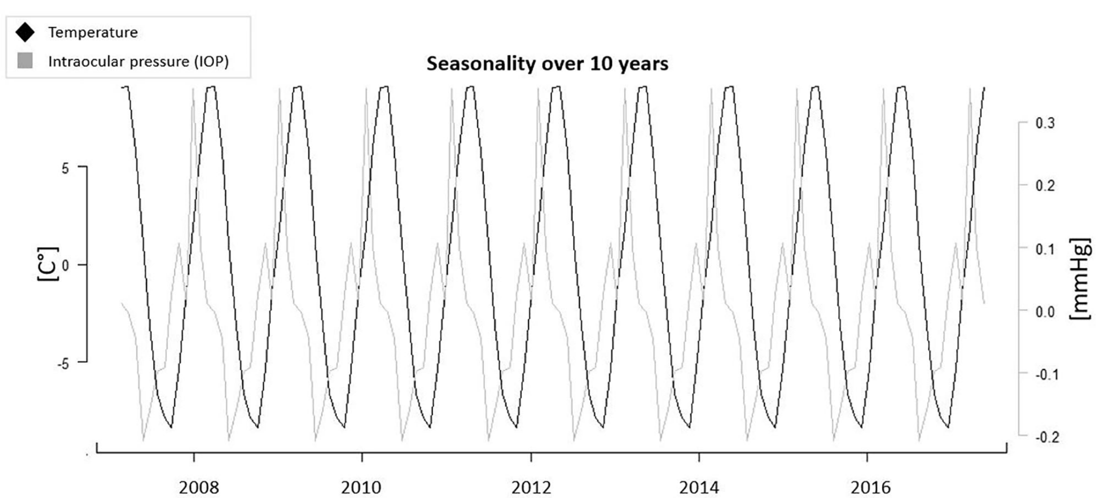

Figure 1. Seasonal component of average temperature and IOP in time series analysis (monthly averages): data from the Gutenberg Health Study (2007–2017) and Department of Astrophysics (2007–2017).

Time Series Analysis

IOP time series over 10 years with monthly averages showed that IOP is subject to seasonality (Fig. 1). The time series of temperature also shows a seasonal component (Fig. 1). Looking at the two time series, an almost inverse relationship between both time series can be seen: at high temperature, the IOP is low and the other way round. The smaller peak of the IOP seasonality arises from a small number of IOP measurements in December, because the study center is not open the whole month. The other components of time series analysis are shown in Supplementary Figures S1 and S2.

Data from the GHS study center also demonstrated seasonality in the measured outdoor temperature (Supplementary Fig. S3a). This was not the case for the indoor temperature (Supplementary Fig. S3b).

The correlation between temperature and IOP is also reflected in the correlation plot of both time series (Fig. 2a) in crude analysis and after removing the trend component (Fig. 2b), although there is a minor correlation after also removing the seasonal component (Fig. 2c). Component models were also created for variables that have been shown to influence IOP. Systolic blood pressure showed a matching seasonality compared to IOP (higher values in winter, lower values in summer). The correlation plots between the outdoor temperature of the GHS and IOP showed comparable results (Supplementary Fig. S4).

Furthermore, we conducted a cosinor analysis to examine the association between IOP and temporal patterns. Our results revealed significant temporal relationship between the 52-week IOP data and both the amplitude (B = 0.12, $P < 0.05$) and acrophase (B = 1.04, $P < 0.05$) within the 52 weeks of a year demonstrating a periodic distribution of IOP.

Associations Between Climate Parameters and IOP

There was a significant association between air temperature and IOP ($r = -0.17$, $P < 0.0001$; Fig. 3a). Higher average daily temperature was associated with a lower IOP. IOP peak was recorded in February (14.9 ± 0.48 mm Hg) and lowest IOP in July (14.3 ± 0.43 mm Hg).

A univariable correlation was also found between air pressure and IOP ($r = 0.07$, $P = 0.031$, Fig. 3b) and air humidity and IOP ($r = 0.07$, $P = 0.031$, Fig. 3c). Linear regression analysis showed in univariable analysis an association between IOP and air temperature and air pressure as climate parameters, whereas in multivariable model with adjustment for potential confounders air temperature and air pressure remained associated with IOP (Table 2).

We further found a significant association of lower systolic blood pressure and higher air temperature (−0.08, 95% confidence interval [CI] = −0.1 to −0.06, $P < 0.001$). Mediation analysis revealed that the relationship between IOP and air temperature is approximately 77% mediated by the lower systolic blood pressure. In the regression model with both temperature and systolic blood pressure, the association between IOP and air temperature remains (−0.0088, 95% CI = −0.01 to 0.00, $P < 0.0012$) significant. In the multivariable model with adjusting for potential confounders the association remains robust. Sensitivity analyses (exclusion of subjects with glaucoma disease, exclusion of subjects with IOP surgery or IOP-lowering medication, only inclusion of participants with phakic lens status) showed comparable results.

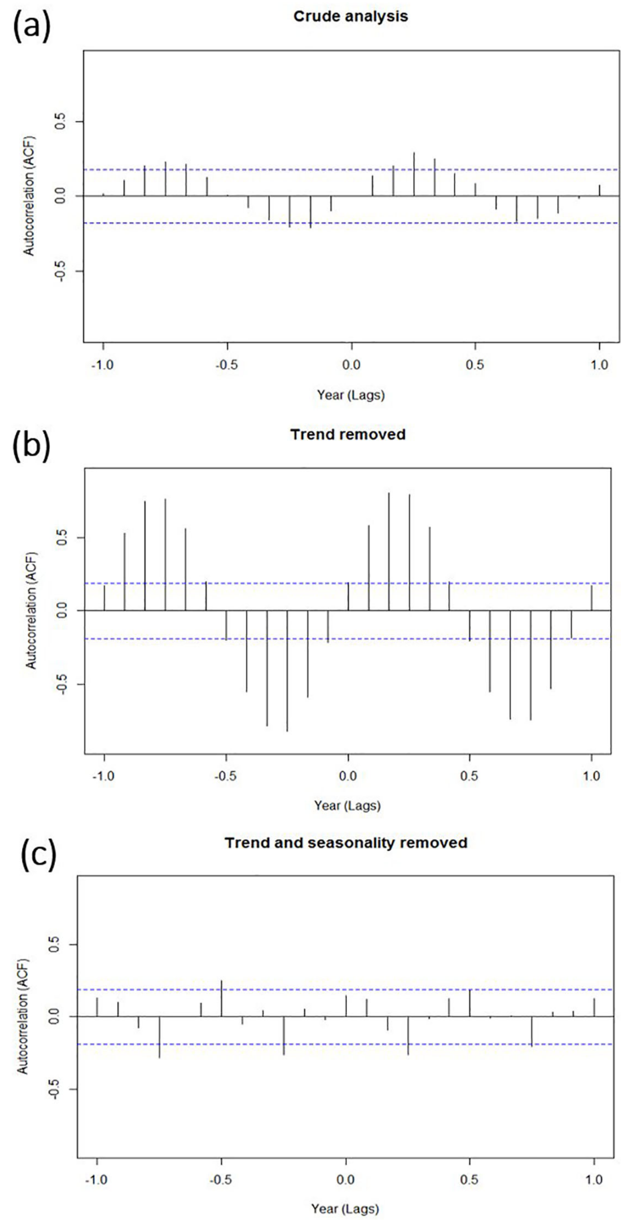

Figure 2. Correlation plot between IOP and air temperature. (**a**) Crude analysis, (**b**) after removing of the trend component, and (**c**) after removing the seasonal component as well.

Within Day IOP Distribution

Within day distribution of IOP (measured between 7:00-18:00) showed no significant difference over the day (Fig. 4), with women showing slightly lower values than men (Supplementary Fig. S5).

Discussion

This study analyzed the relationship between IOP and climate parameters in a large population-based sample over the course of 10 years. We found a periodic change of IOP over the year through the time series and cosinor analysis with higher values in winter and lower values in summer.

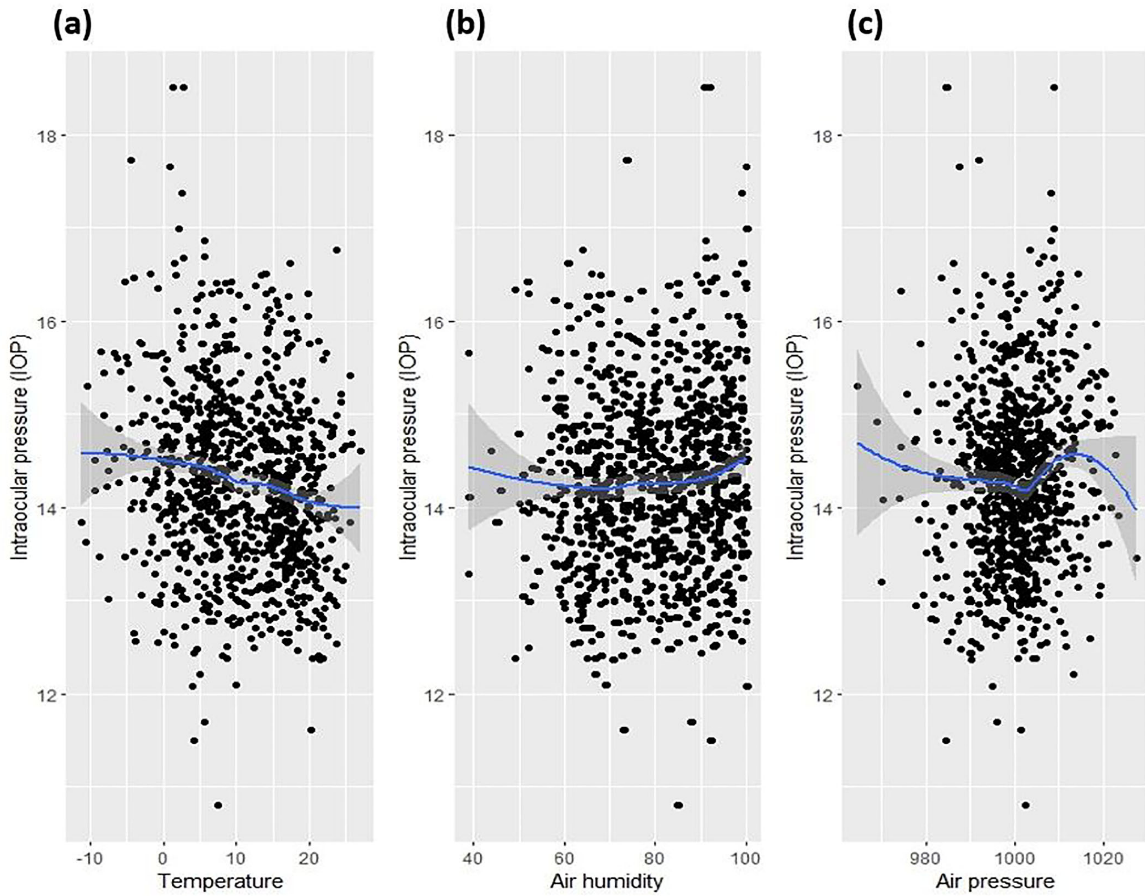

Figure 3. Scatterplot between IOP and air temperature (**a**), air humidity (**b**), and air pressure (**c**). Results from the population-based Gutenberg Health Study (n = 14,632) from baseline examination (2007–2012). The *blue line* illustrates the LOESS line.

Table 2. Multivariable Linear Regression Analysis (With Generalized Estimating Equations) of Climate Parameters With IOP

	Univariable, Unadjusted			Multivariable, Adjustment for Age, Sex, BMI, CCT, and Diabetes			Multivariable, Adjustment for Age, Sex, BMI, CCT, Diabetes, and Systolic Blood Pressure		
	B	95% CI	*P* Value	B	95% CI	*P* Value	B	95% CI	*P* Value
Air temperature	−0.011	−0.02 to −0.01	<0.001	−0.016	−0.02 to −0.01	<0.001	−0.013	−0.02 to 0.01	<0.001
Air humidity	0.002	0.00–0.01	0.16	0.002	0.00–0.01	0.38	0.002	[0.00–0.01]	0.26
Air pressure	0.005	0.00–0.01	0.04	0.006	0.00–0.01	0.03	0.006	[0.00–0.01]	0.02

CCT, central corneal thickness.
Data from the Gutenberg Health Study (2007–2017).

This association can in part be explained by lower blood pressure values at higher air temperature.

Our findings are supported by other studies in healthy subjects[4,17,18]: One study with 103 healthy Chinese participants found an IOP difference of 1.4 ± 0.7 mm Hg between winter and summer, with higher IOP in winter months.[3] Analyses in this subject area in Chicago, Illinois, United States, recorded an IOP peak in December/January (15.7 ± 3.7/15.7 ± 3.8 mm Hg) and lowest IOP in September (14.5 ± 3.1 mm Hg).[20] A study using results from the UK Biobank of 110,573 participants demonstrated seasonality of IOP with lower values in summer and higher values in winter.[29] In this study IOP peak was recorded in February (14.9 ± 0.48 mm Hg) and lowest IOP in July (14.3 ± 0.43 mm Hg).

One retrospective cohort study analyzed a 20-year period through medical records showing significant seasonal changes over the entire period.[17] Similarly, studies examining glaucoma patients concluded that IOP is subject to periodic IOP changes.[4,17,18]

The question arises how this seasonality of IOP might be explained. The present study showed that there is a significant relationship between IOP and air temperature. Seasonality of IOP and temperature showed an almost inverse relationship. Both seasonality curves partially overlap, most likely because the IOP does not react immediately to temperature change but with a time lag. The association was evident in both the correlation plot and the regression analysis, as well as after adjustment for possible confounders. Effect mediation analysis revealed that systolic blood pressure

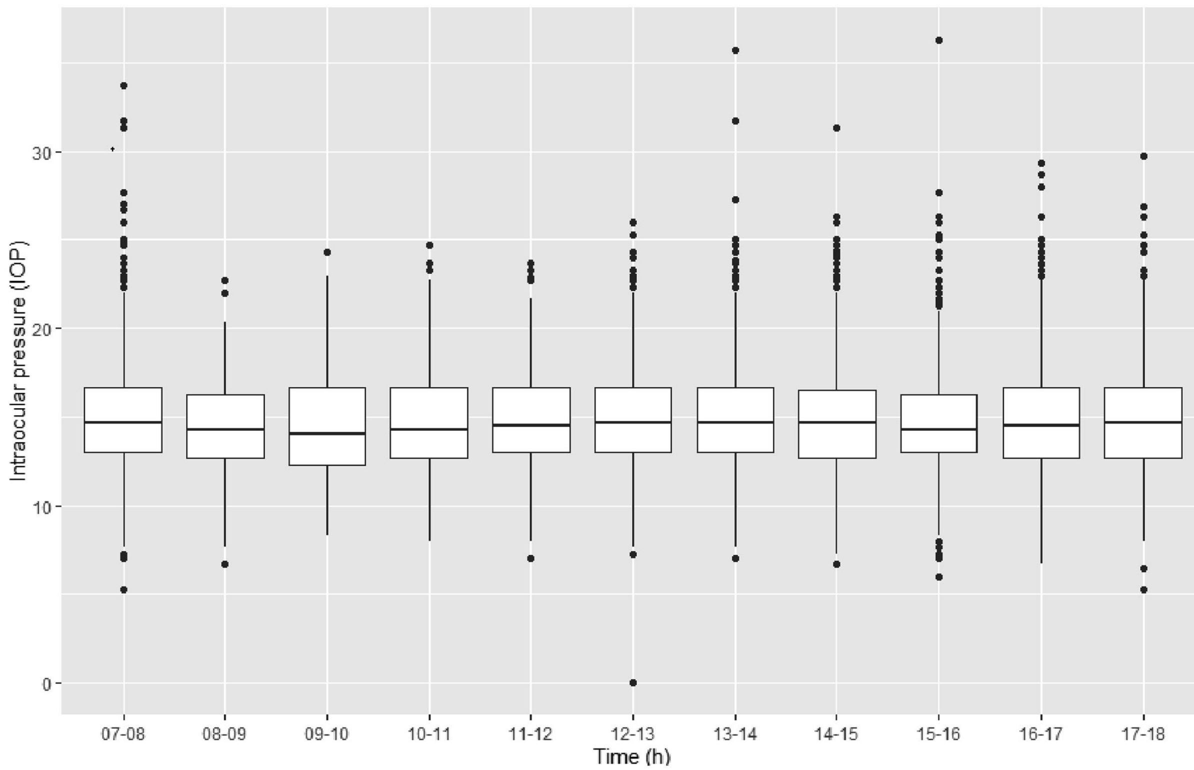

Figure 4. Within day distribution of IOP. Results from the population-based Gutenberg Health Study (n = 14,632), data from baseline examination (2007–2012).

partly mediates this association. Similar to our study data, other studies demonstrated the seasonality of systolic blood pressure with higher values in winter and lower values in summer time.[30–33] The association between IOP and systolic blood pressure has been proven by multiple studies,[34–37] each of these studies indicated that an increase in systolic blood pressure was also associated with an increase in IOP. Temperature and systolic blood pressure showed a relationship in several studies: at high temperatures blood pressure is lower, whereas at low temperatures blood pressure is reported to be higher.[31,38,39] The underlying explanation for this phenomenon is that lower temperature cause temporary constriction of blood vessels, resulting in increased resistance to blood flow and consequently higher blood pressure.[40] It has been hypothesized by several studies that high systolic blood pressure affects aqueous humor by ultrafiltration, which increases IOP.[41–43] Our effect mediation results show that IOP is partially altered because of a change in systolic blood pressure caused by outdoor temperature. However, in our cohort, systolic blood pressure did not fully explain the association of IOP and air temperature.

Little is known about a possible relationship between air humidity and IOP. We didn't find an association between air humidity and IOP in this analysis. Similar results on this subject demonstrating no relationship were reported in another study.[14] With respect to atmospheric pressure, IOP was associated in univariable and multivariable analysis.

This result is partly consistent with the literature on this topic. One study in Germany examined 109 patients with chronic glaucoma or ocular hypertension and found a correlation between IOP and atmospheric pressure. However, a multiple regression analysis showed that the influence of atmospheric pressure on IOP is negligible when taking interindividual variations into account.[14]

One experimental study showed that an increase of air pressure to two bars over 40 minutes in a hyperbaric chamber led to a significant decrease of IOP.[15] This atmospheric pressure corresponds to a dive at a depth of 10 meters. However, this study evaluated the short-term effects of massive air pressure changes and thus is not comparable to the natural slow and much smaller fluctuations. Air pressure regularly fluctuates by approximately 0.003 bars during the day.[44]

Strengths and Limitations

This study analyzed data from a large population-based representative sample. The study contributes results to better understanding of characteristics of IOP over time course and its relation to climate parameters as an environmental influence factor. Compared to other studies on this topic, the large study population and the long observation time of 10 years offer the possibility of obtaining representative findings. Furthermore, the large study sample offers the opportunity to explore the link between systolic blood pressure, temperature, and IOP.

However, there are some limitations of our study, which need to be considered. The included GHS subjects mainly consist of Caucasian origin. Therefore no generalizability to other ethnicities is given. IOP measurement by noncontact tonometry can be recognized as a limitation, although the application of noncontact tonometry is widely used in the clinics but not in full agreement with the reference standard Goldmann applanation tonometry. Moreover, there are IOP measurement techniques incorporating biomechanical properties such as the ocular response analyzer,[45,46] which would allow us to further investigate potential influence of temperature on IOP because of a change in biomechanical characteristics. To reduce this potential influence, we adjusted for central corneal thickness in our statistical analysis. In addition, only daily data on climate parameters were available limiting the time series analysis.

Conclusion

In conclusion, this study demonstrates periodic change of IOP over the time course of 10 years in a population-based sample: IOP is higher in winter and lower in summer time. IOP is associated with air temperature showing an inverse but similar pattern of seasonality. Part of the effect of air temperature on IOP could be explained by systolic blood pressure as an effect mediation.

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References

1. Hashemi H, Khabazkhoob M, Emamian MH, Shariati M, Yekta A, Fotouhi A. Distribution of intraocular pressure and its determinants in an Iranian adult population. *Int J Ophthalmol*. 2016;9:1207–1214.
2. McMonnies CW. The importance of and potential for continuous monitoring of intraocular pressure. *Clin Exp Optom*. 2017;100:203–207.
3. Saccà SC, Rolando M, Marletta A, Macrí A, Cerqueti P, Ciurlo G. Fluctuations of intraocular pressure during the day in open-angle glaucoma, normal-tension glaucoma and normal subjects. *Ophthalmologica*. 1998;212:115–119.
4. Terauchi R, Ogawa S, Noro T, et al. Seasonal fluctuation in intraocular pressure and retinal nerve fiber layer thinning in primary open-angle glaucoma. *Ophthalmology Glaucoma*. 2021;4:373–381.
5. Bengtsson B, Leske MC, Hyman L, Heijl A. Fluctuation of intraocular pressure and glaucoma progression in the early manifest glaucoma trial. *Ophthalmology*. 2007;114:205–209.
6. Drance SM. The significance of the diurnal phasic variation of intraocular pressure in normal and glaucomatous eyes. *Trans Can Opthalmolog Soc*. 1960;23:131–140.
7. Medeiros FA, Weinreb RN, Zangwill LM, et al. Long-term intraocular pressure fluctuations and risk of conversion from ocular hypertension to glaucoma. *Ophthalmology*. 2008;115:934–940.
8. Agnifili L, Mastropasqua R, Frezzotti P, et al. Circadian intraocular pressure patterns in healthy subjects, primary open angle and normal tension glaucoma patients with a contact lens sensor. *Acta Ophthalmol*. 2015;93: e14–e21.
9. Aref AA. What happens to glaucoma patients during sleep? *Curr Opin Ophthalmol*. 2013;24:162–166.
10. Liu JH, Kripke DF, Twa MD, et al. Twenty-four-hour pattern of intraocular pressure in the aging population. *Invest Ophthalmol Vis Sci*. 1999;40:2912–2917.
11. Realini T, Weinreb R, Wisniewski S. Diurnal Intraocular Pressure Patterns are Not Repeatable in the Short Term in Healthy Individuals. *Ophthalmology*. 2010;117:1700–1704.
12. Liao N, Xie YQ, Mao GY, et al. Observation seasonal variation of intraocular pressure in young healthy volunteers. *Int J Ophthalmol*. 2022;15:59–64.
13. Song YK, Lee C-K, Kim J, Hong S, Kim CY, Seong GJ. Instability of 24-hour intraocular pressure fluctuation in healthy young subjects: a prospective, cross-sectional study. *BMC Ophthalmology*. 2014;14:127.
14. Jonas J, Guggenmoos-Holzmann I, Brambring D, Schmitz-Valckenberg P. [Weather influences on intraocular pressure in patients with chronic glaucoma or ocular hypertension]. *Klin Monbl Augenheilkd*. 1986;189:445–449.
15. Van de Veire S, Germonpre P, Renier C, Stalmans I, Zeyen T. Influences of atmospheric pressure and temperature on intraocular pressure. *Invest Ophthalmol Vis Sci*. 2008;49:5392–5396.
16. Cheng J, Xiao M, Xu H, et al. Seasonal changes of 24-hour intraocular pressure rhythm in healthy Shanghai population. *Medicine*. 2016;95:e4453.
17. Ikeda Y, Mori K, Ueno M, et al. Seasonal variation and trend of intraocular pressure decrease over a 20-year period in normal-tension glaucoma patients. *Am J Ophthalmol*. 2022;234:235–240.
18. Kuze M, Ayaki M, Yuki K, et al. Seasonal variation of intraocular pressure in glaucoma with and without dry eye. *Sci Rep*. 2020;10:13949.
19. Mansouri K, Gillmann K, Rao HL, Weinreb RN. Weekly and seasonal changes of intraocular pressure measured with an implanted intraocular telemetry sensor. *Br J Ophthalmol*. 2021;105:387–391.
20. Morettin CE, Roberts DK, Newman TL, et al. Time-of-year variation in intraocular pressure. *J Glaucoma*. 2021;30:952–962.
21. Qureshi IA, Xi XR, Lu HJ, Wu XD, Huang YB, Shiarkar E. Effect of seasons upon intraocular pressure in healthy population of China. *Korean J Ophthalmol*. 1996;10:29–33.
22. Schuster AK, Pfeiffer N, Schulz A, et al. The impact of pseudophakia on vision-related quality of life in the general population—The Gutenberg Health Study. *Aging (Albany NY)*. 2017;9:1030–1040.
23. Schuster AK, Nickels S, Pfeiffer N, et al. Frequency of cataract surgery and its impact on visual function-results from the German Gutenberg Health Study. *Graefes Arch Clin Exp Ophthalmol*. 2020;258:2223–2231.
24. Foster PJ, Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. *Br J Ophthalmol*. 2002;86:238–242.
25. Schlittgen R, Sattarhoff C. *Angewandte Zeitreihenanalyse mit R*. Berlin: De Gruyter Oldenbourg, 2020.

26. Ward MP, Iglesias RM, Brookes VJ. Autoregressive models applied to time-series data in veterinary science. *Front Vet Sci*. 2020;7:604.
27. Cornelissen G. Cosinor-based rhythmometry. *Theor Biol Med Model*. 2014;11:16.
28. Gunzler D, Chen T, Wu P, Zhang H. Introduction to mediation analysis with structural equation modeling. *Shanghai Arch Psychiatry*. 2013;25:390–394.
29. Chan MP, Grossi CM, Khawaja AP, et al. Associations with intraocular pressure in a large cohort: results from the UK Biobank. *Ophthalmology*. 2016;123:771–782.
30. Lewington S, Li L, Sherliker P, et al. Seasonal variation in blood pressure and its relationship with outdoor temperature in 10 diverse regions of China: the China Kadoorie Biobank. *J Hypertens*. 2012;30:1383–1391.
31. Woodhouse PR, Khaw KT, Plummer M. Seasonal variation of blood pressure and its relationship to ambient temperature in an elderly population. *J Hypertens*. 1993;11:1267–1274.
32. Narita K, Hoshide S, Kario K. Seasonal variation in blood pressure: current evidence and recommendations for hypertension management. *Hypertens Res*. 2021;44:1363–1372.
33. Stergiou GS, Palatini P, Modesti PA, et al. Seasonal variation in blood pressure: Evidence, consensus and recommendations for clinical practice. Consensus statement by the European Society of Hypertension Working Group on Blood Pressure Monitoring and Cardiovascular Variability. *J Hypertens*. 2020;38:1235–1243.
34. Klein BE, Klein R, Knudtson MD. Intraocular pressure and systemic blood pressure: longitudinal perspective: the Beaver Dam Eye Study. *Br J Ophthalmol*. 2005;89:284–287.
35. Bakke EF, Hisdal J, Semb SO. Intraocular Pressure Increases in Parallel with Systemic Blood Pressure during Isometric Exercise. *Invest Ophthalmol Vis Sci*. 2009;50:760–764.
36. Dielemans I, Vingerling JR, Algra D, Hofman A, Grobbee DE, de Jong PTVM. Primary open-angle glaucoma, intraocular pressure, and systemic blood pressure in the general elderly population: the Rotterdam Study. *Ophthalmology*. 1995;102:54–60.
37. Zhao D, Cho J, Kim MH, Guallar E. The association of blood pressure and primary open-angle glaucoma: a meta-analysis. *Am J Ophthalmol*. 2014;158:615–627.e9.
38. Barnett AG, Sans S, Salomaa V, Kuulasmaa K, Dobson AJ. The effect of temperature on systolic blood pressure. *Blood Press Monit*. 2007;12:195–203.
39. Alpérovitch A, Lacombe J-M, Hanon O, et al. Relationship between blood pressure and outdoor temperature in a large sample of elderly individuals: the three-city study. *Arch Intern Med*. 2009;169:75–80.
40. Nakagami H, Akiyama H, Otsuka H, Iwamae A, Yamada H. Blood pressure fluctuations and the indoor environment in a highly insulated and airtight model house during the cold winter season. *Hypertens Res*. 2022;45:1217–1219.
41. Yasukawa T, Hanyuda A, Yamagishi K, et al. Relationship between blood pressure and intraocular pressure in the JPHC-NEXT eye study. *Sci Rep*. 2022;12:17493.
42. Bulpitt CJ, Hodes C, Everitt MG. Intraocular pressure and systemic blood pressure in the elderly. *Br J Ophthalmol*. 1975;59:717–720.
43. Shiose Y. The aging effect on intraocular pressure in an apparently normal population. *Arch Ophthalmol*. 1984;102:883–887.
44. Mentzer AP. What is the range of barometric pressure? Available at: https://sciencing.com/range-barometric-pressure-5505227.html. Accessed December 2, 2022.
45. Hoffmann EM, Lamparter J, Mirshahi A, et al. Distribution of central corneal thickness and its association with ocular parameters in a large central European cohort: the Gutenberg health study. *PLoS One*. 2013;8:e66158.
46. McCann P, Hogg RE, Wright DM, et al. Comparison of Goldmann applanation and Ocular Response Analyser tonometry: intraocular pressure agreement and patient preference. *Eye*. 2020;34:584–590.