

Frequency of Cerebral Venous Thrombosis in Dubai, UAE—A Multicenter, Retrospective Study

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Abstract

Background and Purpose: Cerebral venous thrombosis (CVT), also known as cerebral dural venous thrombosis, is not a very common cause of stroke. It has a diverse clinical presentation, with multiple predisposing factors and imaging findings. The incidence of CVT varies in different studies. We hypothesized that the incidence of CVT in Dubai is more than that reported in the West owing to dehydration caused by the high atmospheric temperature.

Methods: We retrospectively reviewed the medical records of all patients aged more than 13 years with appropriate International Classification of Diseases, 9th Revision, codes for the diagnosis of CVT from January 1, 2010 to December 31, 2018 from three major hospitals with an acute stroke service in Dubai, United Arab Emirates.

Results: We identified 138 patients who presented with CVT. The average frequency of CVT was 6.6 per 100,000 population. Fifty percent of the patients presented between May and September, which are considered the hottest months in the UAE. Headache was the most common presentation, followed by seizures. The most important risk factors were the use of oral contraceptive pills, anemia, and polycythemia. Our study showed a higher incidence of anemia, polycythemia, thrombophilia, and abnormal CT brain findings.

Conclusion: In our study, CVT was more common during the months of summer. Anemia and polycythemia were strongly associated with CVT. Public awareness about CVT, its higher incidence during summer months and strategies to avoid dehydration might be considered to reduce the incidence of CVT in summer months. However, larger studies are needed to confirm definite associations.

Keywords

Cerebral venous sinus thrombosis, Imaging & radiology, Seasonal, variation, Thrombophilia

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Introduction

Cerebral venous thrombosis (CVT) is an uncommon cause of cerebral infarction. Venous thrombosis can affect all veins in the body, including the cerebral veins. CVT is a causative mechanism of stroke, particularly in the young and is associated with high mortality rates if left untreated. No population studies have reported the incidence of CVT, while hospital-based studies have reported incidence rates varying from 0.2 to 15.7 per million in various populations, with a higher incidence in women.^{1–12} CVT is reported to be responsible for 3% of all stroke cases and 5% of all intracerebral hemorrhages in the young.³ The clinical presentation varies widely according to the site of thrombosed vein and its area of drainage.¹ The reported incidence varies across countries.

The established risk factors for CVT include infections of the ear, mastoid and paranasal sinuses, intracranial tumors, pregnancy, puerperium, systemic diseases such as malignancies, dyscollagenosis, coagulopathies, oral contraceptive use, and dehydration.⁵ We examined the clinical presentation, risk factors, and etiology of CVT. We also tested the hypothesis that owing to the high atmospheric temperature, the incidence of CVT in Dubai will be much more common than that reported in the West.

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Methods

Standard Protocol Approvals and Registration

The study was approved by the Dubai Scientific Research Ethics Committee (DSREC) and institutional ethics committee. Patient consent was not deemed necessary since it was a retrospective study

Patients

We collected the medical records of all patients admitted with a diagnosis of CVT from January 1, 2010 to December 31, 2018 from three major hospitals with an acute stroke service in Dubai, United Arab Emirates. We reviewed anonymized patient data from the medical records of all patients aged more than 13 years. The inclusion criteria was as per International Classification of Diseases, 9th Revision, codes for the diagnosis of CVT (codes 437.6, 325, 671.5, and 437.8). Only cases with confirmed venous sinus occlusion on CT venograms or MR venograms were included. We examined the time of clinical presentation, clinical features, and risk factors.

Statistical Analysis

IBM SPSS version 21 was used for data analysis. Mean and standard deviation were reported for continuous variables, and frequency was reported for categorical variables. Independent-sample t-tests were used to compare continuous variables, and the chi-square test of independence was used for comparison of proportions for categorical variables. $P < 0.05$ was considered significant. Parameters which were found to be significant risk factors, were separately analyzed for difference in incidence during summer and winter months using chi-square analysis

Results

Demographic Characteristics

The average adult population of Dubai from January 2010 to December 2018 was 2070274, with an average male: female ratio of 2.5:1 population as per the census data from the office of Dubai statistics center, Government of Dubai (Figure 1).¹³ We identified 138 patients who presented with CVT. The average frequency of CVT was 6.6 per 100,000. The mean age at onset was 37.5 years (SD 11.3 years). The majority of the patients were male, accounting for 53.6% ($n = 74$) of the total cases. The majority of the patients were of Asian descent, accounting for 92% of the total number of cases ($n = 127$). The remaining patients were of African (5.1%, $n = 7$) and European or American descent (2.9%, $n = 4$) (Table 1).

The median duration of symptoms before presentation was 3 days. Most patients were diagnosed on the same day of

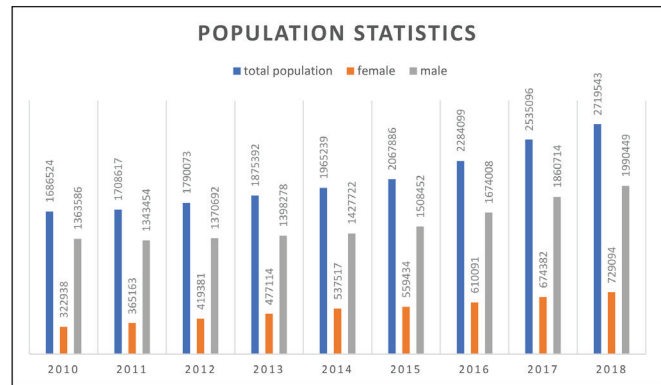


Figure 1. Population statistics for Dubai (2010–2018).

Table 1. Distribution of Nationalities Across the Population of Dubai

Nationality	Number (%)	Male (%)	Female (%)
South Asia (India, Pakistan, Bangladesh)	76 (55.1)	58 (42)	18 (13)
Middle East	27 (18.1)	10 (7.2)	17 (12.3)
Far East Asia	24 (17.4)	2 (1.4)	22 (15.9)
Africa	7 (5.1)	4 (2.8)	3 (2.2)
Others	4 (2.9)	2 (1.4)	2 (1.4)

presentation (median time to diagnosis was 6 hours.). Based on the average monthly temperatures across the UAE, May to September are the hottest months,¹⁴ and about 50% of the patients presented during this time. The highest number of cases was seen in May and June (Fig. 2).

Clinical Findings and Risk Factors

Headache was the most common clinical presentation ($n = 96$; 69.6%). Fifty-six patients reported associated vomiting (40.6%). Isolated headache with or without papilledema (idiopathic intracranial hypertension-like presentation) was seen in 30% ($n = 40$) of the patients. Seizures was the next most common clinical feature ($n = 66$, 47.8%). Altered sensorium was noted in 39.1% of the patients ($n = 54$). Thirty-five patients (25.4%) presented with focal neurological deficits. (Table 2)

Table 3 illustrates the associated predisposing factors identified

Lab Testing

Anemia was detected in 37 patients (28.9%; range, 5.4–11.4 mg/dL), while polycythemia was noted in 33 patients (25.8%; range, 18–22 mg/dL). Anemia was significantly more common in women (53.4%, $p < 0.001$). The majority of

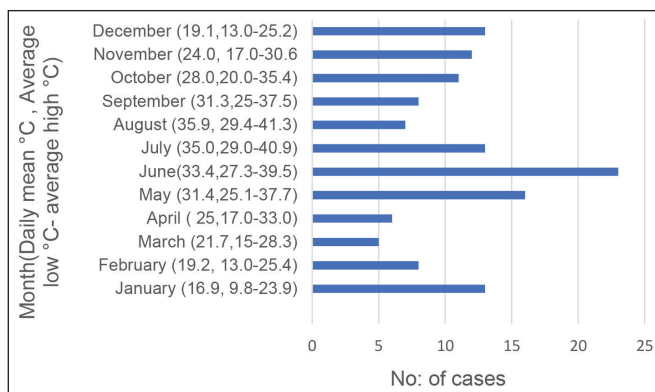


Figure 2. Distribution of the Number of Cases of CVT Throughout the Year (X-axis); The Daily Mean, Average Low and High Temperatures Across Various Months in the City of Dubai.

Table 2. Presenting Symptoms in Patients Diagnosed with CVT

Clinical Feature	Number (%)
Headache	96 (69.6)
Seizures	66 (47.8)
Vomiting	56 (40.6)
Alteration of consciousness	54 (39.1)
Focal neurological deficit	35 (25.4)
Visual blurring	12 (8.7)
Ophthalmoplegia	7 (5.1)
Meningismus	2 (1.4)

Table 3. Distribution of Risk Factors for the Occurrence of CVT

Risk Factor	Number (%)
OCP usage (out of 64 females)	27 (42.2%)
History of dehydration	13 (9.4%)
Nephrotic syndrome	2 (1.4%)
Prothrombotic state	2 (1.4%)
Otogenic infection	4 (2.9%)
Meningitis	3 (2.2%)
Head trauma	2 (1.4%)
Pregnancy	2 (1.4%)
Malignancy	1 (0.7%)

Abbreviation: OCP, oral contraceptive pill

patients had iron-deficiency anemia, while a minority had thalassemia. Three patients had severe anemia (Hb < 7 mg/dL) requiring blood transfusion. One patient had sickle cell anemia and underwent an exchange transfusion. Polycythemia was predominantly seen in men (44.3%, $p < 0.001$). Smoking was the major reason for polycythemia (88%), and nine patients tested negative for the JAK mutation. Two patients

underwent venesection during the hospital stay. An elevated WBC count was noted in 76 patients (55.1%). A low platelet count was noted in 14 patients (10.4%). One patient had idiopathic thrombocytopenic purpura and had a platelet count of 58,000/cmm at presentation. The rest of the patients had low platelet counts in the range of 90,000/cmm to 140,000/cmm, which improved to normal levels within a few days. High platelet counts > 410,000/cmm were seen in 17 (12.6%) patients, whose platelet counts ranged between 410,000/cmm and 620,000/cmm. All patients with a high platelet count also had iron-deficiency anemia. D-dimer was tested at presentation in only 58 patients, of whom 47 (81%) had elevated values. Vasculitic work up including ANA, anti-ds DNA and procoagulant workup, including the antiphospholipid antibody profile (APLA; anti-cardiolipin, lupus anticoagulant, and anti-phosphatidylserine) homocysteine, Factor 5 Leiden mutation, protein C, and protein S deficiency were noted in 69 (50%) cases (Table 4).

Since anemia and polycythemia were found to be significantly high in patients with CVT, their incidence in summer (April to September) and winter months (October–March) were analyzed separately. However there was no statistically significant difference between the incidence in summer and winter months.

Radiology

All patients had a diagnosis confirmed by vessel imaging (either CT venogram, MR venogram, or both). All patients underwent a plain CT scan at presentation. The brain CT scan at presentation showed diffuse cerebral edema in 11.6% ($n = 16$) of the patients, while three patients showed signs of herniation at presentation. Two patients developed herniation within a day of presentation despite the initiation of anticoagulation therapy. Focal hypodensity was observed in 15.2% ($n = 21$) of the patients, mostly in the parietal region, followed by the frontal and occipital cortices. Intracerebral hemorrhages occurred in 42% of the cases ($n = 58$). A hyperdense sinus on a plain CT scan was seen in 52.2% ($n = 72$) of the patients. Thrombosis of multiple sinuses was noted in 103/138 (95%) cases. The superior sagittal sinus was the most commonly affected sinus either in isolation or with thrombosis of other sinuses (68.1%, $n = 94$), followed by transverse and sigmoid sinuses. Isolated superficial vein thrombosis was seen in three patients (Vein of Trolard in 2 and vein of Labbe in 1). Seven patients had superficial vein thrombosis with extension into the superior sagittal plane of the lateral sinuses (Table 6)

Treatment

Anticoagulation with heparin/Low molecular weight heparin (LMWH) was started immediately after presentation in majority of the patients. Patients who presented with signs of

Table 4. Laboratory Findings in Patients with CVT

Lab Parameter	Tested In	Abnormal No (%)
Hematocrit (available for 128 cases)	128	Normal 36–46 (N = 58)–(45.3%) Low <36 N = 37 (28.9%) High >46 (N = 33)–(25.8%)
WBC count (available for 136 cases)	136	Elevated in 76 (55.1%)
Platelets (available for 135 cases)	135	Normal 150–410 N = 104–(77%) Low <150 N = 14–(10.4%) High >410 N = 17(12.6%)
D-Dimer elevated (>0.5)	58	47 (81%)
ANA positive	88	16 (18.2%)
Anti-ds-DNA positive	80	4 (0.05%)
APLA positive	18	0
Anticardiolipin positive	100	2 (2.0%)
Lupus anticoagulant positive	88	4 (4.5%)
Beta-2 glycoprotein positive	84	5 (5.9%)
Homocysteine positive	44	4 (9.1%)
Factor V Leiden mutation positive	83	2 (2.4%)
Protein C positive	119	17 (14.3%)
Protein S positive	119	28 (23.5%)

Abbreviations: WBC, white blood cell; ANA, antinuclear antibody; APLA, anti-phospholipid antibody.

Table 5. Comparison of Parameters Between Summer and Winter Months

	Summer	winter	P Value
Anemia	22	15	0.36
Polycythemia	19	14	0.83

Table 6. Incidence of Radiological Findings in Patients with CVT

Radiological finding	Number (%)
Cerebral edema	16 (11.6)
Hyperdense sinus on plain CT	72 (52.2)
Hemorrhage	58 (42)
Focal hypodensity	21 (15.2)
Delta sign on CT	5 (3.6)
Herniation	3 (2.1)
CTV findings	
SSS	94 (68.1)
TS	82 (59.4)
Sigmoid sinus	67 (48.6)
Straight sinus	20 (14.4)
Confluence	11 (8)
ISS	2 (1.4)
Deep veins	6 (4.3)
Superficial veins	10 (7.2)

Abbreviations: CTV, CT venogram; SSS, superior sagittal sinus; ISS, inferior sagittal sinus; TS, transverse sinus.

herniation underwent decompressive hemicraniectomy and were initiated on heparin 24 h after obtaining neurosurgical clearance. Five patients (3.6%) underwent decompressive hemicraniectomy. LMWH was initiated in 91.7% (n = 121) of the patients, while the rest were started on unfractionated heparin. Anticoagulation was started in patients with a septic etiology, since the clinical symptoms worsened despite antibiotics, and imaging showed worsening of cerebral edema. They responded well after initiation of anticoagulation therapy. All patients received normal saline for hydration in the initial two days of admission. All patients received analgesics for headache relief. Patients with a history of seizures were started on antiepileptic medications. Prophylactic antiepileptic medications were started only in patients undergoing decompressive hemicraniectomy. In a few patients (n = 8) with severe headache and papilledema, a short course of diuretics (acetazolamide) and steroids (dexamethasone) was administered, which provided symptomatic improvement. Follow-up CT venograms at 3 months were available for 18 patients. Twelve showed complete recanalization, while four showed partial recanalization.

Discussion

In this analytical cross-sectional study, we found a CVT frequency of 6.6 per 100 000 person-years. Several studies have reported an incidence between 2 and 15 per million person years.^{1–12} Population-based studies have shown higher

incidences of 13–15 per million person years,^{3,4} while studies similar to ours, which included cases referred to tertiary care centers, showed a lower incidence similar to ours.^{6,12} Although our series included more male patients (male:female ratio of 1:1.15), the overall frequency was still higher in females since the gender ratio in the city of Dubai was 2.5:1. Thus, consistent with previous studies, the incidence was higher in women. Three studies have assessed the differences in the frequencies of CVT in various seasons. Ferro et al.¹⁵ assessed a cohort of 91 Portuguese patients from 20 hospitals and found a unimodal distribution with the highest number of CVT cases during October. The lowest numbers were registered during the spring and summer. The number of cases of CVT during autumn and winter was significantly higher than those in the other two seasons. Stolz et al.¹⁶ assessed a German cohort of 137 consecutive CVT patients and found a bimodal distribution with the highest number of new CVT cases during the summer (June, July, and August) and winter (December, January, and February) months in comparison with that during the spring and autumn months. Janghorbani et al., in their study from Iran, noted a higher incidence of CVT in the autumn months.⁴ Dubai is part of the Arabian Desert and hence has only summer and winter months. We found a higher incidence of CVT in the summer months (May and June). In Dubai, the school summer vacation is in the months of July and August and hence most of the expatriate population travels back to their home countries during these months. Probably this is the reason for reduced incidence noted during these months, despite having higher temperatures during these months. Public awareness about CVT, its higher incidence during summer months and strategies to avoid dehydration would help reduce incidence of CVT in summer months.

Headache was the most common clinical presentation in our study, with an isolated headache with or without papilledema (idiopathic intracranial hypertension-like presentation) observed in 30% of the cases. A previous study by Ameri et al. reported that 40% of patients with CVT present with isolated intracranial hypertension.¹⁷ In another series by Crassard et al., 25% of patients with CVT presented with isolated headache, and another 25% presented with headache in conjunction with papilledema or sixth nerve palsies suggestive of idiopathic intracranial hypertension.^{18,19} Our data show a comparable frequency of cases presenting with headache alone without seizures or focal limb weakness. Focal or generalized seizures have been reported in 40% of patients.¹¹ Our study showed a similar frequency, with 48% of the patients showing seizures at presentation. A previous study showed that the median delay from onset of symptoms to hospital admission was 4 days, and that from symptom onset to diagnosis was 7 days.¹⁰ Our study showed a similar rate, wherein the mean duration of symptoms before presentation was 5.23 days (SD = 7.5). However, most patients were diagnosed on the same day of the presentation, with a mean time to diagnosis of 0.4 days (SD = 1.5). Early diagnosis is probably because of the radiological policy of obtaining a CT venogram in all patients with a new-onset

headache with raised intracranial pressure features, seizures, or focal neurological deficits in the emergency room itself.^{17,18} Oral contraceptive pill intake was the most common risk factor for CVT in females (42.2%). Two meta-analyses reported an increased risk of CVT in oral contraceptive users.^{20,21} A population-based study from Australia reported that 31% of women with CVT had a history of oral contraceptive pill intake,⁴ which is similar to our study. The high incidence of CVT in women taking contraceptive pills warrants alerting the gynecologists of the risk so as to opt for alternative methods for patients who require long term anticoagulation. In addition, they reported that 5% of the CVT cases in women occurred during pregnancy or puerperium. A study from Mexico reported that 50% of CVT cases occurred during pregnancy or puerperium, mostly in the third trimester or during puerperium.²² In our study, pregnancy-related CVT was encountered in only 3.1% of the CVT cases in females, which is more consistent with the study from Australia. A history of dehydration was recorded in 9.4% of patients, which has not been reported in previous studies. Outdoor work without adequate fluid intake was common in male patients presenting with CVT. Nevertheless, our numbers are small to conclude as to whether it is a risk factor or whether it only increases the risk in patients with prothrombotic states. Stam et al. reported that meningeal and parameningeal infections are responsible for 8.2% of CVT cases in their series.¹ This was almost similar to our study, with infection responsible for 5.1% of all cases of CVT. Anemia and thrombocytopenia have been previously reported as risk factors for CVT.¹¹ The overall incidence of hematological risk factors, including anemia, polycythemia, and thrombocytopenia, was reported to be 12%. However, our study showed a high incidence of anemia (29%) and polycythemia (33%). Anemia was significantly more common in women, while polycythemia was more common in men. Iron-deficiency anemia was the most common, with a few patients showing thalassemia and sickle cell anemia. However, the number of subtypes was limited to draw any conclusions. Since anemia and polycythemia were found to be significantly high in our patients, their incidence in summer (April to September) and winter months (October–March) were analyzed separately. However there was no statistically significant difference between the incidence in summer and winter months.

Prothrombotic conditions were noted in 34.1% of the patients in previous studies.¹¹ Our study showed a higher incidence of thrombophilia (50%) in our cases. Testing for D-dimer showed positivity in 81% of the tested cases (47/58), indicating a lower sensitivity than previous studies, which showed a sensitivity of 97.1% and a positive predictive value of 55.7%.^{23,24} Unlike previous studies that reported parenchymal abnormalities in up to 30% of the cases on plain CT,^{2,11,25} our study showed CT scan abnormalities in 69% of the cases. Hyperdense sinuses were noted in 52% of the cases. However, because almost all cases underwent CT venography with the CT scan as per the emergency neurology protocol, this could be an observer bias and cannot be concluded.

Similar to previous studies, superior sagittal thrombosis was the most commonly thrombosed dural sinus, followed by the transverse and sigmoid sinuses. Most cases showed thrombosis at multiple locations (95%), which were higher than those in previous reports.⁴ Very few patients (3.6%) required surgical decompression for elevated ICP. The rest of the patients showed good recovery with anticoagulation and did not encounter any mortality.

Our study had some limitations. We studied the CVT cases in only three major hospitals, and hence the rate could be underestimated since we would have missed patients who sought care outside these hospitals. Population mobility could have resulted in inadequate capture of all cases of CVT. Ours was a retrospective study and hence cannot be an accurate epidemiological study for determination of frequency

Conclusion

In our study, CVT was more common during the months of summer. Anemia and polycythemia were strongly associated with CVT. Public awareness about CVT, its higher incidence during summer months and strategies to avoid dehydration might be considered to reduce the incidence of CVT in summer months. However, larger studies are needed to confirm definite associations.

Authors' Contribution

PS contributed to study concept and design, data acquisition, data analysis, and interpretation, and performed the statistical analysis. SF contributed to data acquisition and critical revision of the manuscript for intellectual content. MJ contributed to data acquisition, analysis, and interpretation of the data. JD contributed to data acquisition, analysis, and interpretation of the data. SA contributed to data acquisition, and JI provided scientific guidance and supervision.

Statement of Ethics

Ethical approval for this study was obtained from the Dubai Scientific Research Approval Committee (DSRAC) with approval DSREC-05/2016_10 on February 15, 2017.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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