# FREQUENCY OF CEREBRAL VENOUS SINUS THROMBOSIS IN PATIENTS PRESENTED WITH HEADACHE AT HIGH ALTITUDE

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## ABSTRACT

***Objective:*** To determine the frequency of cerebral venous sinus thrombosis (CVST) among the patient with headache presenting from high altitude (HA).

***Study Design:*** Cross-sectional study.

***Place and Duration of Study:*** Pak Emirates Military Hospital, Rawalpindi, from 24th Apr 2018 to 24th Jan 2019.

***Methodology:*** The sample population comprised of patients presenting with the headache, living at a height of 3000-8200 meter above sea level. CT-scan brain, MRI brain and MRV brain was performed on all the cases. Carotid Doppler, d-dimers, thrombophillic screen, autoimmune profile, EEG and other relevant investigations were performed of all the cases diagnosed with CVST. Age, altitude, total time spent at HA and acclimatization were correlated with the presence of CVST among the patients of headache at HA.

***Results:*** Out of 60 patients reporting with headache from HA, 9 had presence of CVST on the relevant neuroimaging. Among these cases of CVST 2 had secondary polycythemia, 1 had protein C deficiency and 1 had protein S deficiency. Poor acclimatization had a significant relationship with the presence of CVST when logistic regression was applied.

***Conclusion:*** Cerebral venous sinus thrombosis should be considered a possibility while evaluating the causes of headache among the patients reporting from high altitude. Special attention should be given on acclimatization process for the people who are ascending to high altitude.

**Keywords:** Cerebral venous sinus thrombosis, High altitude, Headache, Risk factors.



## INTRODUCTION

Cerebral venous sinus thrombosis is a rare but life threatening condition with incidence of around 3-4 cases per million[1]. Environment at high altitude affects all the biological functions of the body[2-4]. Decreased atmospheric pressure and low oxygen tension at high altitude causes many changes in normal physiology of the body affecting almost all the organ systems. The saturation of oxy hemoglobin begins to fall at 7000 feet above the sea level[5]. Prolong exposure to low tension oxygen due to stay at high altitude can give rise to multiple health issues including diabetes, heart problems and hypertension[6]. Normal physiology of blood can also be altered in order to adjust at this unusual and harsh environment[7]. Polycythemia and hypercoagul-able states can also occur as a result of this giving rise to the problems like cerebral venous sinus thrombosis[8,9].

Shrestha *et al*. reported a case in 2012 in which a 47 year old male who presented with headache and speech difficulties was ultimately diagnosed as a case of cerebral venous throm-bosis[10]. A meta-analysis comprised of 13 studies was only able to include 17 patients due to rare nature of this phenomenon. Hypercoagul-able state was found among 9 of these 17 patients[11].

A recent case was reported from India in which the patient died of high altitude cerebral edema (HACE) and on autopsy cerebral venous sinus was found thrombosed[12]. Another case was reported from Nepal where patient presented with long duration continuous headache. Symptoms of phtophobia and speech difficulties along with weakness of the right upper limb were

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also present. Superior sagital sinus was found thrombosed on his MRV[13].

Headache has been a frequently reported symptom at high altitude which is usually benign and settles with routine medication. But in some cases it can be an early sign of a dangerous underlying pathology including high altitude cerebral edema and stroke[14,15]. Cerebral venous sinus thrombosis can also present as various physical and neurological symptoms including the headache[16]. Therefore all the headaches at unusual environment like HA should be dealt cautiously by the physician.

Mountaineering and tourism engage a lot of people to work and stay at high altitude. Armed forces of various countries including ours are also protecting their motherland at these high fronts. Though various studies have been done on physiological and psychological aspects of our population at HA[2-4] but limited work has so far been undertaken in our country on patients reporting with headache from high altitude to look for frequency of CVST in them. This study was aimed to investigate this rare and unique phenomenon.

## PATIENTS AND METHODS

After ethical approval from concerned ethical review committee and written consent from all potential participants this cross-sectional study was planned from 24th April 2018 to 24th January 2019. Sample size was calculated by using the WHO calculator and Non probability Consecutive sampling technique was used to collect the sample population. All subjects were male and between the age of 19 and 50 years living at a high altitude (3000 meter above sea level or more). Subjects with the history of trauma, any neurological problem at sea level or family history of CVST or those who were unable to understand/complete the required questionnaire were excluded. Subjects with any co-morbid illness (DM, HTN, IHD, RA, CVA, space occupying lesion Brain, CVST, inflammatory disease of brain etc) were also excluded from the study. After the application of inclusion and exclusion criteria, 60 subjects were included in the analysis.

The consenting subjects were provided with a detailed description of the study. Confounding variables were taken care of by detailed history taking about any current or previous physical or neurological illness and any current or previous evidence of significant head trauma. Those subjects with confounding variables were excluded from the study. Patients who fulfilled inclusion criteria underwent CT-scan, MRI and MRV of brain to detect the presence of cerebral venous sinus thrombosis. Those who showed the presence of CVST underwent further investigations including the carotid doppler, d-dimers, thrombophillic screen, autoimmune profile, EEG and other relevant investigations. The risk factors which were to be related with the presence of CVST and socio demographic data of the full sample of subjects participating in the research was entered in a structured performa; keeping in mind the wish of some subjects for anonymity only initials of their names were kept as record.

Descriptive statistics were used to describe the risk factors and the frequency of CVST. Samples were identified under the categories of presence and absence of CVST. Variables in the study included Age, altitude, time spent at HA and acclimatization. Binary logistic regression analysis was done to evaluate factors related to the presence of CVST. Statistics Package for Social Sciences version 21.0 was used to carry out all the statistical analysis. The $p$-value ≤0.05 were considered as significant.

## RESULTS

A total of 70 patients reported with complaint of headache from high altitude. Out of these 2 had history of trauma, 1 was already diagnosed as a case of CVST, 2 had DM, 2 had HTN and 3 refused to participate in the study. Sixty patients were included in the final analysis which underwent the relevant neuroimaging. Nine out of them were labeled as cases of CVST on the basis of findings on the neuroimaging. Two had secondary polycythemia, 1 had protein

C and 1 had protein S deficiency. No cause was found on investigations of the remaining 5 patients (table-I). Binary logistic regression analysis showed that poor acclimatization had significant association with the presence of CVST while other variables like age, total stay at HA and height of the stay had no significant association in our analysis (table-II).

**Table-I: General characteristics of the study participants.**

| Socio demographic factors | Patients with CVST N(%) | Patients without CVST N(%) |
|---|---|---|
| Total | 09 (15) | 51 (85) |
| **Age** | | |
| <35 | 08 (88.9) | 41 (80.4%) |
| 35 or more | 01 (11.1) | 10 (19.6%) |
| **Acclimatization** | | |
| No | 02 (22.2%) | 25 (68.6%) |
| Yes | 07 (77.8%) | 16 (31.4% |
| **Total stay at HA** | | |
| <2 weeks | 08 (88.9) | 38 (74.5) |
| 2 weeks or more | 01 (11.1) | 13 (25.5) |
| **Altitude at which staying** | | |
| 3000-6000meters | 06 (66.7) | 43 (84.3) |
| >6000 meters | 03 (33.3) | 08 (15.7) |
| **Causes of CVST in diagnosed cases** | Protein C deficiency | 01 |
| | Protein S deficiency | 01 |
| | Secondary polycythemia | 02 |
| | Cryptogenic | 05 |

**Table-II: The correlated factors relating to the presence of cerebral venous sinus thrombosis among the patients of headache at HA: The binary logistic regression.**

| | B | *p*-value | Odds ratio | Confidence interval | |
|---|---|---|---|---|---|
| | | | | lower | upper |
| Age (ref. is >35 years) | 0.585 | 0.624 | 1.794 | 0.173 | 18.635 |
| Acclimatization (ref. is good acclimatization prior to ascent) | 1.870 | 0.034 | 6.489 | 1.151 | 36.587 |
| Total stay at HA (ref. is <2 weeks) | -0.955 | 0.428 | 0.385 | 0.036 | 4.074 |
| Altitude (ref. is 3000-6000 meters) | 0.656 | 0.467 | 1.928 | 0.328 | 11.314 |

## DISCUSSION

To our knowledge this is the first ever study of its kind in our setup on individuals at high altitude exposed to a unique environment, which is challenging, difficult and stressful. The study was an attempt to record the prevalence of cerebral venous sinus thrombosis among the patients suffering from headache at the high altitude. Exposure of individuals to high altitude brings about a lot of changes in the physiology of body which predispose the individuals towards various health issues. CVST is one of the rare but serious complications which can occur at HA[5,8]. A review published by Gambhir *et al*. concluded that both arterial and venous thrombosis can occur at HA and is often difficult to diagnose[17]. Only 9 out of 60 patients with headache at HA included in our analysis showed the presence of CVST. Previously this phenomenon has been reported with same rare incidence[11].

Two of our patients of CVST suffered from secondary polycythemia. This cause of CVST has been reported in the past too among the patients at high altitude[18,19]. Hypoxia is a common condition encountered at HA which stimulated the juxtaglomerular cells of kidney

to increase the production of erythropoietin. Increased production of erythropoietin leads to polycythemia which is an independent risk factor for the thrombosis.

Thrombophiillia have been reported among the cases of CVST in the past[20]. Similar findings were reported among the patients of CVST at high altitude as well[11]. One of our patients had protein C and one had protein S deficiency. Protein C and S serve as natural anticoagulant in the blood and prevents the phenomenon of clotting. Their deficiency prone the individual towards thrombotic phenomenon in any site of the body including the venous sinuses of brain.

Acclimatization is the process by which human body slowly adapts to the unusual environment. It is key process in avoiding all the hazards of high altitude[21]. Our study reported that lack of acclimatization was associated with the presence of CVST. Past literature highlights similar phenomenon that proper acclimatization prevents the drastic changes in blood physiology and can be helpful in prevention of disorders related to change in the blood physiology[22].

The major limitation of our study is that the findings cannot be generalized as our study population was not selected from a randomized sample of all the people at HA at various peaks. We suggest further studies on a broader base and a more representative sample size on the subject in order to look for the causes and risk factors for this potentially life threatening disease.

## CONCLUSION

Cerebral venous sinus thrombosis should be considered a possibility while evaluating the causes of headache among the patients reporting from high altitude. Special attention should be given on acclimatization process for the people who are ascending to high altitude.

## CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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