



## Full Length Article

## Head trauma is the major risk factor for cerebral sinus-vein thrombosis



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## ABSTRACT

**Background:** Cerebral sinus vein thrombosis (CSVT) is a rare disease with significant neurological sequelae and high mortality rate. Incidence of CSVT diagnosis in the western world has increased despite the reduced occurrence of infections.

**Aim:** To identify risk factors that may explain the predisposition to site specific thrombosis.

**Methods:** Ninety consecutive patients diagnosed with acute CSVT in tertiary hospital. As a control group we used the data extracted from the National Trauma Registry and Healthcare Services.

**Results:** Trauma history up to one month prior to diagnosis of CVST was found in 13 (14%) patients. Six patients had skull fractures, the others had blunt trauma. The overall SMR was 941 ( $p < 0.0001$ ); the separate results for men and women were 1206 and 543, respectively. Infections confined to the head and neck in 7% of the cases and brain tumor were observed in 8%. At the time of CVST, 23 of 50 (46%) women had a hormonal risk factor. The SMR for OC use was 1.63 ( $p = 0.0298$ ). Prothrombotic polymorphisms were detected in 16 of 63 (25.4%) patients who were tested for factor V Leiden and prothrombin G20210A mutation ( $OR = 3.47$ ,  $p = 0.002$ ) in comparison to 49% in DVT patients ( $OR = 9.95$ ,  $p < 0.0001$ ).

**Conclusions:** Assessment for CVST in patients with recent trauma and headache even after intact head CT is required. The other risk factors, such as hormone related and prothrombotic polymorphisms, were not specific just for CVST and the latter play a lesser role in CVST than in DVT.

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## 1. Introduction

Cerebral sinus vein thrombosis (CSVT) is a rare disease with significant neurological sequelae and high mortality rate mainly within the first month [1]. The annual incidence is about 1 to 7 cases per million adults [2] and it usually affects more women than men, in particular women at childbearing age. Incidence of CSVT diagnosis in the western world has increased despite the reduced occurrence of infectious sinus thrombosis related to otitis media and mastoiditis. The increased incidence of CSVT nowadays is attributed to increased awareness of the disease, to innovative and sensitive neuro-imaging techniques and the increased use of third generation oral contraceptives.

The etiology and pathogenesis of CSVT is not always apparent and in 30% of the cases it is defined as cryptogenic CSVT [3] interestingly, the predisposing conditions for CSVT are comparable to those for deep vein thrombosis (DVT) of lower limb and/or pulmonary emboli. In fact, the use of oral contraceptives (OC), pregnancy and puerperium, malignancy, infection, inflammatory bowel disease, surgery and trauma and the presence of thrombophilia are altogether risk factors for both events. Rare cases of CVST include hematological disorders like paroxysmal nocturnal hemoglobinuria, myeloproliferative diseases associated with JAK2 V617F mutation [4]. The recurrence rate of CSVT is 2% to 3% and the majority of the cases occur within the first year after discontinuation of anticoagulants, in comparison to 5% to 7% rate of thrombosis in other sites following CSVT [5].

Up to now, the data regarding risk factors, outcome, and treatment of CSVT in adults is primarily based on an International prospective study with 624 patients who experienced CSVT during the years 1998 to 2001 [6].

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It is not known what determines or affects the site of thrombosis or why the incidence of CVST is highest among young adults. The occurrence of CVST in the postpartum period can be attributed to damage of venous sinuses during labor secondary to fluctuations in intracranial pressure in a hypercoagulable state associated with puerperium [7]. Another cause is the epidural anesthesia used before parturition leading to low fluid pressure with loss of buoyancy and mechanical distortion of the vessel wall [8]. In addition, the loss of CSF reduces the absorption of CSF into cerebral venous sinuses resulting in increased blood viscosity [9,10].

In this work, our goal was to identify risk factors that may explain the predisposition to the site specific thrombosis from a single tertiary medical center. Conceivably identifying risks associated with CVST will allow us to prevent or diagnose it at an early stage, thus ameliorating the prognosis.

## 2. Material and methods

### 2.1. Patients with CSVT

The study included consecutive patients aged 15 and up that were diagnosed with acute CSVT from January 2002 to September 2014 at the Sheba Medical Center, a tertiary referral hospital with highly specialized medical care, either upon admission or during hospitalization. Only patients with confirmed CSVT by one of the imaging modalities e.g., computed tomography venography, magnetic resonance or magnetic resonance venography were recruited. The enrollment of patients was retrospective and was based on the database of the archive of the medical center. All medical charts were thoroughly reviewed with particular attention to potential risk factors attributed to CSVT, location of thrombus and number of sinuses involved and any parenchymal lesions, following a questionnaire created specifically for this study. The Institutional Review Board of the Sheba Medical Center approved the study according to the declaration of Helsinki.

### 2.2. Controls

Data on population frequencies were used in assessing the importance of potential risk factors.

Data on the frequency of major head and neck trauma requiring hospitalization was extracted from the national trauma registry for the years 2012 and 2013.

Data on the frequency of OC use in childbearing age and hormone replacement therapy (HRT) and the frequency of hypertension, diabetes and hyperlipidemia during 2012 and 2013 were retrospectively extracted from Maccabi HealthCare Services, the second largest health care maintenance organization (HMO) in Israel.

Data on the frequency of thrombophilia in Israeli patients with idiopathic DVT were extracted from our previous work [11].

### 2.3. Laboratory tests

The prothrombotic polymorphisms i.e., factor V Leiden and prothrombin G20210A were determined using methods previously described [11].

### 2.4. Statistical analysis

Numerical variables are summarized with averages and standard deviations, or with medians for skewed variables. Categorical variables are summarized by percentages. Standardized morbidity ratios (SMR's) were used to assess trauma, the use of OC or hormonal replacement therapy (HRT), and the presence of hypertension, diabetes mellitus or hypercholesterolemia as risk factors for CVST. The SMR's were computed using age- and sex-specific population rates for these factors. The population data on trauma came from the Israel national

registry; a three-month window was assumed following the instigating event. The population sizes were taken from the web site of the Israel Central Bureau of Statistics. Relations between clinical factors and outcomes were assessed using Wilcoxon tests (for numerical outcomes), chi-squared tests with Yates adjustments (for binary outcomes) and Spearman correlations (when both the clinical factor and the outcome were numerical).

## 3. Results

### 3.1. Patient characteristics

The study included 90 patients with documented CVST and jugular vein thrombosis. The clinical characteristics of the patients are outlined in Table 1.

The predominant sinus involved was the transverse followed by the sigmoid sinus. In 81% of the patients more than one sinus was involved and in 52% of the patients at least 3 sinuses were involved. Jugular vein thrombosis was observed in 42 patients (7 bilateral) in addition to CVST; in another 2 patients it was the only affected site (both unilateral).

Eight patients had venous infarct on the same side of the CVST and in another 2 patients it was present on the opposite side. Thirty-four patients had cerebral hemorrhage but only 4 of those patients had a decompressive craniotomy.

The most common neurological deficit when first admitted was diplopia, which presented in 12 (13%) patients, followed by plegia in 9 (10%) patients. Eighteen (20%) patients were discharged with at least one neurological deficit. Five (6%) patients died and one of these had brain trauma.

In 9 patients (10%) CVST was not the first thrombotic event as shown in Table 1. There were 2 patients who had multiple sclerosis and in one of those patients diagnosis was made after head MRI was carried out as per follow-up after CT venography.

Atherosclerotic risk factors were observed in 29 (32%) patients as shown in Table 1. Seven (8%) patients had all 3 risk factors i.e., hypertension, diabetes and hypercholesterolemia.

### 3.2. Risk factors

Trauma history up to one month prior to diagnosis of CVST was found in 13 (14.4%) patients as shown in Table 1. The median age of the male trauma patients was 30 and of the female patients was 33 years. Six patients had skull fractures, the others had blunt trauma. For eight patients, CSVT was diagnosed the day of the trauma, for 3 patients,

**Table 1**  
Clinical characteristics and risk factors of patients.

Characteristic	Number of cases
Sex and mean age (SD)	50 women 43.2(18.1) 40 men 41.7 (17.6)
Diabetes (%)	11 (12%)
Hypertension (%)	18 (20%)
Hypercholesterolemia (%)	19 (21)
Previous thrombotic events (%)	9 cases, 5-superficial vein thrombosis, 2 DVT, 1-portal vein thrombosis, 1-kidney infarct
Risk factors (%)	Head and neck trauma—14.4% Head and neck infection—7% Systemic infections—7% Intracranial tumor 8% Puerperium, oral contraceptives and hormone replacement therapy—46% Hematological disease: 4.4%
Occluded sinus/vein	Transverse sinus—39 bilateral, 16 unilateral Sigmoid sinus—22 bilateral, 32 unilateral Jugular vein—42 unilateral, 7 bilateral
Venous infarct	10 cases
Cerebral hemorrhage	34 cases

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