

# The significance of atherosclerosis in hypertensive patients with epistaxis

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## Abstract

**Background:** The relationship between hypertension and epistaxis is controversial and poorly understood. The present research investigated atherosclerosis as a potential risk factor in hypertensive patients with epistaxis.

**Methods:** A prospective study of 141 hypertensive patients with epistaxis was conducted. The laboratory tests included full blood count, lipid profile and coagulation profile. All patients underwent fundoscopic examination of the eye and were classified in terms of four retinopathy grades.

**Results:** There were strong positive correlations between the number of nosebleeds and retinopathy grade and low-density lipoprotein cholesterol level. There were weak correlations between the number of nosebleeds and blood pressure readings and triglycerides levels. Patients with grade III retinopathy, suggesting atherosclerosis, suffered from more frequent nosebleeds than other patients.

**Conclusion:** Atherosclerosis is one of the potential risk factors in hypertensive patients with epistaxis. This may have an impact on treatment choices.

**Key words:** Hypertension; Epistaxis; Retina; Atherosclerosis; Cholesterol

## Introduction

Epistaxis is one of the frequent symptoms in our practice. It is reported that 8–60 per cent of people will experience at least one episode of epistaxis in their life. Surprisingly, the cause of epistaxis is diagnosed in only 15 per cent of cases.<sup>1</sup> Anterior nosebleeds constitute about 80 per cent of cases, while 15–20 per cent are posterior; the latter are more common in elderly patients and are more difficult to manage.<sup>1</sup>

Hypertension is increasing in prevalence worldwide, affecting about one-quarter of the general adult population. Several factors may predispose to epistaxis.<sup>2</sup> Hypertension is traditionally considered as one of these factors. However, the connection between hypertension and epistaxis is still unclear.<sup>3</sup> The prevalence rates of hypertension among patients with epistaxis range from 17 to 67 per cent.<sup>4</sup> Dal Secchi *et al.* found that arterial hypertension was the most frequent prevailing factor in their patients with severe epistaxis.<sup>5</sup> In a systematic review by Kikidis *et al.*, six out of nine studies reported that arterial pressure was higher at the time of epistaxis, as compared to the control group or to the general population.<sup>6</sup>

Epistaxis in hypertensive patients is usually posterior and more difficult to control than anterior nosebleeds. Some hypertensive patients tend to have recurrent episodes of epistaxis even though their coagulation profile

is within normal levels. In a small study, Ibrashi *et al.* suggested that hypertension and atherosclerosis seem to maintain and increase the severity of epistaxis.<sup>7</sup> Herkner *et al.* made a similar conclusion, and highlighted the relationship between hypertension and the frequency of epistaxis.<sup>8</sup>

Retinal arteriolar narrowing is a known marker of chronic hypertension and of microvascular disease.<sup>9</sup> Some hypertensive retinopathy signs are associated not only with concurrent blood pressure levels, but also with past blood pressure levels, suggesting that they reflect chronic hypertensive damage. Two studies suggested that arterial hypertension results in structural alterations of the nasal vessels similar to those found in cerebral circulation and on retinal examination, but they did not address the issue in detail.<sup>5,10</sup>

The present research investigated atherosclerosis as a potential risk factor in hypertensive patients with epistaxis. However, we did not intend to address treatment options for these patients.

## Materials and methods

The research was performed prospectively on 141 hypertensive patients with epistaxis who were treated in a tertiary care hospital from January 2010 to March 2015. The sample size was based upon an a priori power calculation.<sup>11</sup> All patients signed informed

consent forms approved by the institutional review board (ethics committee) of our institution, and the faculty ethics committee approved the research.

None of the patients had any identifiable local pathology on endoscopic examination that accounted for the bleeding. The study group did not include patients with bleeding disorders or those receiving medications that may interfere with haemostasis.

All patients had chronic hypertension, as confirmed based on medical records and reports for the previous three years. The blood pressure of each patient was measured three times on the day of admission using a mercuric manometer, and the mean measurements were calculated and recorded. We also retrieved blood pressure readings from the patients' records and reports of treating physicians, and compared these statistically to our readings in order to exclude effects of stress and white coat phenomenon on blood pressure. The history of previous epistaxis episodes was retrieved from patients' out-patient and in-patient records.

All patients underwent full rhinological and medical examinations. The following laboratory tests were performed: full blood count, including platelet count; lipid profile (total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein (LDL) cholesterol and triglycerides); and coagulation profile (bleeding time, prothrombin time, activated partial thromboplastin time, fibrinogen and thrombin time).

All patients underwent funduscopic examination by an expert ophthalmologist. The patients were classified

into four groups according to the Keith–Wagener–Barker classification of funduscopy.<sup>12</sup>

#### Statistical analysis

Data entry and analysis were performed using SPSS® statistical software version 15. Sample size calculation was based on a power of 0.8 and an alpha level of 0.05. Lin's concordance correlation co-efficient was calculated to test the agreement of blood pressure readings taken at the time of admission and the readings in the reports of the treating physicians. Continuous variables are presented as means  $\pm$  standard deviations, and categorical variables are shown as percentages. Mean values were compared using *t*-tests. Comparisons between retinopathy groups were conducted using a Kruskal–Wallis test. Pearson's correlation co-efficient was used to test for correlations between variables. A *p*-value of less than 0.05 was considered statistically significant.

#### Results

The study included 141 patients with epistaxis who were admitted to the hospital between January 2010 and March 2015. There were 105 males (74.4 per cent) and 36 females (25.6 per cent). Pertinent demographic, clinical and laboratory data are shown in Table I.

Comparisons between blood pressure readings taken at the time of admission and those retrieved from medical reports (Table II) did not reveal any significant differences between the readings regarding either systolic or diastolic blood pressure measurements ( $p = 0.3281$  and  $p = 0.4420$  respectively). The concordance correlation co-efficient also showed good agreement between the two groups of measurements (the concordance correlation co-efficient was 0.9441 for systolic blood pressure and 0.9811 for diastolic blood pressure).

There was a weak positive correlation between the number of epistaxis episodes and the level of blood pressure ( $R = 0.3050$  for systolic blood pressure and  $R = 0.2287$  for diastolic blood pressure; Tables III and IV).

The LDL cholesterol levels in blood (Table V) were strongly correlated with the number of epistaxis episodes ( $R = 0.9354$ ,  $p = 0.0196$ ). There was a weak positive correlation between triglyceride concentration

TABLE I  
PATIENTS' DEMOGRAPHIC, CLINICAL AND  
LABORATORY DATA\*

Parameter	Value
Age (mean $\pm$ SD; years)	54.5 $\pm$ 8.56
Sex ( <i>n</i> )	
– Male	105
– Female	36
Duration of hypertension (mean $\pm$ SD; years)	16.4 $\pm$ 8.63
Number of previous epistaxis episodes (range)	1–5
Blood pressure level (mmHg)	152.2 / 105.1
Total cholesterol level (mean $\pm$ SD; mg/dl)	234.9 $\pm$ 2.55
LDL cholesterol level (mean $\pm$ SD; md/dl)	161.6 $\pm$ 3.05
HDL cholesterol level (mean $\pm$ SD; mg/dl)	58.53 $\pm$ 2.11
Triglyceride level (mean $\pm$ SD; mg/dl)	266.5 $\pm$ 3.01

\*Total of 141 patients. SD = standard deviation; LDL = low-density lipoprotein; HDL = high-density lipoprotein

TABLE II  
COMPARISON BETWEEN MEAN BLOOD PRESSURE READINGS AT TIME OF ADMISSION AND READINGS PROVIDED BY  
TREATING PHYSICIANS

BP type	BP reading at time of admission (mean $\pm$ SD; mmHg)	BP reading provided by treating physicians (mean $\pm$ SD; mmHg)	<i>p</i> *	Concordance correlation co-efficient†
Systolic	152.2 $\pm$ 11.9	149.8 $\pm$ 10.8	0.3281	0.9441
Diastolic	105.1 $\pm$ 15.0	104.6 $\pm$ 13.7	0.4420	0.9811

\*No significant differences between the means of the two groups. †Concordance correlation co-efficient shows strong agreement between the two groups. BP = blood pressure; SD = standard deviation

Epistaxis episodes ( <i>n</i> )	Patients ( <i>n</i> )	BP reading (mean ± SD; mmHg)
1	36	149.13 ± 11.23
2	28	154.46 ± 12.09
3	59	151.54 ± 11.48
4	13	150.34 ± 17.02
5	5	153.17 ± 15.22

Pearson correlation co-efficient (*R*) = 0.3050, *p* = 0.6177. BP = blood pressure; SD = standard deviation

Epistaxis episodes ( <i>n</i> )	Patients ( <i>n</i> )	BP reading (mean ± SD; mmHg)
1	36	104.21 ± 9.03
2	28	99.21 ± 19.40
3	59	103.62 ± 10.47
4	13	102.14 ± 15.06
5	5	104.65 ± 14.11

Pearson correlation co-efficient (*R*) = 0.2287, *p* = 0.7113. BP = blood pressure; SD = standard deviation

(Table V) and the number of epistaxis episodes (*R* = 0.4293, *p* = 0.4068).

The funduscopic examination results are shown in Table VI. Patients with grade III retinopathy constituted 48.2 per cent of patients, and those with grade II retinopathy constituted 32.6 per cent of patients. There was a significant difference between retinopathy groups regarding the number of epistaxis episodes (*p* = 0.0417, Kruskal–Wallis test). Patients with grade III retinopathy suffered from more frequent nosebleeds than other patients.

## Discussion

The association between epistaxis and hypertension is still controversial.<sup>13–15</sup> Some studies, however, have

Epistaxis episodes ( <i>n</i> )	Patients ( <i>n</i> )	LDL cholesterol level (mean ± SD; mg/dl)*	Triglyceride level (mean ± SD; mg/dl)†
1	36	142.06 ± 5.05	255.53 ± 6.01
2	28	138.32 ± 4.97	271.25 ± 5.92
3	59	169.54 ± 2.91	269.68 ± 5.47
4	13	182.72 ± 5.23	264.01 ± 3.98
5	5	186.17 ± 3.87	267.11 ± 4.08

\**R* = 0.9354, *p* = 0.0196; †*R* = 0.4293, *p* = 0.4068. LDL = low-density lipoprotein; SD = standard deviation

Epistaxis episodes ( <i>n</i> )	Retinopathy grade				Total
	I	II	III	IV	
1	20	12	4	0	36
2	3	13	12	0	28
3	2	20	36	1	59
4	0	1	12	0	13
5	0	0	4	1	5
Total	25	46	68	2	141

Data represent number of patients, unless indicated otherwise. *p* = 0.0417 (Kruskal–Wallis test).

confirmed a relationship between epistaxis and hypertension.<sup>16</sup> Isezuo *et al.*<sup>3</sup> and Herkner *et al.*<sup>17</sup> reported that patients with epistaxis had higher blood pressure measurements compared to control patients. Pollice and Yoder reviewed the medical records of 249 hospitalised epistaxis patients in 7 hospitals, and found that 46.9 per cent of patients had a positive history of hypertension.<sup>18</sup> Viducich *et al.* also provided evidence for the association between hypertension and epistaxis.<sup>16</sup> The present study investigated the significance of hyperlipidaemia and atherosclerosis risk factors in hypertensive patients with epistaxis.

In the present study, we included only patients with confirmed chronic hypertension, in order to avoid the confounding effects of temporary hypertension due to stress and the white coat effect. Furthermore, we compared blood pressure readings on the day of admission with those reported by the treating physicians, and found no significant differences between the two groups of readings.

Our results showed a weak positive correlation between the levels of systolic and/or diastolic blood pressure and the frequency of epistaxis episodes. However, there was a strong positive correlation between LDL cholesterol levels and the number of epistaxis episodes.

Hypertensive retinopathy has long been considered to increase the risks of systemic morbidity and mortality.<sup>19,20</sup> An abundance of data from clinical and population-based studies shows strong, graded and consistent associations between retinal changes and hypertension and atherosclerosis.<sup>21,22</sup> In the present study, we found that grade III retinal changes, signifying atherosclerosis, were significantly more frequent in patients who suffer recurrent episodes of epistaxis. In addition, LDL cholesterol, which is also a risk factor for atherosclerosis, was positively correlated with recurrent epistaxis. These findings are in line with those of Ibrashi *et al.*, who highlighted the possible association between epistaxis and atherosclerosis.<sup>7</sup> Another study, by Lubianca Neto *et al.*, also reported an association between long-lasting hypertension and the state of the nasal arteries in hypertensive patients with a history of epistaxis.<sup>10</sup>

The statistically significant relationship between advanced retinal arterial changes and epistaxis recurrence in hypertensive patients, and the weak correlation between blood pressure level and number of epistaxis episodes, may suggest that the state of the arterial wall is more important as a risk factor for epistaxis than simply the blood pressure level in hypertensive patients. This may help explain the conflicting results of studies investigating the relationship between epistaxis and hypertension, as these studies concentrated mainly on blood pressure readings and ignored the factor of associated atherosclerosis. Our view is also potentially supported by several studies which suggest that typical signs of hypertensive retinopathy are related to degenerative processes in the arterial wall rather than blood pressure level.<sup>23,24</sup>

- **The relationship between epistaxis and hypertension remains controversial**
- **Hypertensive patients suffering from atherosclerosis were more prone to recurrent and recalcitrant bleeding**
- **Atherosclerotic retinopathy grade and low-density lipoprotein cholesterol level correlated positively with epistaxis frequency**

Based upon our results, we suggest that atherosclerosis can be a risk factor in hypertensive patients with epistaxis. Hypertensive patients with atherosclerosis appeared to be prone to recurrent or recalcitrant bleeding episodes. The relationship between atherosclerosis, hypertensive retinopathy and epistaxis has been reported in previous publications.<sup>7</sup> The present cohort study, which included a larger number of patients and more detail, confirmed these findings. The impact of our results on our treatment decisions will be the subject of further evaluation and research.

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