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ORIGINAL ARTICLE

Is the site of hemorrhage an indicator of the cause of hemorrhage in cases with non-traumatic subconjunctival hemorrhage?

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Abstract

Purpose: To our knowledge, no study has so far assessed in detail the relationships between subconjunctival hemorrhage (SCH) sites and SCH causes in patients with non-traumatic SCH (NTSCH). Therefore, in this study, we aimed to investigate comprehensively these relationships.

Methods: Four-hundred nineteen cases were included. SCH sites were classified as superior (n = 109), nasal (n = 114), temporal (n = 84), and inferior (n = 112) areas. Etiological factors associated with NTSCH were determined as hypertension, diabetes mellitus, coagulation system disorders, conditions causing sudden venous congestion (CCSVC), and idiopathy. Relationships between SCH sites and causes were analyzed. In addition, evaluations were made according to age (≤60 and >60 years).

Results: In cases aged ≤60 years, nasal site hemorrhage was more frequent than temporal (35.0% vs. 21.7%, P = 0.016) and inferior (35.0% vs. 15.2%, P < 0.001) site hemorrhages. In individuals aged >60 years, inferior site hemorrhage was more frequent than superior (39.1% vs. 23.8%, P = 0.012), nasal (39.1% vs. 18.8%, P < 0.001), and temporal (39.1% vs. 18.3%, P < 0.001) site hemorrhages. In cases aged ≤60 years, etiological factors were seen with similar frequency in superior, temporal, and inferior site involvements (P > 0.05), while hemorrhage in nasal site was most frequently associated with CCSVC (46.1%, P < 0.01). In individuals aged >60 years, etiological factors were observed with similar frequency in superior, nasal, and temporal site involvements (P > 0.05), while hemorrhage in inferior site was most frequently associated with hypertension (48.1%, P < 0.02).

Conclusion: We determined that nasal NTSCH was most frequently associated with CCSVC in cases aged ≤60 years, while inferior NTSCH was most frequently associated with hypertension in individuals aged >60 years.

Keywords: Conjunctiva; hypertension; non-traumatic; subconjunctival hemorrhage; sudden venous congestion.

Subconjunctival hemorrhage (SCH) is the leakage of blood between the conjunctiva and episclera as a result of the conjunctival vessel rupture.[1] The hemorrhage usually occurs in the bulbar conjunctiva due to the loose subconjunctival tissue structure.[2] SCH may be associated with a trauma or non-traumatic causes.[2,3] In non-traumatic SCH (NTSCH), there is a spontaneous rupture of the conjunctival vessel.[2] NTSCH may be associated with the systemic vascular diseases such as hypertension or diabetes mellitus, the coagulation system disorders including

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anticoagulant or antiplatelet therapies, and the sudden severe venous congestion due to Valsalva maneuvers such as weight lifting, aerobic exercise, sexual activity, blowing musical instruments, vomiting, coughing, and constipation.[1-8] Conjunctival tumors, ocular amyloidosis, and hereditary hemochromatosis are among the rarer causes of NTSCH.[1,9-12] These hemorrhages can sometimes occur without obvious reasons (idiopathy).[2,3]

When the hemorrhage is noticed by the person and/or his surroundings, it may worry the patient due to its appearance and may cause the patient to consult a physician. In cases admitted to the health-care institution and diagnosed with NTSCH, this hemorrhage may sometimes be a clinical clue for a systemic disease that will be newly diagnosed or for an uncontrolled condition. Therefore, knowing the conditions, which may be frequently associated with the hemorrhage according to age and bleeding site, may be important in terms of taking the necessary precautions for those conditions first. Also when necessary, it may guide the physician in directing the patient to the related branches. Most studies in the literature were conducted on the causes and/or incidence of SCH,[2,5,13-16] and there were very few studies partially analyzing the SCH sites.[17,18] Moreover, to our knowledge, no study has so far assessed in detail the relationships between the SCH sites and SCH causes in patients with NTSCH. Therefore, in this study, we aimed to investigate comprehensively these relationships.

Materials and Methods

This study was performed with the approval of Izmir Tepecik Training and Research Hospital's Medical Research Ethical Committee and in line with the ethical principles of the Declaration of Helsinki. Written consent form was received from the participants and/or their families. The cases who were diagnosed with NTSCH after admission to the ophthalmology clinic and who had follow-up examinations were included in this study. The diagnosis of SCH was made by biomicroscopic examination. At presentation, the patient's age, gender, affected eye, histories of topical/systemic drug and/or contact lens usage, ocular and/or systemic diseases, the conjunctival location where the hemorrhage occurred, the history of major trauma, the history of minor trauma such as eye rubbing, and the recent surgical histories were noted. The visual acuity and intraocular pressure levels and the anterior-posterior segment examinations including a fluorescein staining test were recorded. The traumatic cases involving eye, head and/or other organ injuries, the individuals with a history of contact lens usage, the cases with diagnoses of dry eye, conjunctivitis, conjunctivochalasis, glaucoma or uveitis, the patients using a topical eye medication, and the cases having histories of ocular or other organ surgeries in the past 2 months before the hemorrhage were not included in the study. In addition, the cases with multiple SCH sites, multiple SCH causes, and/or bilateral involvement were also not included in this study. The medical history, hospital/health system records, and the consultation answers were used in the diagnoses of systemic disorders. Four-hundred and nineteen cases who met the inclusion criteria and who had routine control examinations within 2 months after the admission were evaluated. In the determination of SCH sites, the bulbar conjunctival area was divided into superior and inferior sites according to the imaginary horizontal line tangent to the corneal limbus at 12 and 6 o'clock, while the intermediate conjunctival area was divided into nasal and temporal sites. The classification of SCH sites was made by a single researcher (BÖ) according to a standard chart [e.g., Figure 1 for the right eye] from anterior segment photographs in a masked fashion. For the determination of etiological factors associated with NTSCH, the clinical information involving the medical history, hospital/health system records, and consultation answers was evaluated by another researcher (HÖ) blinded to the information of the conjunctival location where the hemorrhage occurred. SCH sites were classified as the superior (n = 109), nasal (n = 114), temporal (n = 84), and inferior (n = 112) bulbar conjunctival areas. Etiological factors associated with NTSCH

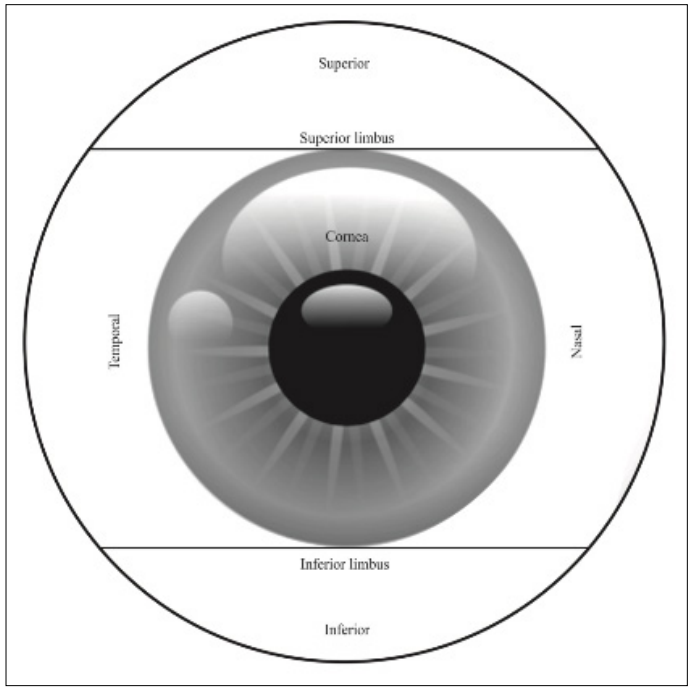

Fig. 1. The division of the bulbar conjunctival area into the superior, nasal, temporal, and inferior conjunctival sites for the right eye

Table 1. Clinical characteristics of the cases according to NTSCH sites

	NTSCH sites				P-value
	Superior	Asal	Temporal	Inferior	
Gender (Female/Male)	50/59	58/56	39/45	51/61	P=0.423
Age (years) (median [minimum–maximum])	54 (34–75)	49 (30–78)	52 (31–74)	65 (36–80)	4–1: P<0.001
					4–2: P<0.001
					4–3: P<0.001
					Opc: P>0.05
Affected eye (Right/Left)	56/53	53/61	44/40	52/60	P=0.504
Distribution of cases	61 (28.1%)	76 (35.0%)	47 (21.7%)	33 (15.2%)	2–3: P=0.016
≤60 years old (n, %) (Total n=217)					2–4: P<0.001
					1–4: P=0.009
					Opc: P>0.05
Distribution of cases	48 (23.8%)	38 (18.8%)	37 (18.3%)	79 (39.1%)	4–1: P=0.012
>60 years old (n, %) (Total n=202)					4–2: P<0.001
					4–3: P<0.001
					Opc: P>0.05

NTSCH: Non-traumatic subconjunctival hemorrhage; n: Number of cases; Opc: Other pairwise comparisons; P<0.05 statistically significant.

were determined as hypertension, diabetes mellitus, coagulation system disorders, conditions causing sudden venous congestion (CCSVC), and idiopathy (not attributable to any cause). The relationships between the SCH sites and SCH causes were analyzed. In the literature, it was reported that NTSCH incidence gradually increased with aging.[2,18] Moreover, the highest incidence of NTSCH was detected after 60 years of age.[2,18] Hence, we chose 60 years of age as the limit, and the evaluations were also made according to the age of ≤60 years and >60 years.

The Statistical Package for the Social Sciences (SPSS Version 25.0; IBM, USA) software was used for the statistical analysis. The assumption of normality was tested by the Shapiro–Wilk test. Non-normally distributed continuous variables were reported as the median and range (minimum-maximum). Categorical variables were presented with the number and percentage. The Chi-square test with a Bonferroni correction was used to evaluate any potential association between the categorical variables. The Kruskal–Wallis test was employed to analyze the data of three or more independent measurements, and also, Dunn's test was used for pairwise comparisons. The results were assessed with a 95% confidence interval and at the $P < 0.05$ significance level.

Results

There were 198 (47.3%) females and 221 (52.7%) males in our study ($P = 0.397$). The median age of all individuals was 55 (30–80) years. The right eye was affected in 205 (48.9%) cases, and the left eye in 214 (51.1%) cases ($P = 0.681$). The median age of the individuals with inferior site involvement was significantly higher than those of the individuals with superior (65 vs. 54 years, $P < 0.001$), nasal (65 vs. 49 years, $P < 0.001$), and temporal (65 vs. 52 years, $P < 0.001$) site involvements. However, there was no significant difference between the ages of the cases with superior, nasal, and temporal site involvements ($P > 0.05$). Both gender distributions ($P = 0.423$) and right/left eye involvement rates ($P = 0.504$) of the individuals with superior, nasal, temporal, and inferior site involvements were similar. In cases aged ≤60 years, the nasal site hemorrhage was detected more frequently than the temporal (35.0% vs. 21.7%, $P = 0.016$) and inferior (35.0% vs. 15.2%, $P < 0.001$) site hemorrhages. In addition, the superior site hemorrhage was more frequent than the inferior site hemorrhage (28.1% vs. 15.2%, $P = 0.009$). In individuals aged >60 years, the inferior site hemorrhage was found more frequently than the superior (39.1% vs. 23.8%, $P = 0.012$), nasal (39.1% vs. 18.8%, $P < 0.001$), and temporal (39.1% vs. 18.3%, $P < 0.001$) site hemorrhages. The clinical characteristics of the cases according to NTSCH sites were given in Table 1.

In cases aged ≤60 years, the rates of the SCHs associated with hypertension, diabetes mellitus, coagulation system disorders, CCSVC, and idiopathy were similar in superior,

Table 2. Distributions of the etiological factors associated with NTSCH according to ages and conjunctival sites

	Etiological factors associated with NTSCH (n, %)					P-value
	Hypertension (%)	Diabetes mellitus (%)	Coagulation system disorders (%)	Conditions causing sudden venous congestion (%)	Idiopathy (%)	
NTSCH sites of cases ≤60 years old						
Superior (n=61)	13 (21.3)	7 (11.5)	8 (13.1)	17 (27.9)	16 (26.2)	P=0.389
Nasal (n=76)	11 (14.5)	9 (11.8)	8 (10.5)	35 (46.1)	13 (17.1)	4–1: P=0.002 4–2: P<0.001 4–3: P<0.001 4–5: P=0.005 Opc: P>0.05
Temporal (n=47)	7 (14.9)	7 (14.9)	6 (12.8)	16 (34.0)	11 (23.4)	P=0.158
Inferior (n=33)	8 (24.2)	5 (15.2)	8 (24.2)	6 (18.2)	6 (18.2)	P=0.673
NTSCH sites of cases >60 years old						
Superior (n=48)	13 (27.1)	8 (16.7)	7 (14.5)	8 (16.7)	12 (25.0)	P=0.432
Nasal (n=38)	9 (23.7)	6 (15.8)	6 (15.8)	9 (23.7)	8 (21.0)	P=0.695
Temporal (n=37)	10 (27.0)	5 (13.6)	6 (16.2)	6 (16.2)	10 (27.0)	P=0.492
Inferior (n=79)	38 (48.1)	11 (13.9)	7 (8.9)	6 (7.6)	17 (21.5)	1–2: P<0.001 1–3: P<0.001 1–4: P<0.001 1–5: P=0.011 4–5: P=0.032 Opc: P>0.05

NTSCH: Non-traumatic subconjunctival hemorrhage; n: Number of cases; Opc: Other pairwise comparisons; P<0.05 statistically significant.

temporal, and inferior site involvements (P > 0.05). On the other hand, in nasal site involvement. the rate of the SCH associated with the CCSVC was significantly higher than the rates of the SCHs associated with hypertension (46.1% vs. 14.5%, P = 0.002), diabetes mellitus (46.1% vs. 11.8%, P < 0.001), coagulation system disorders (46.1% vs. 10.5%, P < 0.001), and idiopathy (46.1% vs. 17.1%, P = 0.005) in this age group.

In individuals aged >60 years, the rates of the SCHs associated with hypertension, diabetes mellitus, coagulation system disorders, CCSVC, and idiopathy were similar in superior, nasal, and temporal site involvements (P > 0.05). However, in inferior site involvement, the rate of the SCH associated with hypertension was significantly higher than the rates of the SCHs associated with the diabetes mellitus (48.1% vs. 13.9%, P < 0.001), coagulation system disorders (48.1% vs. 8.9%, P < 0.001), CCSVC (48.1% vs. 7.6%, P < 0.001), and idiopathy (48.1% vs. 21.5%, P = 0.011) in this age group. The distributions of the etiological factors associated with NTSCH according to ages and conjunctival sites were given in Table 2.

Discussion

In clinical practice, NTSCH is one of the conditions observed by ophthalmologists as well as other branch physicians such as family physician, internal specialist, and emergency physician. In spite of that, according to our knowledge, no study has analyzed comprehensively the relationships between the SCH sites and SCH causes in cases with NTSCH until our study. In the literature, different results were reported in terms of the gender distributions of the SCH cases.[2,13,15,17-19] Some authors stated that NTSCHs were seen more frequently in women compared to men.[2,15,19] Hu et al. thought that the presence of some female-only etiologies such as childbirth might contribute to this situation.[2] On the other hand, there were some studies that found similar gender distributions in SCH patients.[13,17,18] The distributions of the female and male were also similar in our study. The reason for reporting the different results in terms of the gender distribution among the studies may be due to the different demographic characteristics of the regions where the studies were conducted.

Joshi and Bandgar found that the right eye was affected

more frequently than the left eye in patients with NTSCH. However, they interpreted this condition as an incidental finding.[18] Some authors stated that the right or left eye was not predominance for spontaneous SCH.[15,19] In our study, the rate of right-eye involvement was also similar to the rate of left-eye involvement in cases with NTSCH. In the literature, SCHs were reported to be seen more frequently in individuals over 50 years of age.[13,16] Similarly, the median age of all cases in our study was 55 years. The reason for this rise in SCH after the age of 50 may be the increase of the frequencies of both the etiological diseases such as hypertension, diabetes mellitus, and the complications related to the anticoagulant treatment with advancing age.[16]

Wa Kaimbo stated that the temporal or nasal area was involved in 19 of 28 spontaneous SCH patients with a mean age of 35 years.[15] Sahinoglu-Keskek et al. reported that the nasal, temporal, and inferior areas were affected similarly in 16 spontaneous SCH patients with a mean age of 50 years.[19] However, in our study, we determined that the nasal site hemorrhage was more frequent than the temporal and inferior site hemorrhages in NTSCH cases aged ≤60 years. In addition, we found that a hemorrhage detected in the nasal site was most frequently associated with CCSVC in individuals aged ≤60 years. In the literature, the density of the superficial conjunctival vessels was shown to be highest in nasal quadrant.[20] Mimura et al. stated that the connections between the conjunctiva and Tenon's capsule were strong in younger individuals, and therefore, the blood remained at the site of the origin after the bleeding in younger individuals.[17] Contrary to some etiological diseases such as hypertension and diabetes mellitus, which can be seen more in the elderly,[21-23] the CCSVC can be derived from the actions such as weight lifting, aerobic exercise, sexual activity, blowing musical instruments, vomiting, coughing, and constipation, which may be more relevant to the younger age group.[1-3,8,16] Moreover, it was thought that young individuals could produce sufficiently high reflux venous pressure which might lead to small vessel ruptures.[24] The reasons, why the nasal site is affected more frequently and the Valsalva maneuvers are determined more commonly in our study, may be the age factor as well as, the lack of eyelid support effect and the presence of denser conjunctival vessels in that site. In addition, the strong connections between the conjunctiva and Tenon's capsule in younger individuals may also have contributed to this result by causing the blood to remain in the nasal site after the bleeding.

Hu et al. reported that the incidence of NTSCH reached its maximum value between the ages of 60–69 years.[2] In the literature, it was shown that SCHs seen in elderly individuals were associated with common systemic vascular diseases such as hypertension and arteriosclerosis.[13,16] Pitts et al. determined that the incidence of the hypertension was higher in patients with spontaneous SCH than in healthy controls. The authors also reported that spontaneous SCH might be an indicator of undiagnosed hypertension.[14] Similarly, Mimura et al. thought that some of the SCHs with unknown etiology in elderly patients might be a predictor of future hypertension.[16] Joshi and Bandgar stated that the nasal area was affected more frequently in their study including 70 NTSCH patients with a mean age of 66 years. The authors could not find any etiological factor in 34.3% of all cases, while they detected the presence of hypertension in only 8.6% of all cases.[18] On the other hand, Mimura et al. reported that SCHs were seen more frequently in the lower areas than in the upper areas.[17] In our study, the inferior site was the most frequently involved area in NTSCH cases aged >60 years. In addition, a hemorrhage detected in the inferior site was most frequently associated with hypertension in individuals aged >60 years. In the literature, it was stated that the prevalence and incidence of hypertension increased with age.[21,22,25] Both age-related effects and vascular disorders caused by hypertension may damage the vessels over time and may make them fragile. Therefore, conjunctival vessels may rupture spontaneously more easily in elderly individuals.[3] The reason why the inferior site is affected more frequently in our study may be that the fibrous connections between the conjunctiva and Tenon's capsule become more fragile with increasing age, and therefore, the blood can move to the inferior site with the effect of gravity, even if the origin of the bleeding is in the upper areas.[17]

There were some limitations in our study. First, this study included only the cases who were admitted to the hospital and diagnosed with NTSCH. Second, the idiopathic causes of SCHs might also have contained undiagnosed diseases as well as minor traumas that the patients did not remember or made unconsciously. In addition, there might be some conditions or diseases associated with SCH, which were not written in consultation answers and hospital/health system records. To our knowledge, the main difference of our study from the previous studies was that the causes of the hemorrhage according to SCH sites were investigated comprehensively for the first time in patients with NTSCH.

Conclusion

We determined that the nasal site hemorrhage was more frequent than the temporal and inferior site hemorrhages in cases aged ≤60 years. In this age group, etiological fac-

tors were seen with similar frequency in superior, temporal, and inferior site involvements, while the hemorrhage detected in the nasal site was most frequently associated with the CCSVC. On the other hand, we found that the inferior site hemorrhage was more frequent than the superior, nasal, and temporal site hemorrhages in individuals aged >60 years. In this age group, etiological factors were observed with similar frequency in superior, nasal, and temporal site involvements, while the hemorrhage detected in the inferior site was most frequently associated with hypertension. Besides a well-taken history, the bleeding site and individual's age may give an idea about the etiologies. NTSCH may sometimes be a clinical clue for a systemic disease that will be newly diagnosed or for an uncontrolled condition. In addition, it may guide the physician and the patient to take the necessary precautions for those conditions first.

Ethics Committee Approval: This study was approved by Tepecik Training and Research Hospital Faculty of Medicine Ethics Committee (12,10.2020; 2020/12-34).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: H.Ö., B.Ö.; Design: H.Ö., B.Ö.; Supervision: H.Ö., B.Ö.; Resource: H.Ö.; Materials: H.Ö., B.Ö.; Data Collection and/or Processing: H.Ö.; Analysis and/or Interpretation: H.Ö., B.Ö; Literature Search: B.Ö.; Writing: H.Ö., B.Ö.; Critical Reviews: H.Ö., B.Ö.

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