# Seasonal and Diurnal Variations of Ocular Pressure in Ocular Hypertensive Subjects in Pakistan

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## ABSTRACT

**Background:** Studies have been shown that intraocular pressure (IOP) shows a diurnal variation in ocular hypertensive subjects, but the amount of change differs from study to study. In recent years it has been noted that intraocular pressure is a dynamic function and is subjected to many influences both acutely and over the long term. The variability in the results may be due to negligence of factors that can affect IOP. Moreover, seasonal variations in the ocular hypertensive subjects have never been described. After placing control on those factors that can affect IOP, this study investigated seasonal and diurnal variations in IOP of ocular hypertensive subjects.

**Patients and Methods:** IOP was measured each month over the course of 12 months with the Goldmann applanation tonometer in 91 ocular hypertensive male subjects. To see the diurnal changes, subjects were asked to stay in the hospital for 24 hours.

**Results:** The average IOP in the winter months was higher than those in spring, summer, and autumn. The IOP difference between winter and summer was (mean $\pm$ sem) 2.9 $\pm$ 0.9 mmHg ($p < 0.001$). The peak of mean IOP in diurnal variation curve (25.7 $\pm$ 1.2 mmHg) appeared in the morning when the subjects had just awaken. The mean diurnal variation was found to be 4.2 $\pm$ 0.6 mmHg ($p < 0.001$).

**Conclusions:** This study confirms that seasons influence IOP and it shows diurnal variations. As compared to other nations, diurnal variations in ocular hypertensive subjects seem to be somewhat less in Pakistan. Knowledge of the seasonal and diurnal variations in IOP may help glaucoma screeners.

**Keywords:** applanation pressure, diurnal variations, ocular hypertensive subjects, seasonal variations, tonometry

## INTRODUCTION

Intraocular pressure (IOP) is one type of chronobiological rhythms similar to other physiological values in the human body, such as body temperature, heart rate, blood pressure, hormone secretion, etc. Many investigators[1-4] have reported diurnal variations in ocular hypertensive (OHT) subjects. However, the results differed from study to study. Some studies reported that the momentary IOP elevation was associated with awakening[4]. In contrast to these, other investigators have shown that IOP was highest at 2 pm[2]. The variability in the results of previous studies may be due to negligence of some factors. In recent years, it has been noted that intraocular pressure is a dynamic function and is subjected to many influences both acutely and over the long term. Many investigators have reported that IOP varies with age and sex[5]. It has been reported that drinking of water, coffee, or alcohol before IOP measurement have a significant effect on it[6]. Acute hyperglycaemia decreases[7], while chronic hyperglycaemia in diabetes increases IOP[8]. It has been shown that IOP is positively related with systemic blood pressure[8]. Recently, it has been shown that IOP decreases even by simple exertion such as walking[9].

It has been shown in both normal and glaucoma patients that intraocular pressure has a seasonal variation, being low in summer and high in winter[10-14]. However, seasonal variations in the ocular hypertensive subjects have never been described. After taking into account the above mentioned factors, we investigated diurnal and seasonal variations in IOP of ocular hypertensive subjects of Karachi, the largest city in Pakistan.

## PATIENTS AND METHODS

All experimental procedures adhered to the Declaration of Helsinki of the World Medical Association. Ninety-one ocular hypertensive subjects with open angle glaucoma were chosen from the out-patient Ophthalmology Department at Jinnah Postgraduate Medical Centre, Karachi, Pakistan. To exclude the effects of age and sex, all subjects were males and in the same age group, ranging between 35 and 45 years, (mean $\pm$ sem 41.1 $\pm$ 1.2). No ocular hypertensive subject was on any medicine. A medical history was taken from each subject, including questions concerning previous ocular diseases, presence of diabetes mellitus, and the occurrence of glaucoma in the family. The criteria met by the subjects were absence of any history of eye surgery and diabetes, normal body temperature and blood pressure. The OHT subjects had at least three IOP readings equal to or greater than 22 mmHg, but normal visual fields and normal optic nerves without evidence of asymmetric cupping.

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The measurements of seasonal variation were taken at a fixed time between 9.00 am and 10.00 am, to minimise the effect of diurnal variations. The subjects were checked monthly for a period of 12 months. In order to see the diurnal variations, during winter months (November to January), the subjects were asked to stay in the hospital for 24 hours for examinations. The subjects stayed in bed during their regular sleeping hours. They could sleep in-between measurements and were awaken for 5 to 10 minutes for each examination and in most instances, they promptly fell asleep again until the next measurement. After arising in the morning, the IOPs were measured immediately. The second measurements were taken at 10.00 am. Subsequently, measurements were taken after every three hours until they awoke the next day. In order to minimise the effect that food and water has on the results of IOP readings in the 8 hours where no measurement was done, subjects were allowed to eat and drink in the first hour. Before each measurement, the subjects were rested for 30 minutes in a supine position. The blood pressure was taken in a sitting position. After installation of 0.25% fluorescein and 0.4% benoxinate hydrochloride (Fluress) eye drops, the IOP was measured with the Goldmann applanation tonometer (Goldmann Topocon, Germany), first in the right eye and then in the left eye. The measuring drum was turned until the inner borders of the fluorescein rings (adjusted for equal size) just touched each other at the midpoint of the ocular pulse and the overlap and separation of the mires with each pulse swing was equidistant from the midpoint on both sides. The measuring drum was not to be observed until this defined point was reached. Three consecutive readings of each eye were taken. After each reading, the tonometer was removed from the contact and the measuring scale was returned to 10 mmHg. The practice of returning the tonometer to 10 mmHg, after each reading was to minimise observer bias.

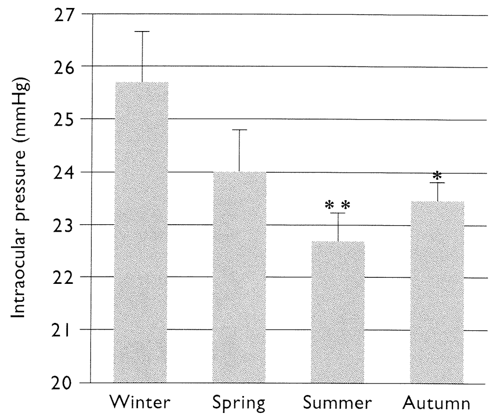


**Fig 1** – Intraocular pressure measurements over a course of one year.

The distribution of intraocular pressures for each three-month period. The bars represent the mean, and the vertical lines above the mean, represent one standard error of the mean. Decreases are significant (* $p < 0.02$; ** $p < 0.001$) as compared to the highest mean value in winter.

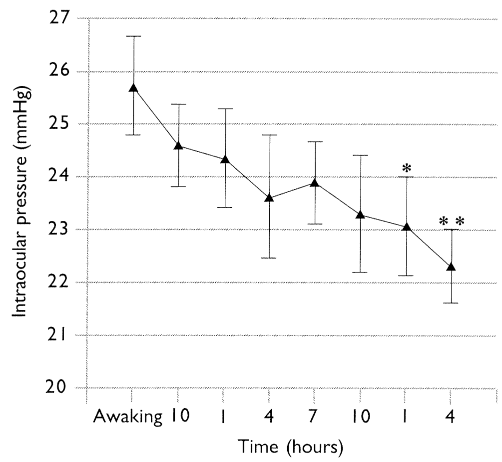


**Fig 2** – Twenty-four hour variations of IOP in ocular hypertensive subjects.

Mean IOP recorded at various times in ocular hypertensive subjects. The symbol (▲) represents the mean, and the vertical lines above and below the mean, represent one standard error of the mean. Decreases are significant (* $p < 0.05$; ** $p < 0.001$) compared to the highest mean value in the morning.

### Statistical analyses

The mean of the three readings was computed separately for each eye. For statistical accuracy, the mean values were expressed up to one decimal point. All variable descriptive statistics (mean, standard deviation, standard error of mean) were calculated by Statistical Analysis System 76[15]. All data are expressed as mean and standard error of the mean. Analysis of variance (ANOVA) was used to compare results between the different months and between different hours of a day. Differences were regarded as significant when the p value was less than 0.05. Actual p values were given where appropriate.

## RESULTS

The effects of seasons and diurnal variations of IOP are represented in Figs 1 & 2 respectively. The effects of seasons and diurnal variations were found to be similar on each pair of eyes. The average intraocular pressure in winter was higher than those in spring, summer and autumn. Out of 91 subjects, only two showed significantly higher value of IOP in summer than in winter ($p < 0.05$). Nine subjects showed no significant variations during the study, while in 80 subjects, intraocular pressure was 2 to 5 mmHg higher in winter than in summer. The IOP difference between winter and summer was found to be (mean ± sem) 2.9 ± 0.9 mmHg ($p < 0.001$). Seasonal IOP and blood pressure variations were of different magnitudes depending on the individual. The systolic blood pressure varied between 114.5 ± 3.7 and 122.1 ± 2.8 mmHg, while diastolic blood pressure varied between 74.4 ± 3.1 and 71.1 ± 2.5 mmHg, both insignificantly lower in summer. The blood pressure of all the subjects fell within the normal range. The change in IOP did not correlate with the variation of blood pressure (data not shown). The peak of mean IOP in diurnal variation curve (25.7 ± 1.2 mmHg) appeared in the morning when the subject was awaken, and the trough of mean IOP (21.5 ± 1.4 mmHg) happened between 2 and 4 am. The mean diurnal variation was 4.2 ± 0.6 mmHg ($p < 0.001$).

## DISCUSSION

Different seasons influence IOP in ocular hypertensive subjects. In our study, it was highest in winter, reaching the lowest values in summer. This finding is similar to previous studies of normal subjects and glaucoma patients[10-14]. Studies of seasonal variation in normal individuals have shown that in the overwhelming majority, IOP was lower by 1 – 3 mmHg in summer than in winter[10]. Bengtsson[14] conducted a seasonal study of IOP in normal subjects and found that the levels were higher by about 2 mmHg in winter than in summer. In Japan, Shiose[11] compared IOP readings monthly and found that there was a significant difference in the seasons, the IOP being 1.5 mmHg lower in summer than in winter. In a glaucoma survey conducted in Israel, Blumenthal et al[13] found that the average IOP in clinical cases was 15.7 mmHg in summer and 18.0 mmHg in winter. In the present study, the IOP difference of ocular hypertensive patients in winter and summer was found to be 2.9 ± 0.9 mmHg.

This study demonstrates the IOP peak of diurnal variation curve upon awaking. Review of previous studies of diurnal variation in IOP shows considerable variation, ranging from 5.4 to 8.5 mmHg[14]. In the current study, the mean diurnal variation was found to be 4.2 ± 0.6 mmHg, much lower than previous studies. The large difference between the present and previous studies may be due to the fact that they did not control the effect of drinking, acute hyperglycaemia and even seasonal variations.

In populations of different races and countries, IOP is higher in the cold season[10-14,16], showing that this finding is related to climatic changes and not to local factors. The physiological mechanism responsible for the seasonal variation of intraocular pressure is not clearly known[10,11]. The presence of an elevated IOP upon awaking is also puzzling. However, a mechanism that accounts for both the rise and decline of IOP can be suggested. The time of exposure to light may be the reason for both the seasonal and diurnal variations. In winter, the time of exposure to light is much shorter than in summer. Gloster and Poinoosawmy[17] concluded that 1 hour in darkness can cause an increase in IOP but decreases upon exposure to light. They also pointed out that the dilatation and constriction of the pupil were not the main causes of IOP variations. Stoupel et al[18] showed that environmental conditions have a significant influence on IOP. They reported that intraocular pressure is related to levels of daily geomagnetic and extreme yearly solar activity. Recently, Giuffre et al[16] reported that mean hours of daily sunlight exposure are slightly and inversely related with the mean IOP.

The pineal gland is controlled by the amount of light seen by the eyes each day. The pineal gland secretes melatonin and several other similar substances. Melatonin or one of the other substances then passes either by way of blood or through the fluid of the third ventricle to the anterior pituitary gland to control gonadotropic hormone secretion. This causes excessive secretion of FSH and LH. These hormones in turn, increase the secretion of progesterone and estrogen. This is what presumably occurs in animals in winter, when there is more darkness[19]. It has been reported that blind girls are prone to an early onset of menstruation, showing that light deprivation in human beings has an effect on sex hormones[20]. Several studies have reported the effect of progesterone and estrogen (alone or in combination) on IOP values[21]. It seems quite possible that in summer, when there is more light, less secretion of pineal gland may be the cause of lower IOP and therefore its effect on sex hormones.

Correlations between diurnal fluctuations in intraocular pressure and plasma glucocorticoid levels have been found in normal individuals and in patients with glaucoma. There seemed to be a four-hour lag between the peak level of the plasma glucocorticoids and the peak in intraocular pressure[22]. Administration of SU4885, an inhibitor of glucocorticoid and mineralocorticoid synthesis, diminished the diurnal fluctuation of intraocular pressure[22]. In one review, Waitzmar[23] concluded that the hypothalamus might be the major central nervous system controlling site for changes in IOP. Certainly, the 24-hour correlative relationships with differing hypothalamic controlled circadian events, such as neuroendocrine processes, body temperature, sleep-waking functions, autonomic activity, etc., would support the fact that this central nervous system area may be critically involved.

We realise that starting the diurnal variation curve of IOP in the clinic around 8 am is less than ideal, because the highest IOP occurs immediately after awaking. It is also possible that the home tonometry, as advocated by Zeimer[24], covers a larger portion of the 24-hour cycle. The clinical importance of our finding, that peak IOPs occur in the early morning, raised a serious question as to the necessity of extending the diurnal IOP curves beyond the usual working time. More importantly it emphasises the fact that solitary IOP examination taken in the afternoon may miss most of the IOP peaks. This finding indicates that a revision of the timetable for IOP examination in the ocular hypertensive patients may be warranted.

## ACKNOWLEDGEMENTS

The authors gratefully acknowledge Professor Ahmad Kamal Ansari and Professor Abdul Baseer for their technical guidance and assistance and Dr Nusrat Pasha for his statistical assistance.

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