Cerebral venous thrombosis in Saudi Arabia

Clinical variables, response to treatment, and outcome

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ABSTRACT

الأهداف: استقصاء الأعراض الإكلينيكية للتجلط الوريدي الدماغي (CVT) و التعرف على عوامل و مدى استجابة المرضى للعلاج.

الطريقة: أجريت دراسة استطلاعية من خلال قاعدة البيانات للجلطات الحادة في مدينة الملك فهد الطبية خلال الفترة ما بين أبريل من عام 2005 و فبراير 2008 و أظهرت 22 مصاب بالتجلط الوريدي الدماغي (CVT). تم إجراء تحاليل التخثر المفرط للدم و الأشعة الدماغية.

النتائج: تكونت عينة الدراسة من 16 مريض من الإناث (72.7%)، و كان متوسط العمر 35 سنة. شملت الأعراض الإكلينيكية ما يلي: الصداع (77.3%)، تشنجات (54.5%)، علامات عصبية بؤرية في (54.4%) من أفراد العينة، انخفاض مستوى الوعي في (50%). أكثر من ثلثي عينة الدراسة (n=11; 69%) من الإناث سبق وأن استخدمن حبوب منع الحمل، حيث كان هذا العامل هو الأكثر شيوعا من عوامل الخطر. كما أظهرت النتائج نقص بروتين س (n=3)، متلازمة ضد الفسفورية الشحميه المرافقة لمرض الذئبة الحمراء (n=1) (SLE)، الإصابات الفطرية في الأنف (n=1)، لوكيميا (n=1)، الورم الليمفاوي الغير هودجكن (n=1)، تسمم الدم (n=1)، غير معروف (n=6). وقد أشارت النتائج إلى أن أكثر المناطق المتضررة هي الجيب السهمي العلوي (n=13)، الجيب المعترض (n=16)، الجيب السهمي (n=14)، المستقيم (n=6)، والجيب الكهفي الغائر (n=1)، الوريد المخي الغائر (n=2)، شريان جالين المخي (n=3)، الأوردة المخية (n=10)، الوريد الوداجي الباطن (n=12). كما أظهرت الدراسة إصابة 2 من المرضى بالشلل الجزئي الرباعي وتوفي 2 آخرين. بينما أشارت إلى تحسن حالة بقية أفراد العينة (18 فرد أي ما يعادل 81.8%) لتلقيهم جرعات الهيبارين المسيلة للدم. و قد تبين أن استجابة المرضى للعلاج كان أقل فعالية في المرضى الذين كان لديهم نزيف داخل الدماغ أو تجلط وريدي أو تجلط في الأوردة العميقة أو أورام خبيثة.

خاتمة: أن الأعراض الإكلينيكية لهذه الفئة من المرضى مماثلة لتلك التي نشرت في دراسات سابقة، و لكن كانت أعراض تغير في الوعي و التشنجات أكثر شيوعا في هذه العينة. كما أن ارتباط الوريد الدماغي كان أكثر شيوعا في هذه الفئة من المرضى. استخدام موانع الحمل للإناث من عوامل الخطر الرئيسية. كانت استجابة المرضى للعلاج جيدة في 81.8% من المرضى.

Objective: To investigate cerebral venous thrombosis (CVT) clinical presentations, risk factors, and response to treatment in Saudi Arabia.

Methods: Retrospective analysis of the King Fahad Medical City, Riyadh, acute stroke database from April 2005 through February 2008 revealed 22 patients with CVT. Hypercoagulable work-up and neuroimaging were performed.

Results: Sixteen patients were female (72.7%), and the median age was 35 years. Clinical presentations included: headache (77.3%), seizures (54.5%), focal neurological signs (54.5%), and decreased level of consciousness (50%). Over two-thirds (n=11; 69%) of female patients had a history of oral contraceptive use, which was the most common risk factor. Protein S deficiency (n=3), antiphospholipid antibody syndrome secondary to systemic lupus erythematosus (SLE) (n=1), rhinocerebral mucormycosis (n=1), leukemia (n=1), non-Hodgkin's lymphoma (n=1), sepsis (n=1), and unknown (n=6) were causes. Affected areas included superior sagittal (n=13), transverse (n=16), sigmoid (n=14), straight (n=6), and cavernous sinus (n=1); internal cerebral vein (n=2); vein of Galen (n=3); cortical veins (n=10); and internal jugular vein (n=12). Two patients had quadriparesis, and 2 patients died. The remainder (n=18, 81.8%) improved. Bilateral hemorrhagic presentation or venous infarction, deep venous system thrombosis, and underlying malignancy had less favorable results.

Conclusions: Presentations in our series were similar to those in other reports, although altered consciousness and seizures were more common. Cortical vein involvement was also higher than commonly reported. Oral contraceptive use was a primary risk factor in female patients. Outcomes were favorable in 81.8% of patients.

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Cerebral venous thrombosis (CVT) is a unique and uncommon condition that usually affects young adults and children.[1] Precipitating causes are many, and additional risk factors are emerging as are reports of its occurrence. Recent reports indicate that CVT is more common than previously assumed, although it is still estimated to affect no more than 5 per million population.[2] Varied, nonspecific presentation often delays diagnosis, although enhanced technologies such as CT, MRI, and magnetic resonance angiography (MRA) now allow non-invasive emergency diagnosis, which has contributed to reducing associated mortality from between 30-50% to between 5-10%.[3,4] A single publication in 1995 of a series of 40 patients seen over 9 years in 2 hospitals in Riyadh, Saudi Arabia, comprises the literature on CVT in the Arabian peninsula.[5] Accordingly, we believed a more current review of the presentation, associated risk factors, and treatment status of CVT in a tertiary care hospital in the same catchment area was warranted.

Methods. A retrospective review of the King Fahad Medical City in Riyadh (KFMC) acute stroke database from April 2005 through February 2008 revealed 22 patients with CVT. Twenty patients (90.9%) were admitted to the acute stroke unit, and 2 were seen on consultation for new neurological symptoms. Patient files were collected, and data were abstracted anonymously for this review, which was given "exempt" status by the KFMC Institutional Review Board not requiring consent from the patients. Due to the lack of established diagnostic criteria, the diagnosis of CVT was made based on clinical presentation of headache, seizures, focal neurological signs, decreased level of consciousness, and was corroborated by imaging modalities: CT, MRI, and venography (MRI/V) including the following sequences: T1, T2, FLAIR images, SE, DWI, ADC map, T2* gradient echo, FRFSF T2, Angio vein SPGR, 3 DTOF, T1 memp GD, MRA, and MRV using a 1.5 tesla GE sigma machine. Four-vessel cerebral angiogram, and CT angiogram/venogram were carried out in selected patients. Four patients who were unable to tolerate MRI/V initially due to their general condition had CT venogram, with MRI/V performed later when possible. Other patients with concomitant diseases underwent additional imaging including carotid Doppler, transthoracic echocardiography (TTE), and transesophageal echocardiography (TEE). All patients had a complete blood count, coagulation profile, and blood biochemistry performed. Twenty patients had hypercoagulable workup that included protein C, protein S, antithrombin III, factor V Leiden, homocysteine, prothrombin gene mutation, anticardiolipin antibodies, antinuclear antibodies, and double stranded DNA. Erythrocyte sedimentation rate, rheumatoid factor, C3, and C4 were performed per discretion of the attending physician. Selected patients presenting with papilledema or in febrile condition had CSF examination. We recorded the following information: demographic data, date of symptom onset, date of admission, symptoms and signs from clinical onset to diagnosis of CVT, concomitant diseases, laboratory results, imaging methods used, presence of possible CVT risk factors, location of the thrombus and number of sinuses/veins occluded, treatment modalities used, outcome, length of hospital stay, duration of anticoagulant use, and follow up. Information was collected also in regards to OC use, their type, content, name, and duration of use.

All patient data were collected in a database and analyzed with standard software (Excel, Microsoft).

Results. Of 22 patients, 16 (72.7%) were female (**Figure 1**), with a median age of 35 (interquartile range: 29-45) and mean age of 38.3 ± 16.3 (range 15-81) years. Presenting symptoms that occurred in at least half of the patients included headache, seizure, focal neurological signs, and altered consciousness (**Table 1**). Fifteen patients (68.2%) had focal deficits and/or seizures. Headache was the earliest symptom in 14 (63.6%) patients. Other presenting signs and symptoms included weakness in at least half of the patients (n=12; 54.5%), vomiting/nausea, and vision deficits with papilledema. Isolated intracranial hypertension with headache mimicking idiopathic intracranial hypertension was seen in 8 patients (36.3%). Unusual clinical manifestations were seen in 2 patients: simulating an acute ischemic attack in one; and the other with the classical thunderclap headache of subarachnoid hemorrhage. All patients

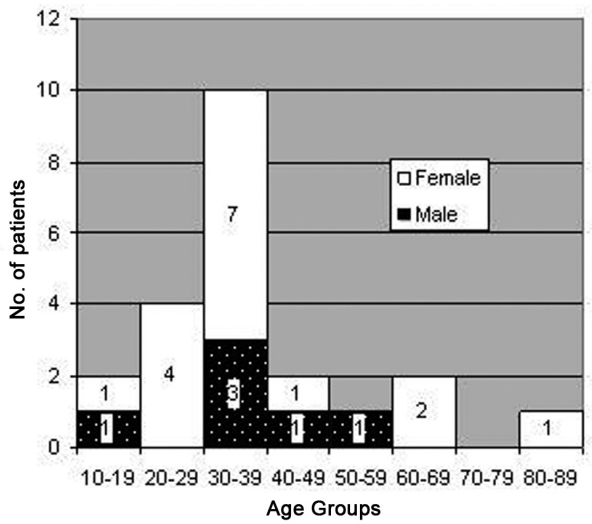

Figure 1 - Distribution of cases by age and gender.

presenting with headache had other symptoms, including neurological. The mean NIH Stroke Scale (NIHSS) was 12.1 ± 11.2 (range 0-30). The mode of symptom onset was variable. Seven patients (31.8%) had acute onset of neurological symptoms, 11 (50%) had subacute onset, 3 (13.6%) were chronic, and one (4.5%) patient had a recurrence of CVT 5 days after stopping warfarin (**Table 1**). Five patients initially were admitted to the ICU, requiring either intubation or close observation. Two patients who were admitted under hematology for management of acute myeloid leukemia (AML) and non-Hodgkin's lymphoma, developed CVT during their hospital stay. Twenty patients were admitted under the care of the neurology team; out of these, 2 patients were initially admitted under the care of the neurosurgery team: one for presumed brain tumor, and one treated with the impression of subarachnoid hemorrhage. Fourteen patients were previously healthy. Comorbidities occurring in one patient each included hypertension, diabetes mellitus, mucormycosis of the clivus, longstanding gastroesophageal reflux disease and anemia, previous CVT, hypercholesterolemia, and benign prostate hypertrophy, AML, and non Hodgkin's lymphoma. Six patients had a normal CT scan of the brain. Hemorrhagic venous infarction (detected either by CT and/or MRI) was observed in 7 patients, 3 patients had bland venous infarcts, 3 had intracerebral hemorrhage, 3 had arterial ischemic lesions in addition to venous infarction, and 6 patients had no parenchymal changes. Direct signs of thrombosis (empty delta sign and cord sign) were seen in 11 patients, and indirect signs (parenchymal changes: hemorrhagic venous infarction, venous infarction, edema) in 7 patients. An MRI/V brain was performed in 21 patients and was confirmatory in 19 (86.4%) patients. In the 3 doubtful cases, conventional 4-vessel

Table 1 - Characteristics of cerebral venous thrombosis (CVT).

Variable	n (%)	
Age, years, mean (SD)	38.3	(16.3)
Age >45 years	4	(18.2)
Female gender	16	(72.7)
NIH Stroke Scale, mean (SD)	12.09	(11.2)
Mode of onset		
Acute (<48 h)	7	(31.8)
Subacute (≤1 month)	11	(50.0)
Chronic (>1 month)	3	(13.6)
Recurrence of CVT	1	(4.5)
Neurological findings		
Headache	17	(77.3)
Papilledema	8	(36.3)
Seizures	12	(54.5)
Focal neurological signs	12	(54.5)
Altered consciousness	11	(50.0)
Non-neurological findings		
Vomiting/nausea or diarrhea	9	(40.9)
Brain imaging		
Hemorrhagic venous infarction	7	(31.8)
Bland venous infarction	3	(13.6)
Intracerebral hemorrhage	3	(13.6)
Arterial ischemic lesions	3	(13.6)
No focal lesion	6	(27.2)
Risk factors		
Oral contraceptive (OC) use	11	(50.0)
Alone	8	(36.3)
With protein S deficiency	2	(9.1)
With antiphospholipid antibody syndrome secondary to SLE	1	(4.5)
Protein S deficiency without OC use	1	(4.5)
Rhinocerebral mucormycosis	1	(4.5)
Septicemia	1	(4.5)
Leukemia	1	(4.5)
Non-Hodgkin's lymphoma	1	(4.5)
Unknown	6	(27.2)
Length of stay, days, mean (SD)	24.8	(29.8)
Median (IQR)	14	(8-21)
Range	3-111	

NIH - National Institute of Health, IQR - interquartile range

Table 2 - Site of involvement of 22 patients with cerebral venous thrombosis.

Site	No. of patients
1 site (1 patient)	
Transverse sinus	1
2 sites (7 patients)	
Superior sagittal + cortical vein	5
Superior sagittal + transverse sinus	1
Sigmoid + internal jugular vein	1
3 or more sites (14 patients)	
Superior sagittal + transverse + straight + cortical vein	1
Superior sagittal + transverse + sigmoid + cortical vein	1
Superior sagittal + right transverse + sigmoid + internal jugular vein	1
Superior sagittal + transverse + sigmoid + internal jugular vein + cortical vein	2
Superior sagittal + right transverse + right sigmoid + straight + vein Galen + right internal jugular vein	1
Superior sagittal + transverse + sigmoid + straight + internal cerebral vein + vein of Galen + cortical veins	1
Transverse + sigmoid + internal jugular vein	3
Transverse + sigmoid + straight + internal jugular vein	2
Transverse + sigmoid + cavernous + internal jugular vein	1
Transverse + sigmoid + straight + internal cerebral + vein of Galen + internal jugular vein	1

cerebral angiogram confirmed venous thrombosis. More severe presentations; that is, NIHSS scores of 19 to 30, occurred in 9 (40.9%) patients with bilateral hemorrhagic or venous infarcts (n=6), concomitant arterial infarcts (n=1), underlying malignancy (n=1), or deep venous system thrombosis (n=1). Seven patients had a CSF study that revealed 0-929/mm^3 white blood cells (median 3), 0-1152/mm^3 red blood cells (median 250), and 0.2-2.54 g/L protein (median 1.04). For 5 of these patients (71.4%), protein concentration was abnormally high, ranging from 0.66-2.54 g/L (normal range: 0.20-0.45 g/L). High white blood cell counts (12 and 929/mm^3) in 2 patients suggested a possible CNS infection; however, cultures were negative for both patients. Affected sites were superior sagittal (59.1%), transverse (72.7%), sigmoid (63.6%), straight (27.3%), and cavernous sinus (4.5%); and internal cerebral vein (9.1%), vein of Galen (13.6%), cortical veins (45.4%), and internal jugular vein (54.5%) (**Table 2**). Of 16 patients with transverse sinus thrombosis, 14 (87.5%) were left-sided. Presentations of the 10 patients who had cortical vein involvement associated with their sinus thromboses were similar to those of the entire series regarding headache (80% versus 77.3%) and seizures (50% versus 54.5%); while more (70% versus 50%) had a decreased level of consciousness. Cortical veins involvement was assessed by T2* gradient echo images of MRI in addition to CT brain.

Sixteen patients (72.7%) had typical risk factors for CVT (**Table 1**); 3 (13.6%) patients had more than one. The most common risk factor was OC use. Eleven of 13 women (84.6%) of reproductive age had a current history of OC use ranging from 3 months to 15 years. In 8 patients for whom the brand of OC was known, formulations used contained 25-30 µg of ethinylestradiol (EE) and 25-150 µg of synthetic progestins including desogestrel (25 µg; n=1), levonorgestrel (150 µg; n=1), and gestodene (75 µg; n=6). Three patients (13.6%) had low levels of protein S, of whom 2 also had a history of concomitant OC use. Another patient with a history of OC use had antiphospholipid antibody syndrome secondary to SLE. Oral contraceptive use was the only risk factor identified for 8 of the 13 (61.5%) women of reproductive age. Two patients had malignancies (leukemia and non-Hodgkin's lymphoma), one had rhinocerebral mucormycosis with thrombosis of the cavernous sinus, one had septicemia, and no common risk factors were found in 6 patients despite extensive workup. All patients except one were fully anticoagulated. In 13 patients, heparin infusion was used for anticoagulation, followed by warfarin. Eight patients were initially started on therapeutic doses of low molecular weight heparin followed by warfarin. Duration of warfarin use varied among patients. Eleven patients remained on warfarin from 1-36 months (median 11 months; IQR 5.5-16.5), and one is on lifelong anticoagulation due to antiphospholipid antibody syndrome. Single patients took warfarin for 6, 7, and 8 months each, and 2 were on warfarin for one year. Two patients were discharged on a therapeutic dose of low molecular weight heparin, and one patient was lost to follow up. Phenytoin was used in 8 patients for seizures in the acute stage in combination with other antiepileptic drugs. The other antiepileptic drugs used alone or in combination were carbamazepine in 5, valproic acid in one, levetiracetam in 2, and topiramate in 2 patients. Dexamethasone was used in 2 patients and acetazolamide in 2 for the symptoms of increased intracranial pressure. The mean hospital stay was 24.8 ± 29.8 days (median 14 days; IQR 8-21, range 3-111). Sixteen patients (72.7%) recovered completely, and 4 (18.2%) were left with mild (n=2) or severe (n=2) disability. The former 2 patients, both elderly women aged 66 and 81 years, had mild, right-sided weakness; the patient aged 66 years had underlying non-Hodgkin's lymphoma. The latter 2 patients had quadriparesis: a patient with venous and arterial infarcts and an elderly woman aged 66 years with underlying rhinocerebral mucormycosis. Two patients (9.1%) died: a man aged 45 years with underlying AML complicated by deep venous thrombosis (DVT), chest infection, respiratory failure, febrile neutropenia and seizures; and a woman aged 33 years who was transferred to our hospital 3 weeks after presentation in a comatose state without brainstem reflexes, and died 3 days after admission to our unit.

Discussion. The neurological symptoms and signs encountered in our series were those classically associated with CVT. Headache was the most frequent symptom, occurring in over three-fourths (77.3%) of our patients, and was the earliest symptom in 63.6% of our patients. Headache is a common presenting symptom for CVT, and was reported to occur in at least 80% of cases.[6] Two more recent series reported headache in 77.1% (27/35)[7] and 75% (36/48) of patients.[8] Cumerciuc and colleagues[9] reported that 17 of 123 consecutive patients with CVT had headache as the only neurological sign, although 10 of these patients also had at least nausea or other gastrointestinal symptoms. The 17 patients with presenting headaches in our series had associated neurological symptoms. Isolated intracranial hypertension with headache mimicking benign intracranial hypertension was seen in 36.3% of our cases, similar to that seen in recent studies where it was reported to range between 27-47%.[3,10] Fifty-four percent of our cases had focal neurological signs, which is similar to the 47% reported by Breteu et al,[11] and

somewhat larger than the 37% reported by Ferro et al.[12] However, half (n=11) of our patients had altered consciousness, compared with 18.2% and 22%, in the above-mentioned studies. Also, more of our patients presented with seizures when compared with the recent large cohort (n=624) reported by Ferro et al[12] (54.5% versus 39.4%).

We observed a large proportion (59.1%) of patients with superior sagittal sinus involvement, which is similar to the 50.1% (313/624) reported by Ferro et al[12] and 67.2% (37/55) reported by Breteu et.[11] Almost three-fourths (72.7%) of our patients had transverse sinus thrombosis, which was more than 44.7% reported by Ferro (279/624)[12] and similar to the 69% (38/55) reported by Breteu et al.[11] In addition, almost half (45.4%) of our patients had cortical vein thrombosis, which is much higher than the 6.2% (3/48) reported by Terazzi et al,[8] 6.3% (5/79) reported by Stolz et al,[13] and 17.1% (107/624) reported by Ferro et al.[12]

Oral contraceptive use is considered a risk factor for CVT. A meta-analysis of 8 studies evaluating the role of OCs in CVT included 263 women with CVT compared with 2862 women without CVT, and reported a summary odds ratio (OR) of 4.79 (95% confidence interval 2.40, 9.58; $p<0.001$) for OC users.[14] In a recent single center case control study of 63 CVT patients reported by Libourel et al,[15] 78% of non-pregnant fertile cases were OC users, and an earlier multicenter study by deBruijn et al[16] reported that 34 of 40 (85%) women with CVT were current OC users. Similarly, 84.6% of our cases that were women of reproductive age were current OC users. In our series, OC use was the only identified risk factor in almost two-thirds (61.5%) of reproductive age women, compared with another report where OC use was found to be the only etiologic factor in approximately 10% of cases.[6] Several studies suggest that the risk of venous thromboembolic events is greater with increasing amounts of ethinyl estradiol.[17] The OC users in our series for whom the formulation was known (n=8) were all taking products with 35 µg ethinyl estradiol, which is less than the 50 µg threshold proposed by Speroff[18] as producing no increased thrombolytic risk.

Three of our patients (13.6%) had protein S deficiency; 2 of these had a history of concomitant OC use. Although protein S deficiency has been associated with CVT, it is usually reported in lesser frequency than appeared in our subjects. For example, Stolz et al[13] summarized results of 4 studies comprising 160 CVT patients, where 1.9% of patients had protein S deficiency. More recently, Bombeli and colleagues[19] compared the prevalence of coagulation defects among different thrombosis groups, and reported that all groups had higher prevalence of defects compared with control patients, with 2% and 0.8% protein S deficiency in CVT patients and controls. Oral contraceptive use was the most frequent risk factor among the 51 CVT patients in that series, and was reported for 51.3% of patients without a coagulation defect compared with 33.3% of the 12 patients with any defect. Cantu et al[20] reported a higher prevalence (6.7%) of protein S deficiency, affecting 3 in a series of 45 CVT patients. No risk factors were identified in 4 (18.2%) of our patients despite extensive workup, which is similar to the 15% reported by Bousser and Ferro.[2]

Although we cannot attribute any unique risk factors to our population based on this series of patients, our sample characteristics are in contrast to those of patients comprising an earlier report from 2 hospitals in Riyadh.[5] That study included 40 patients diagnosed with CVT from 1985 through 1994 in the same catchment area as our study. Gender distribution was different in their cohort, where only half of the patients were female, versus 72.7% of our 22 patients ($p=0.08$). Significantly, only one of the 20 women in the earlier study was an OC user, compared with 11 of the 16 total women in our series ($p<0.001$). Three of their patients (7.5%) had probable protein S deficiency, which was slightly more than half that found in our patients (13.6%). In addition, 25% of the patients reported on by Daif et al[5] had Behçet's disease as the attributed cause of the CVT, compared with none from our group.

Mortality in our series of patients (9.1%) was similar to that reported in the cohort of 625 CVT patients (8.3%) studied by Ferro and colleagues,[12] which included all deaths during a median follow-up interval of 16 months. They list 8 risk factors for unfavorable outcome, of which one of our patients who died had 5: male, age >37 years, mental status disorder, thrombosis of deep cerebral venous system, and cancer; while the other had 3: coma, mental status disorder, and intracranial hemorrhage. Of 1180 patients in a systematic review by Dentali et al,[14] 66 (5.6%) died during the first month (range 0-15.2%). Of these early deaths for which information was available, 28.9% died as a consequence of an underlying disease rather than as a direct result of the CVT. One of our 2 cases that died succumbed to his underlying disease (AML) complicated by DVT, chest infection, respiratory failure, febrile neutropenia, and seizures.

In a recent review of CVT, Ehtisham and Stern[21] stated that the present "gold standard" for the diagnosis of CVT is no longer cerebral angiography but MRI, which visualizes the thrombosed sinus as increased signal on both T1 and T2 weighted imaging. This has been recently challenged by Linn and colleagues,[22] who recommend the use of multidetector-row CT angiography (MDCTA) as an alternative diagnostic measure in CVT, being faster, more widely accessible and more cost-effective than MR imaging.

In our patients MRI/V brain was confirmatory in 19 (86.4%) patients. Conventional angiogram may be needed; however, in patients with cortical vein involvement or equivocal MRI studies, which is a case in our series, where in the 3 doubtful cases, conventional 4-vessel cerebral angiogram confirmed venous thrombosis. This is stated also in the 2006 European Federation of Neurological Societies guidelines on the treatment of cerebral venous and sinus thrombosis.[23] In addition, for urgent cases or with sick patients CT angiogram/venogram is an appropriate choice. Four of our patients who were unable to tolerate MRI/V initially due to their general condition had CT venogram, with MRI/V performed later when possible.

In conclusion, our series provides an updated overview of risk factors, presentations, and outcome in CVT patients at a tertiary care center in Riyadh, Saudi Arabia. Risk factors, especially OC use, were similar to those reported from other centers internationally, and were different from those in an earlier report from Saudi Arabia. More women had OC use as the only risk factor compared with other reports, and more of our patients had protein S deficiency than reported elsewhere. More severe presentation was observed with deep venous system thrombosis, bilateral hemorrhagic or venous infarcts; but most had a favorable outcome. We also observed greater cortical vein involvement than is usually reported. Patients with underlying malignancy had a poor outcome; one of the cases that died, succumbed to his underlying disease (AML) complicated by DVT, chest infection, respiratory failure, febrile neutropenia, and seizures. The other one with underlying non-Hodgkin's lymphoma remained with right-sided weakness. A 33-year-old female, who was transferred to our hospital 3 weeks after presentation in a coma, died due to inadequate anticoagulation, stressing the importance of early diagnosis and treatment. Heparin was supported as the treatment of choice. Prospective, multicenter studies are needed to determine the incidence and prevalence of CVT and to further evaluate risk factors in this environment.

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