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ROLE OF NON-ENHANCED BRAIN CT IN DIAGNOSIS OF CEREBRAL VENOUS SINUSES THROMBOSIS WITH THE CORRELATION OF POTENTIAL PREDICTIVE LABORATORY TESTS

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Abstract:

Introduction: *Non-enhanced computed tomography (NCCT) is the first "preliminary" neuroimaging test. It is a rapid examination that aids the radiologist in identifying the defect area and the clinician in decision-making about treatment. Cerebral Venous Sinus Thrombosis (CVT) may be suspected if there is an apparent hyperattenuating of the venous sinus.*

Objectives: *Measurements of the radio density area using Hounsfield Units readings of the NCCT were taken from patients with and without a cerebral venous sinus thrombus as confirmed by CT venography, as well as determining laboratory predictors such as Hematocrit (HCT), Blood Urea Nitrogen (BUN), and creatinine (Cr) for an accurate and effective diagnosis of CVT.*

Methodology: *A retrospective case-control study of patients who presented with acute neurologic symptoms to the emergency department at Prince Sultan Military Medical City (PSMMC), Riyadh, Saudi Arabia, from May 2016 to April 2021 was included in this study. A total of 200 patients participated in this study.*

The study included 99 CVT patients and 101 control patients aged 14 to 80 years with newly onset neurological symptoms, confirmed venous sinus thrombosis by CT Venogram, and NCCT at presentation. Attenuation of venous sinuses was measured by technologists and radiologists. A region of interest (ROI) measuring 1-2 mm (based on sinus size) was used to measure the attenuation of the Dural sinuses.

To analyze the data, we used IBM SPSS Statistics for Windows by IBM Corp. Descriptive statistics are used to explore the relationship between NCCT brain and laboratory data (BUN, HCT, and Cr) to assess the incapacitated CVT.

As a result, CVT was observed in 77 (77.8%) of the females and 22 (22.2%) of the males. The median age of CVT ***Main Result:*** *patients was 40.7 years, while the median age of controls was 35.9 years. Gender and age differences were significant, with a p-value for the age 0.023 and p-value for gender 1. Headache was the most frequently reported symptom in clinical presentations, accounting for 47.5% of the total. Furthermore, the highest risk factor was oral contraceptives with 5.1%. In our study, we found among patients. The superior sagittal sinus represents the most defective area of CVT (21.9%). An independent t-test was used to compare the differences in CT attenuation between the control group and the CVT group at the sites of thrombus in each sinus. The optimal cut-off attenuation value for Dural sinuses was 62 HU, with a sensitivity of 66.82%, specificity of 89.45 %.*

Conclusion:*Hounsfield units' values can be affected by different factors such as the location of the thrombosis, the hydration status of the patient, and coagulopathy. The HU Opportunity Measurements of suspected cerebral venous sinus provide radiologists with an additional tool for increasing reporting confidence of the relatively rare clinical start of CVT, guiding further imaging and management.*

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INTRODUCTION AND LITERATURE REVIEW:

1.1 Introduction

Cerebral venous sinuses thrombosis CVT is rare form of the cerebrovascular disease can strike anyone regardless of age (Bousser & Ferro, 2007). The accounts for 0.5–1% of strokes that have a preponderance occurring in women, with a peak in young women due to gender-specific risk factors, especially oral contraceptives, pregnancy, puerperium, and in vitro fertilization (Stam, 2005). Adult patients are dominated by gender hormonal 75% of all CVT patients are female, with a 3:1 ratio among men (Ferro et al., 2004). CVT presents with a more diverse range of symptoms (headache, seizures, focal signs, disturbance of consciousness, and mental status) than other stroke types (Ferro & Canhao, 2014). The most frequently reported complaint was headache, affecting up to 90% of all patients (Bousser & Ferro, 2007). A timely diagnosis and treatment of CVT was critical for reducing morbidity and increasing survival (Bousser, 1999) . Clinically, CVT has a broad spectrum of presentation, and the presence of the condition often requires a high level of suspicion (Bousser, 1999) . Radiological studies were crucial to establishing a definitive diagnosis (Bousser, 1999). As a result of a delayed diagnosis, infarction, hemorrhage, coma, and even death can be caused, so rapid diagnosis of CVT is crucial (Zaheer et al., 2016). The variety of signs and symptoms makes the diagnosis of CVT challenging for clinicians as well as radiologists (Shayganfar, Azad, & Taki, 2019). The gold standard for diagnosing CVT was no longer routinely used and has been replaced by computed tomography CT (Saposnik et al., 2011). In emergencies, non-enhanced brain CT scans have become a cost-effective, fast, and available alternative diagnostic test (Buyck et al., 2013). An increase in attenuation of the occluded sinus on NCCT, which is considered a sign of CVT, indicates newly formed thrombi, and is best detected within the first week of the disease (Linn et al., 2009). This sign has been linked to the detection of CVT, even though the levels of hematocrit (HCT) and hemoglobin are related to blood attenuation, and a high level of HCT has been shown to be the cause of false-positive interpretation of CVT on NCCT (Provenzale & Kranz, 2011). Measurement of attenuation in the sinus and normalization of measured attenuation regarding HCT (H:H) can be a more reliable method and improve CVT detection on NCCT (Provenzale & Kranz, 2011).

1.2 Epidemiology

Few epidemiologic studies of CVT meet the current standards for a high-quality epidemiologic study 2–7, so the true incidence of CVT was probably underestimated (J. M. Coutinho, Zuurbier, Aramideh, & Stam, 2012). The prevalence of CVT was only 1% over consecutive autopsies (Ferro et al., 2001). CVT incidence among women between 31 and 50 years (J. M. Coutinho et al., 2012). In adults, CVT occurs more frequently among younger individuals than those with other strokes, and its incidence decreases with age (Ferro et al., 2004). In the most extensive international study of CVT patients, the International Study on Cerebral Veins and Dural Sinus Thrombosis (ISCVT) study, the median age was 37 years, with only 8% of the patients older than 65 years. A higher proportion of women than men were affected by CVT female-to-male ratio 2,9:1 (Ferro et al., 2004). The prevalence of CVT in Portugal was higher in autumn and winter, suggesting upper respiratory infections may be the reason for CVT (Stolz, Klotzsch, Rahimi, Schlachetzki, & Kaps, 2003). On the other hand. In Germany, CVT were more common in winter and summer (Stolz et al., 2003). Finally, there were approximately 5% of CVT cases among the young stroke population (Janghorbani et al., 2008)

1.3 Causes and Risk Factors

Causes and risk factors for CVT is a multifactorial disorder with sex-related specific causes (Bousser & Crassard, 2012). Virchow's triad of thrombogenesis constitutes the three risk factors of hypercoagulability, vessel wall damage, and blood stasis in any thrombotic

process (Saposnik et al., 2011). In developed countries, the most frequently associated factor was congenital thrombophilia (Bousser & Ferro, 2007). Furthermore, there were acquired risks factors such as any local head infection (Bousser & Ferro, 2007), pregnancy, and Puerperium (Bousser & Crassard, 2012). Gender-specific risk factors, particularly (OCP) and, to a lesser extent, pregnancy, puerperium, and menopause, are frequently blamed for the substantial discrepancies between genders. Conclusions had been obtained from research in age groups that lack these gender-specific risk factors, such as children and elderly patients, and have shown no gender predilection (J. M. Coutinho et al., 2009; deVeber et al., 2001) . A total of 44% of the patients had at least one risk factor, and 34.1% had congenital or genetic thrombophilia. In 65% of the women, there were gender-specific risk factors (Ferro et al., 2004). Approximately 85% of patients with CVT had prothrombotic risk factors or direct causes. Risk factors for thrombophilia include inherited or acquired thrombophilia, as well as OCP used (Ferro et al., 2004). Antiphospholipid syndrome was the most common diagnosis in the group of acquired thrombophilia (5.9%), followed by hyperhomocysteinemia (Ferro et al., 2004). There were 54.3% of patients who used OCP (Ferro et al., 2004). RENAMEVASC a registry run between 2002 and 2004 in 25 Mexican hospitals found that thrombophilia assessment and acute treatment was suboptimal due to gender-specific risk factors (Ruiz-Sandoval et al., 2012). The results of those studies contrast with registries conducted in developed countries, where there was a standard protocol for treating thrombophilia and actively seeking patients with oncology and hematology conditions (Ruiz-Sandoval et al., 2012). To summarize, CVT was a multi-factor problem, and there were several factors to identify. Intentional search for co-existing causes that may potentially increase the probability of recurrence (Ruiz-Sandoval et al., 2012).

1.4 Pathophysiology

Pathophysiology of CVT can be caused by many factors that should be considered, thrombophilia, infections, inflammatory states such us, autoimmune disorders, transient physiological states including dehydration and pregnancy, medication, especially OCP, smoking, and head trauma (Ferro et al., 2004; Stam, 2003). Most data on CVT epidemiology comes from the International Study on Cerebral Vein and Dural Sinus Thrombosis (Canhao et al., 2005). Thrombosis of the cerebral veins and venous sinuses induces the formation of a predominantly red clot in the acute stage (Ameri & Bousser, 1992) . It consists of red blood cells and fibrin within the Dural venous sinuses(Ameri & Bousser, 1992) . The clot prevents absorption of the cerebrospinal fluid through the arachnoid granulations and distends the superficial and deep veins that drain into the venous sinuses (Ameri & Bousser, 1992). These distended cerebral veins may rupture into the brain parenchyma or into the subarachnoid space and cause intracerebral or subarachnoid hemorrhage(Ameri & Bousser, 1992). If the thrombotic process extends from the sinus into the superficial or deep cerebral veins, it could cause focal signs and symptoms secondary to the localized vasogenic or cytotoxic edema and venous infarction, which undergoes hemorrhagic transformation (Ameri & Bousser, 1992). In venous congestion, disturbances of neuronal functional metabolism are tolerated for a much longer time than in arterial occlusion, and full recovery from severe focal and generalized neurological signs and symptoms may be observed in CVT even after weeks (Ameri & Bousser, 1992). Intracranial hemorrhage was often observed in CVT, and its incidence may reach 40–50% (de Bruijn & Stam, 1999).

1.5 Signs and Symptoms

Clinical presentation for CVT can be acute, subacute, or rarely chronic (Ferro & Canhao, 2014) . The most frequent symptoms include headaches, seizures, motor, sensory, and language dysfunction, and altered mental status or diminished consciousness (Ferro & Canhao, 2014) . Symptoms and signs can be grouped into three major presentation syndromes: first isolated intracranial hypertension, which includes headache that could be accompanied by nausea or vomiting, papilledema, tinnitus, and visual symptoms such as transient visual obscuration, visual field defects, or rarely nowadays decreased visual acuity(Ferro & Canhao, 2014). Headache was often severe and unremitting and increasing in severity with Valsalva's maneuver and recumbence, but patients may also present with other types of headaches, including migraine with aura (Ferro & Canhao, 2014) . A secondary, focal syndrome consisting of focal deficits and seizures (Ferro & Canhao, 2014) . The third is encephalopathy, when the patient presents with multifocal signs, mental status changes, or is stuporous or comatose (Ferro & Canhao, 2014). The isolated intracranial hypertension syndrome was more common in lateral sinus occlusion, focal syndrome, and bilateral pyramidal signs in Superior Sagittal Sinuses (SSS) thrombosis, while encephalopathy and coma occur in deep venous thrombosis (Ferro & Canhao, 2014). The clinical picture was more severe when parenchymal lesions were present, particularly hemorrhages, with focal signs, seizures, and lowered

vigilance (Ferro & Canhao, 2014). The incidence of seizures and encephalopathy was higher in newborns and young children, while headaches were less common among elderly patients, and mental changes tend to be more prevalent (Ferro & Canhao, 2014). Patients that presented later were more likely to have isolated intracranial hypertension syndrome and presented with papilledema (Ferro & Canhao, 2014).

1.6 Diagnoses CVT

Diagnosis of CVT was verified by showing evidence of thrombi in the cerebral veins or sinuses (Bousser & Ferro, 2007). The first diagnostic test usually was a non-enhanced computed tomography (NCCT), and particularly if patients were evaluated in an emergency setting, CT was useful to rule out acute or subacute cerebral disorders that CVT may imitate, such as a tumor, subdural hematoma, and abscess (Buonanno, Moody, Ball, & Laster, 1978). CT was unremarkable in up to 30% of cases of CVT, and most of the findings were non-specific (Buonanno et al., 1978). We perform a CTV after NCCT, which provides excellent anatomic detail of the venous circulation, allowing the detection of defects in the Dural sinus and cortical veins, as well as anomalous sinus wall enhancement and collateral vein drainage (Ozsvath et al., 1997; Rodallec et al., 2006). The advantage of a CTV is less invasive and less expensive, and easy to be carried out immediately after brain CT (Wetzel et al., 1999). Furthermore, NCCT/CTV has several advantages in diagnosing CVT: fewer motion artifacts, no contraindication for patients with ferromagnetic devices, and easier use in patients with claustrophobia (Rodallec et al., 2006). On the other side, there were drawbacks to NCCT /CTV: limited visualization base of skull structures 3D display, poor resolution for small parenchymal abnormalities ,poor detection of cortical and deep venous thrombosis, exposure to ionizing radiation , adverse reactions to iodine contrast agent, such as in patients with diabetes, kidney failure, and may restrict in pregnant women and children (Rodallec et al., 2006).

CVT has increased the attenuation of the occlusive sinus on NCCT (Linn et al., 2009). A direct sign of CVT usually occurs in the first week after forming the thrombus (Linn et al., 2009). This sign reported to be useful in the detection of CVT (Black, Rad, Gray, Campeau, & Kallmes, 2011; Provenzale & Kranz, 2011). In addition, HCT and hemoglobin levels are correlated with blood attenuation and the high level of HCT has been reported to be one of the main causes of false positive interpretation of CVT on NCCT (Black et al., 2011; Provenzale & Kranz, 2011). A more reliable method of detecting CVT on NCCT is to measure the attenuation in the sinus and regarding HCT (H: H)(Provenzale & Kranz, 2011) .The H:H ratio has suggest these signs are sensitive and potentially useful to diagnose CVT (Black et al., 2011; Buyck et al., 2013). On the other hand, the blood urea nitrogen and Creatinine BUN/Cr ratio increases, and it was often regarded as an indicator of dehydration (Black et al., 2011; Buyck et al., 2013). The INR was used to assess bleeding risk and coagulation status in patients (Shikdar, Vashisht, & Bhattacharya, 2022)

The aim of this study is to measure the density (Hounsfield Units) of cerebral venous sinuses by NCCT examinations in patients with and without a CVT as confirmed on CT venography to reach quantitative criteria for more rapid and accurate diagnosis.

METHODS AND MATERIALS:

2.1 Study design

The Research Ethics Review Board has approved as the case-control retrospective study, and the need for informed consent was waived as part of the study approval. IRB approval number is 1553. Data were collected at Prince Sultan Military Medical City (PSMMC) from May 2016 to April 2021. The PSMMC has a capacity of 1162 beds and 303 beds in emergency service, serving as a tertiary care center. All laboratory results and NCCT were confirmed by CTV conducted during this period.

2.2 Patient selection:

Using a standard picture archiving and communication system (PACS) workstation, a search for the words "CT Brain Venogram" performed during a 5-year period starting from May 1st, 2016, to April 30th, 2021, resulted in a total of 1380 CTV examinations. All CTV examinations were reviewed to identify patients with a radiologically confirmed CVT diagnosis.

Inclusion criteria: patients must be present with new-onset neurologic symptoms such as headaches, focal neurological signs, and seizures. They confirmed venous sinus thrombosis by CTV, NCCT performed at presentation, HCT, (BUN), and International normalized ratio (INR) evaluation within 24 hours of NCCT. Age older than 13 years. The diagnosis of CVT was confirmed on a CTV during the hospital admission.

Exclusion criteria: Any intracranial pathology, such as intracranial hemorrhage, skull fracture, increased intracranial pressure, intra or extra-axial mass, or recent brain surgery (1/52), as well as intravenous

iodinated contrast material administration within 72 hours of NCCT, or patients who have received a blood transfusion within the previous 48 hours.

The total number of NCCT and venogram patients is 1380. However, we excluded 535 patients who did not have a CTV to confirm thrombosis. Therefore, there were 845 patients with CTV, and 99 patients had CVT. On the other hand, out of 746 patients, 101 were chosen as the control group based on their age and gender. We excluded 496 patients due to chronic thrombosis and follow-up exams. 68 patients did not have NCCT within 24 hours, and they had hypoplastic venous sinuses, tumors, or intracranial pathology.

In contrast, 81 children aged 0 to 13 were excluded from the study because they were considered children by the hospital system. Patient age, gender, thrombus location, CT density in the Hounsfield unit of the superior sagittal, right transverse, left transverse, right sigmoid, left sigmoid sinuses, HCT, INR, BUN, and Cr were recorded for each patient in both groups. Furthermore, if the patient had a thrombus, the CTV was used to determine the location of the thrombus, which was then matched with the NCCT and measured by HU. In contrast, in the control group, the HU of the superior sagittal sinus (SSS) and the transverse and sigmoid sinuses were measured from NCCT.

2.3 Data Interpretation and Training

Hounsfield units quantify the density of tissue in the CT modality. The attenuation of cerebral venous sinuses was measured by a technologist and by both junior and senior radiologists. They used the Hounsfield unit to measure each venous sinus. CTV and NCCT were obtained from (Centricity PACS radiology Healthcare Barrington, USA). Furthermore, we get laboratory results from the Paratal Portal System v2.0. A HCT was obtained from a complete blood count (CBC), whereas (Cr) and BUN were obtained from a kidney function test. The international normalized ratio (INR) is derived from prothrombin.

The technologist was given multiple hands-on, one-on-one workshops and tutorials for PACS (two sessions), neuroanatomy emphasizing the cerebral venous sinuses (two sessions), and density measurement (three sessions) by a consultant neuroradiologist. After density measurement training was accomplished, the first ten patients with CVT and control group density measurements were done by technologist, who was under the direct supervision and evaluation of the consultant neuroradiologist. After the consultant neuroradiologist approved the measurement technique, the rest of the data density measurement was completed by the technologist. Then the data was reviewed by the consultant neuroradiologist supervisor, and, randomly, he chose 10% of the density measurement data and re-measured it blinded from the technologist measurement data. Technologist have difficult (hypoplastic) areas to measure. The consultant neuroradiologist measured it properly

2.4 Measurement of the Region of Interest (ROI):

Density measurements were taken by utilizing the region of interest ROI in all patients according to the following criteria. Given the wide range of patient ages and skull and venous sinus sizes, the ROI size was selected using "best fit" criteria to maximize accuracy while minimizing volume averaging with adjacent tissues. An ROI was created by manually drawing a circular or elliptical ROI on a PACS workstation using a standard density cursor. The ROI does not include the sinus wall or artifacts from the adjacent bone and sinus wall. The ROI for CVT patients was taken at the best-fit region within the thrombosed sinus on non-enhanced brain CT.

In contrast, the ROI for the non-thrombosed sinus in control group patients was placed within the distal part of the superior sagittal sinus, the middle third of the transverse sinus, and the proximal third of the sigmoid sinus. If an accurate density measurement for the sinus could not be reliably made, the neuroradiologist discussed the case to decide the possibility of an accurate density measurement or exclude the case from the study. To determine the region of interest, we identify landmarks for each sinus. For example, the region of interest (ROI) for superior sagittal sinus is 2–2.5 mm (depending on sinus size) and is a landmark at the beginning of the lateral ventricle. On the other hand, the right and left transverse sinuses (TS) in the coronal plane, tentorium cerebelli, and regions of interest of 1–2.5 mm avoid overlapping bone or vessels. The last sinus right and left sigmoid (SS) is at the level of the internal auditory canal (IAC), and the ROI is 1-2 mm.

2.5 CT protocol

CTV and NCCT examinations were done via two scanners by Siemens Medical Solutions, Forchheim, Germany, in the emergency department (ED). The other scanner used for inpatient is the GE Healthcare System. The scans were performed from the base of the skull to the vertex, parallel to the floor of the anterior fossa, avoiding the eyes. The patient was positioned supine on the bed, with the head supported by appropriate support with flexion of 20–30 degrees. Following the acquisition of lateral scout images, a

spiral technique was used to acquire NCCT of the brain caudo-cranially. We reconstructed raw data using back-projected filtered data and a convolution kernel dedicated to brain tissue 40. For Siemens Medical Solutions, the standard CT used the kV120 & mA180-300 for NCCTs, whereas for CTV, the standard CTs were 300 & 550. The GE healthcare system uses 120 kV for NCCT and CTV. The mA varies according to the patient's age. The NCCT brain protocol is axial, sagittal, and coronal. The patient's position was supine, and the headfirst coverage area from the base of the skull to vertex slice thickness is 2.5 to 5mm. recon destination PACS with the following parameters: kV120, mA 160–250 depending on patient age. A collimation width ranged from 14.4 to 20. If the patient required an IV, there was a 90-second delay. Images of the axial, coronal, and sagittal planes from Scout STD. Axial, Sagittal, and Coronal CVT Brain, we apply venogram Protocol. Plain CT scans should be completed within 48 hours. Converge the area between the skull's base and the vertex. The thickness of the slices varies depending on the section. The axial slice thickness is 2.5 mm and 0.625 mm. Sagittal and coronal measurements are 0.625mm. The following parameters are affected by the patient's age: kV120, mA300-550, and patient age are also factors. 38-40 collimation width CTV were performed 45 seconds after intravenous iodinated contrast was administered at a rate of 3/4 ml/s. Scout, brain routine, axial 0.625, coronal and sagittal 1/1STD imaging process.

2.6 Collecting Data and Statistical Analysis:

The data includes both qualitative and quantitative information. We obtained the patient's number, age at the time of examination, clinical presentation, diagnosis, and laboratory results such as Cr, HCT and BUN. In addition, we also measured Hounsfield units (HU) for each sinus. We used IBM SPSS Statistics for Windows by IBM Corp. to analyze our data. We used a t-test to match age and gender and found a correlation between Hounsfield unit HU and hematocrit HCT. Furthermore, attenuation means in positive and control patients. We determine the thrombosis sites. Maximum and minimum values for each sinus in the positive and control groups, as well as the cut-off point. We conducted CVT distribution on both male and female subjects.

RESULT:

3.1 Age and gender distribution

The study included 200 patients for the CVT and control group at Prince Sultan Military Medical City. Of these, there were (n=99, 49.5%) patients that were confirmed to have CVT identified by CTV. The remaining (n = 101, 50.5%) patients were in control groups; they didn't have CVT confirmed by CTV. Furthermore, 155 (77.5%) of the total included patients were female, with 78 (77.2%) in the control group and 77 (77.8%) in the CVT group. 45 (22.5%) were males, of which 23 (22.8%) were controls and 22 (22.2%) were CVT patients. The patients had a mean age of 38.3 years (±15.00), 99 had a median age of 40.7 (17%), and 101 were controls, with a median age of 35.9 (12.3%). There was a significant difference in gender and age, with a *p*-value for the age of 0.023 and *p*-value for gender 1 (Table 1 & Fig 1).

3.2 Characteristics of CVT and Control Groups

The patients' lab values for BUN, Cr, HCT, and INR were recorded. The normality test revealed non-normal distributions for BUN, Cr, H: H ratio, and INR. The median and interquartile ranges for BUN were 3.8 [2.8, 4.8] and 59.0 [48.0, 70.0] for Cr. The differences between the two studied groups for Cr and BUN levels were not statistically significant ($p > 0.05$). The mean HCT in the CVT and control groups was similar (37.6 versus 37.7, respectively; $p = 0.880$), HCT was 37.7% (±6.8). On the other hand, the INR of 1.1 [1.0,1.2] was statistically significant ($p < 0.001$) (Table 1). The Hounsfield Unit: hematocrit ratio (H: H ratio) was calculated for all patients with a median value and an interquartile range of 1.5 [1.2,1.7]. The H: H ratio in control patients had a median value of 1.4 [1.2,1.6], which was significantly lower ($p = 0.005$) when compared to the confirmed CVT group, 1.6 [1.3,1.8]. There was a weak correlation between the hematocrit reading and attenuation levels ($r = 0.13$). However, this weak correlation was statistically significant in our sample ($p<0.001$). (Table 1, Fig. 2)

3.3 Location of the thrombus in CVT patients

In patients that were identified to have CVT, the most defected area was in the superior sagittal sinus in 47 (21.9%) patients. Then, a thrombus in the left transverse sinus was found in 45 (20.9%) patients, and 46 (21.4%) patients had a thrombus in the right transverse sinus. Thrombus was identified in the right Sigmoid Sinus in 42 (19.5%) patients and in the left Sigmoid Sinus in 43 (20.0%) patients. (Fig 3).

3.4 Clinical presentation and Risk Factor of CVT

Among patients' clinical presentations, the most frequently reported symptom was headache. Headache was reported in a significantly higher number of patients in the control group 74 (73.3%) compared to the confirmed CVT group 47 (47.5%). Additionally, nausea and vomiting were noted in 12 of the patients who had CVT but were not statistically significant in

the control group (6.9%) and the confirmed CVT group (12.1%). On the other hand, seizures were reported at the presentation of 10.1 (10) patients. Seizures were not significant in control and confirmed CVT groups. The patients' presenting signs were focal motor deficit and papilledema. The focal motor deficit was reported in 9 patients. It was similar in confirmed CVT and control groups (8.9% versus 9.1%, respectively). Furthermore, papilledema was reported at 9.9% for the control group (Table 4). The highest risk factor was OCP. It was eight patients, 7.9% for the control group and five patients 5.1% for the CVT group. There was no significant difference in the reported risk factors between the control and CVT groups Table 5, Figure 6. The differences in the patient's CT attenuation levels between the control and CVT groups at the site of thrombus in their respective sinuses were significantly different, and the differences were compared using an independent t-test. In SSS, HU was different between the control and CVT groups at 53.9 (6.7%) and 57.9 (9.7%), respectively, and was found to be statistically significant (p<0.001). The HU difference for the left transverse sinus in control was 52.1 (6.1%), and the HU in confirmed CVT was 55.8 (8.5%) and found to be statistically significant (p<0.001). Moreover, the HU for the control group in the right transverse sinus was 52.5 (6.4%), while the HU for the CVT group was 59.0 (9.8%), which is statistically significant (p<0.001). Furthermore, the LT and RT sigmoid had almost the same HU in the control and CVT groups, with a statistically significant (p=<0.001) (Table 6).

3.5 ROC analysis for each sinus

Identified at the presentation ROC analysis reveals the potential cut-offs for attenuation levels for each sinus. First, the attenuation value for SSS of 62.9HU was the optimal cut-off with an AUC of 0.789 and had a sensitivity of 55.32% and a specificity of 93.45%. Furthermore, the attenuation cut-off for Rt TS was 62 HU with an AUC of 0.891 and had 70.9% sensitivity and 92.9% specificity. Lt TS had a cut-off point of 59HU and an AUC of 0. 802. It had 68.89% sensitivity and 86.47% specificity. Then, the best optimal cut-off point for Rt SS was 62.1HU with an AUC of 0.879 and had 78.57% sensitivity and 85.55% specificity. The last cut-off point for Lt SS was 62 HU with an AUC of 0.576. It had 72.9% sensitivity and 85.47% specificity. Finally, the CVT optimal cut off attenuation value for all Dural or superficial sinuses was 62 HU with a sensitivity of 66.82%, a specificity of 89.45%, a positive predictive value (PPV) of 64.5%, a negative predictive value (NPV) of 90.38%, and an AUC of 0.831.

The boxplot in Figure 8 shows the 25th and 75th percentiles and the maximum and minimum attenuation levels represented by the whiskers for each of the sinus and a comparison between the control and CVT groups. First, for SSS, the maximum value for CVT was 82 HU, and the minimum value was 36 HU, with a median of 58 HU. However, for the control group, the maximum value was 65HU, and the minimum value was 36HU with a median of 50HU.

Table 1: Characteristics of CVT and Control Groups

		Total	Control	CVT	*P*-Value
n		200	101	99	
Gender, n (%)	F	155 (77.5)	78 (77.2)	77 (77.8)	1.0
	M	45 (22.5)	23 (22.8)	22 (22.2)	
Age, mean (SD)		38.3 (15.0)	35.9 (12.3)	40.7 (17.0)	0.023
BUN, median [Q1, Q3]		3.8 [2.8,4.8]	3.8 [2.8,4.8]	3.7 [2.7,4.8]	0.597
Cr, median [Q1, Q3]		59.0 [48.0,70.0]	60.0 [48.0,74.0]	58.0 [49.5,68.0]	0.750
HCT, mean (SD)		37.7 (6.8)	37.6 (6.7)	37.8 (6.9)	0.880
INR, median [Q1, Q3]		1.1 [1.0,1.2]	1.0 [1.0,1.1]	1.1 [1.0,1.3]	<0.001
H:H ratio, median [Q1, Q3]		1.5 [1.2,1.7]	1.4 [1.2,1.6]	1.6 [1.3,1.8]	0.001

Figure 1: Age and gender distribution

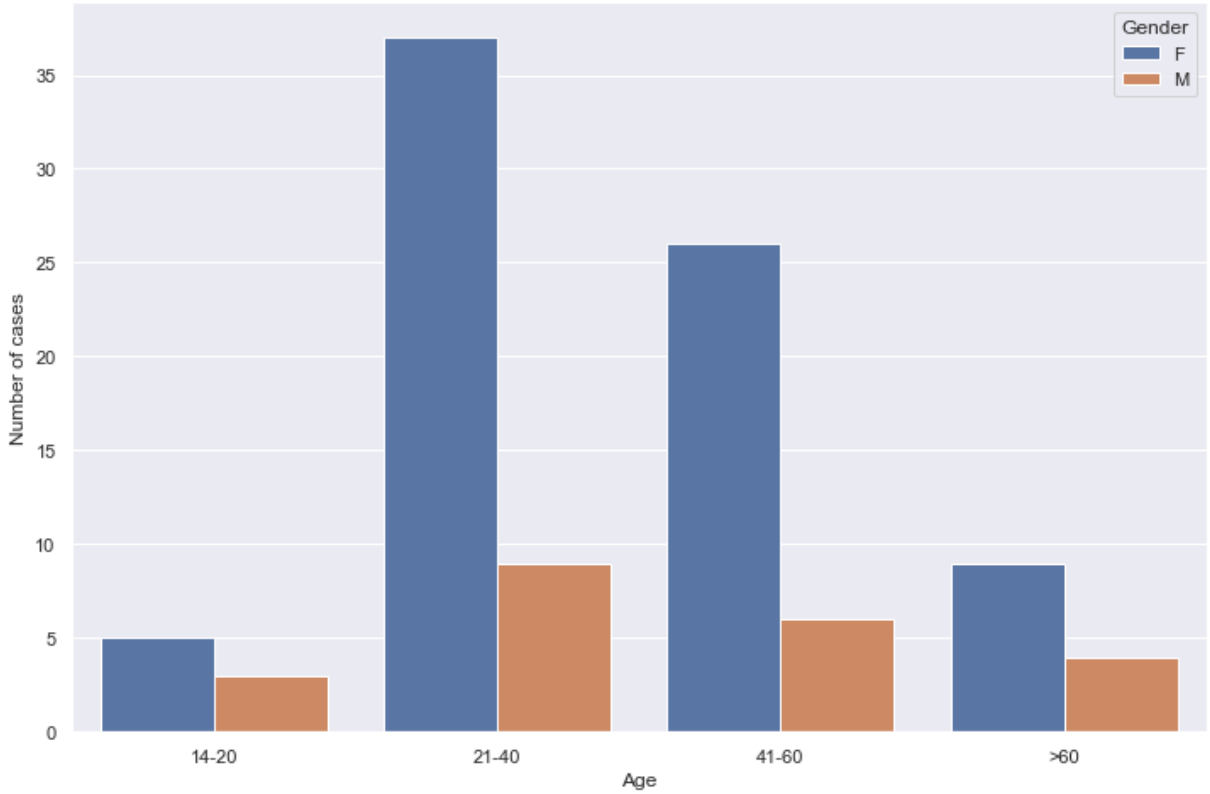


Figure 2: Correlation between Hematocrit and Attenuation level

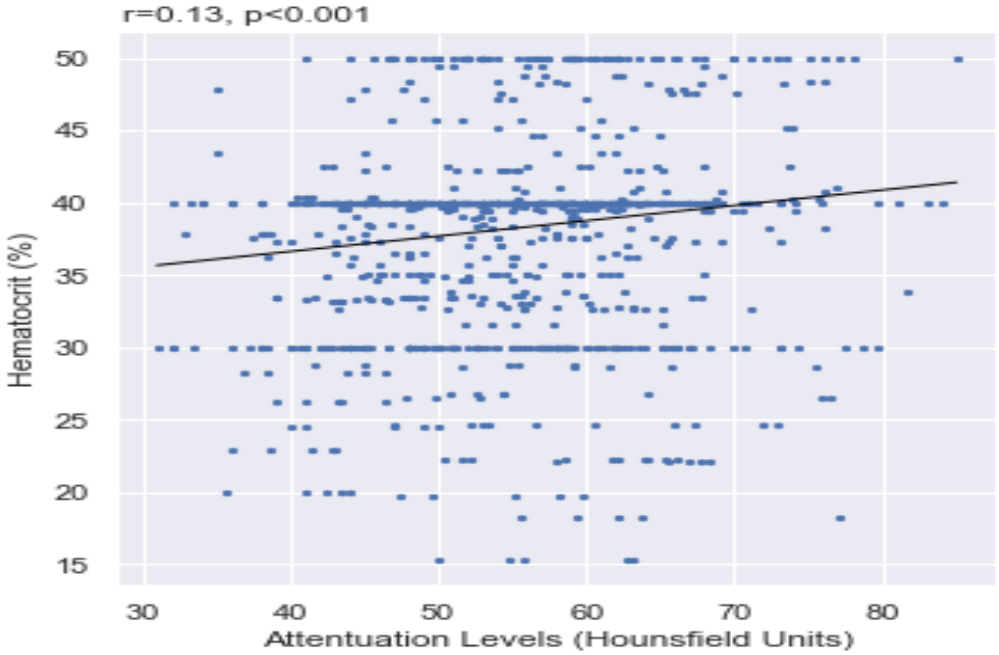
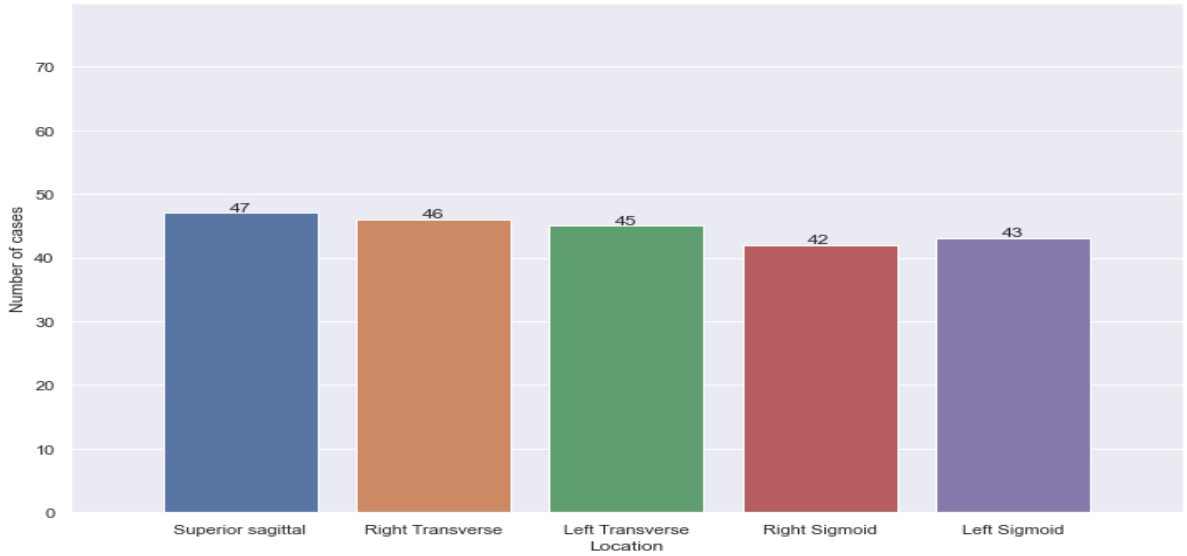


Table 2: Location of the thrombus in CVT patients

	CVT
N	219
SSS, n (%)	46 (46.5%)
LTTS, n (%)	45 (45.5%)
RTTS, n (%)	44 (44.4%)
LTSS, n (%)	43 (43.4%)
RTSS, n (%)	41 (41.4%)

Figure 3: Site of the thrombi in patients with confirmed CVT



❖ Some patients have more than on location of thrombosis at the same time

Table 3: Presenting symptoms among all patients with suspected CVT

	Control	CVT
N	101	99
Headache, n (%)	74(73.3%)	47(47.5%)
Nausea & vomiting, n (%)	7(6.9%)	12(12.1%)
Seizures, n (%)	10(9.9%)	10(10.1)
Visual disturbance, n (%)	14(13.9%)	7(7.1%)
Photophobia, n (%)	6(5.9%)	1(1.0%)
Altered mental status, n (%)	6(5.9%)	4(4.0%)
Impaired speech, n (%)	1(1.0%)	3(3.0%)
Dizziness/vertigo, n (%)	2(2.0%)	1(1.0%)
Numbness, n (%)	6(5.9%)	2(2.0%)

Figure 4: Presenting symptoms in patients with confirmed CVT

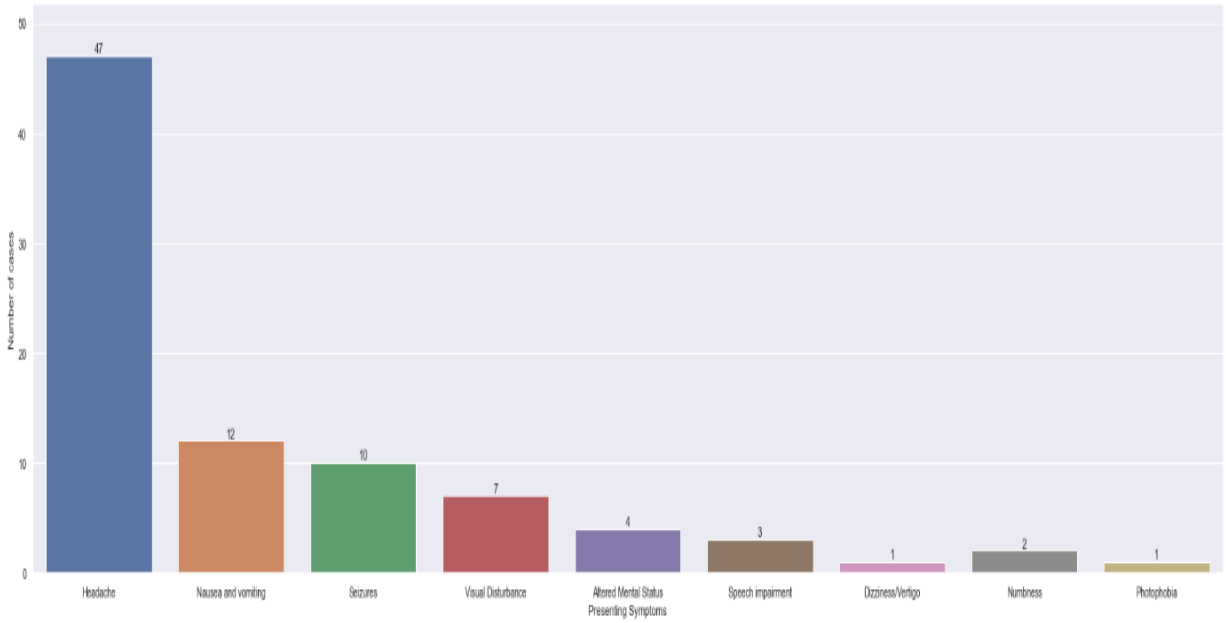


Table 4: Presenting signs among all patients with suspected CVT

	Control	CVT
Focal motor deficit, n (%)	9 (8.9)	9 (9.1)
Papilledema, n (%)	10 (9.9)	0 (0.0)

Table 5: Risk factors among patients with suspected CVT

	Control	CVT
Antiphospholipid, n (%)	2 (2.0%)	2 (2.0%)
SLE, n (%)	0 (0.0)	3 (3.0%)
RA, n (%)	1 (1.0%)	1 (1.0%)
OCP Use, n (%)	8 (7.9%)	5 (5.1%)
SCD, n (%)	2 (2.0%)	1 (1.0) %
Postpartum, n (%)	2(2.0%)	4(4.0%)
Bechet's Disease, n (%)		2 (2.0%)

Figure 5: Comparing risk factors between control and CVT patients

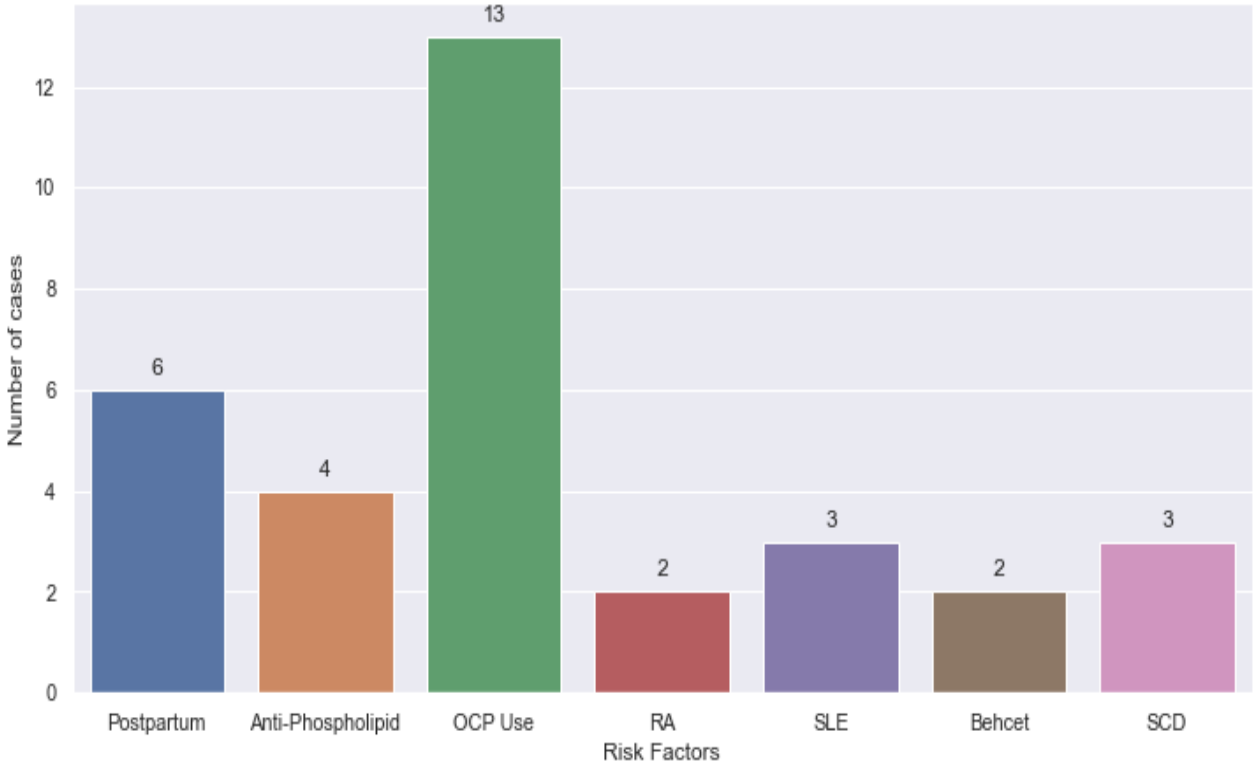


Table 6: Comparing the cerebral venous sinus CT Attenuation levels between control and CVT patients. The differences were compared using the independent t-test

	Grouped by CT			
	Total	**Control**	**CVT**	**P-Value**
N	200	101	99	
SSSHU, mean (SD)	55.9 (8.6)	53.9 (6.7)	57.9 (9.7)	0.001
LTSSHU, mean (SD)	55.2 (9.7)	52.3 (8.4)	58.2 (10.2)	<0.001
RTSSHU, mean (SD)	55.4 (10.5)	53.2 (8.8)	57.5 (11.6)	0.004
LTTSHU, mean (SD)	53.9 (7.6)	52.1 (6.1)	55.8 (8.5)	<0.001
RTTSHU, mean (SD)	55.7 (8.9)	52.5 (6.4)	59.0 (9.8)	<0.001

- Using the site of thrombus in CVT and the corresponding site in the control group

Figure 7: ROC curves all Dural sinuses

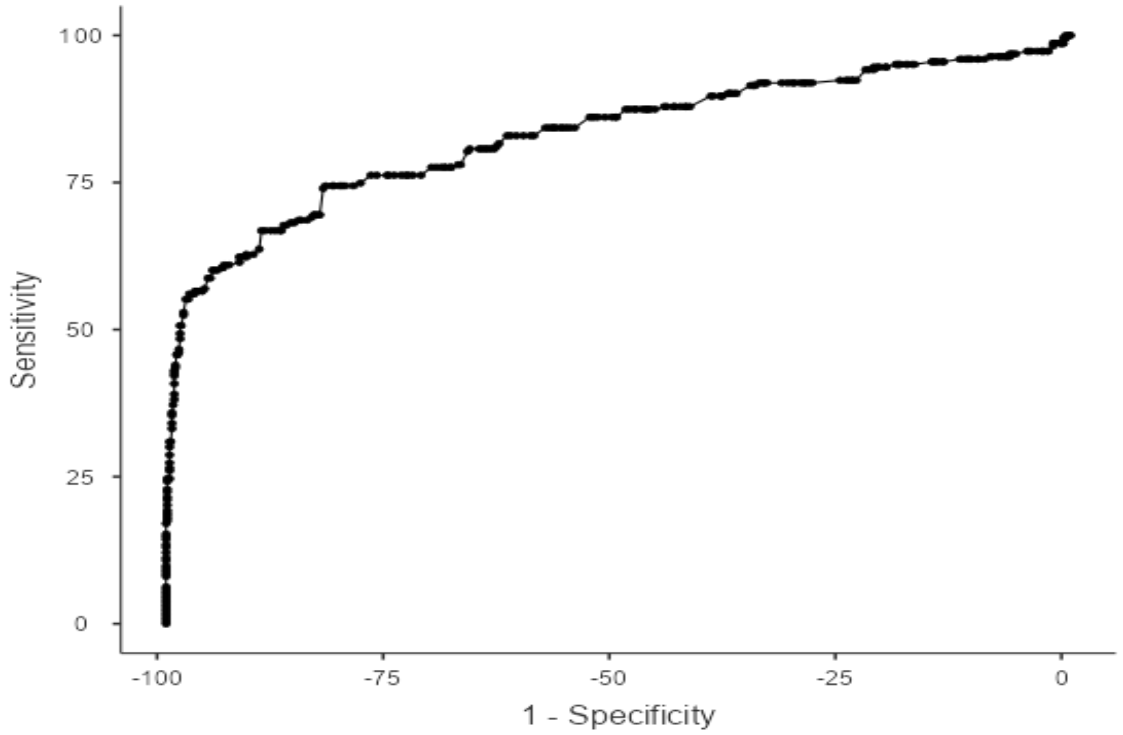
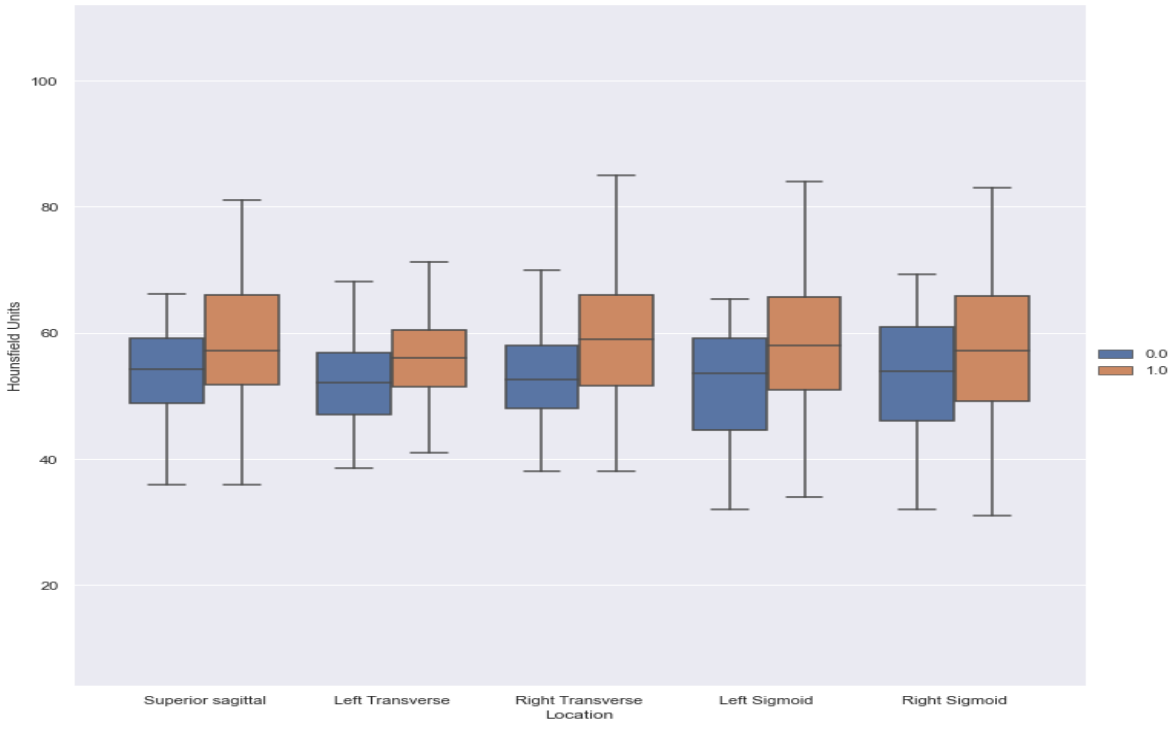


Figure 8: Box plots showing the interquartile range and median of the attenuation levels of different sinuses



4.1 DISCUSSION

NCCT scans are used as the first-line imaging modality in the emergency department when neurologic symptoms are present. The CT scan was cost-effective, fast, and a readily available modality. The appearance of CVT on NCCT showed increased attenuation (Buyck et al., 2013). However, measurement of the attenuation values of the sinuses in HU may be more objective and reliable as a moderate increase in attenuation may not always be detected by the radiologists (Roland et al., 2010). Despite the importance of a prompt CVT diagnosis to begin appropriate treatment and prevent sequelae (J. Coutinho, de Bruijn, Deveber, & Stam, 2011). It can occasionally diagnose as a false positive, masking the correct diagnosis and causing patient anxiety and inappropriate treatment options (J. Coutinho et al., 2011).

According to Ferro et al (2004) CVT was significantly more prevalent in women than in men, with a ratio of 3:1 partly due to gender-specific risk factors, such as pregnancy and preputium (Ferro et al., 2004). As well Canakci et al found that (39%) of patients in the CVT group were male, and (61%) were female (Canakci et al., 2021). Furthermore, the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) cohort found that 75% of the patients were women and older than men (Ferro et al., 2004). Similarity to our result indicates 77.2% were female and 22.5% were male (Table 1 fig 1). On the other hand, age was an independent factor for the attenuation levels of cerebral venous sinuses, an association that has not been established in the literature. Another study points HCT levels decrease with age (Al-Ryalat et al., 2016). Weinstein & Anderson explains that aging causes gradual kidney loss that may cause a decrease in HCT levels (Weinstein & Anderson, 2010). According to Provenzale & Kranz (Provenzale & Kranz, 2011) when serum hematocrit is elevated, the attenuation in the sinuses may increase, and false-positive readings may occur. Consequently, Weinstein & Anderson (Weinstein & Anderson, 2010) explained hematocrit has been shown to affect attenuation, and this age-related decrease in HCT may underestimate the level of attenuation of cerebral venous sinuses. Another study discovered a mean hematocrit of 36.76, which was not statistically significant with the age *p*-value 0.808 (Akhavan et al., 2019). In our study, the mean hematocrit for positive patients was 37.7, with a *p*-value of 0.880, and the patients had a mean age of 38.3 years (15.00), with 99 patients having a median age of 40.7 (17%) and 101 patients having a median age of 35.9 (12.3%). There was a significant difference in gender and age between the two groups, with *p*-values 1.0 for gender and a *p*-value for the age of 0.023. Subsequent study found 26 patients had CVT with a median age of 38.7, while 224 patients had control (Alsafi, Lakhani, Carlton Jones, & Lobotesis, 2015). They had a median age of 43.3. There was no significant difference in age, gender, and two groups with *p* values of 0.3800 (Alsafi et al., 2015). Thus, radiologists should consider the patient's age when correlating laboratory findings with attenuation values and deciding whether to confirm or exclude CVT (Alsafi et al., 2015).

In the study 20 patients with acute CVT, initiate a cut-off value of 61 HU (Buyck et al., 2013). Our result suggests that the average potential cut-off for attenuation level for all sinuses with CVT was 62 HU. Another study established attenuation above 65 HU in the Dural sinuses was able to make a diagnosis of CVT with a sensitivity of 84% and specificity of 96% (Besachio, Quigley, Shah, & Salzman, 2013). Alsafi et al (Alsafi et al., 2015) study reported that attenuation in patients with CVT was 68 HU. The study Shayganfar et al, (Shayganfar et al., 2019) found the non-enhanced diagnosis CVT, was reliable and accurate. The attenuation value was > 60.4 HU with 71.4% sensitivity, and the H: H ratio was > 1.42 with 94.3% sensitivity . Furthermore, in our study, we recommend 62 HU as a the CVT optimal cut off attenuation value for all Dural or superficial sinuses with a sensitivity of 66.82%, specificity of 89.45%, positive predictive value PPV 64.5%, negative predictive value NPV 90.38%, and an AUC of 0.831.

An increase in attenuation based on the H:H ratio may be misleading if it is influenced by other factors. First, Black et al. (Black et al., 2011) looked at the H:H ratio on CT scans of patients with CVT and showed that these patients have a higher mean H:H ratio of 2.20 than those without CVT of 1.44. Consequently, H:H ratio of >1.8 was strongly associated with the presence of thrombosis. Buyck et al (Buyck et al., 2013) who reported that patients with and without CVT have H: H ratios of 1.91 and 1.33, respectively. Our study proposes the Hounsfield Unit: hematocrit ratio (H: H ratio) was calculated for all patients with a median value and interquartile range of 1.5. The H: H ratio in control patients had a median value of 1.4 which was significantly lower p =0.005 when compared to the CVT group 1.6. Furthermore, study of Bonatti et al. (Bonatti et al., 2021) noticed that the mean attenuation of patent sinus segments correlated significantly with hematocrit values, but the correlation was only weak Spearman r = 0.19. In our study, we got a correlation between significant hematocrit with attenuation levels, but the correlation was weak (r = 0.13). However, this

weak correlation was statistically significant in our sample (p<0.001).

When the blood urea nitrogen/creatinine BUN/Cr ratio increases, it is often regarded as an indicator of dehydration. Although a negative correlation was initially observed between BUN/Cr and average HU, this correlation disappeared when the results were controlled for HCT (Black et al., 2011; Buyck et al., 2013). There were other reasons for dehydration, such as anima patients, steroid therapy, gastrointestinal bleeding, and nitration (Uchino, Bellomo, & Goldsmith, 2012). According to Shayganfar et al. (Shayganfar et al., 2019) the mean BUN/Cr ratio was 18.07, ranging from 1.5 to 110. There was a significant and negative correlation between the BUN/Cr and average attenuation for the sinuses, with p values of 0.004, 0.000, 0.002, 0.008, and 0.01, respectively (Shayganfar et al., 2019). We also observed a negative correlation between BUN/Cr (p > 0.05). The significant correlation between BUN/Cr and average attenuation in the four sinus segments disappeared upon controlling for HCT level. In our results, we noticed BUN readings of 3.8 [2.8, 4.8] and creatinine 59.0 [48.0, 70.0]. The differences between the two studied groups for creatinine and BUN levels were not statistically significant (p > 0.05).). According to Shikdar et al. (Shikdar et al., 2022) INR usually ranges between 1.0 and 1.1 for non-anticoagulated patients I observed 99 patients, most of whom had an INR of 1.1 [1.0,1.2]. Therefore, there was no correlation between INR and CVT.

Shayganfar et al (Shayganfar et al., 2019) point out thrombosis in each sinus, such as SSS, which occurred in 31.4% of patients, while I detected 21.9% of patients had thrombosis in SSS. Secondly it was also reported by Shayganfar et al (Shayganfar et al., 2019) that LSS was found in 28.6% of patients, whereas I observed it in 20.0% and they found RSS in 31.4% of patients, while I got 19.5% in RSS. In Shayganfar et al (Shayganfar et al., 2019), thrombosis of the left transverse sinus was point out in 48.6% of patients, and the right transverse sinus was affected in 51.4%. In my study, I observed that the left transverse sinus had a thrombus in 20.9% of patients, and the right transverse sinus had a thrombus in 21.4% of patients (Fig 3).

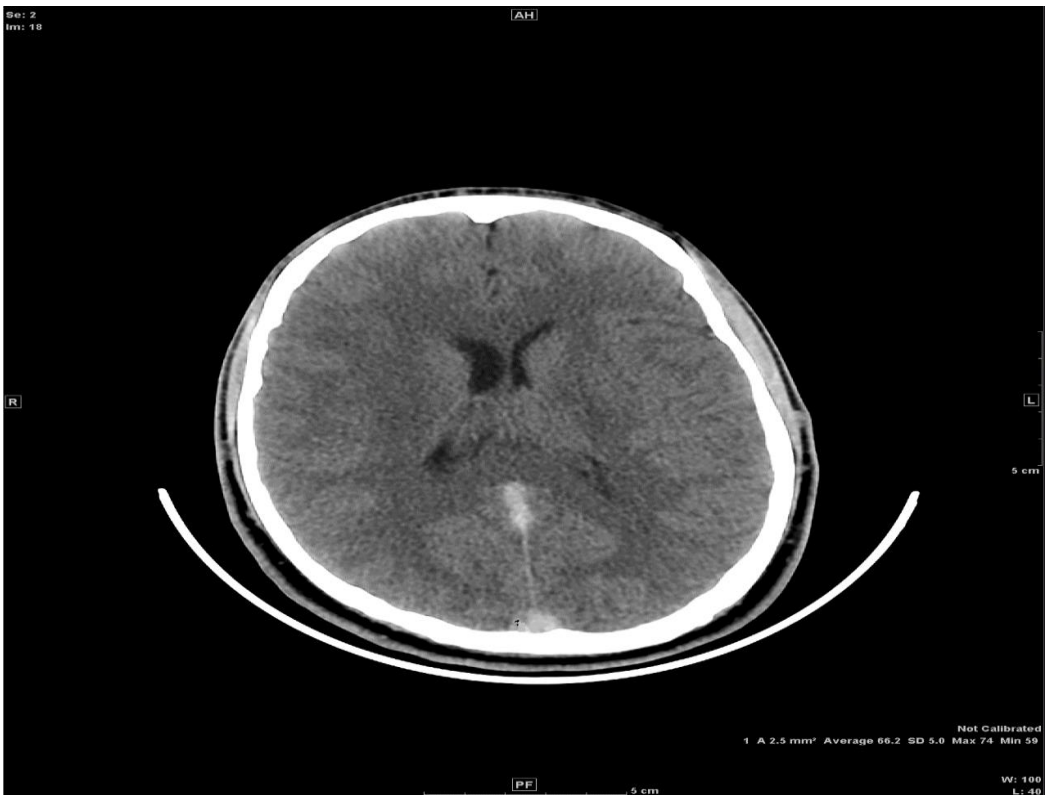


Fig9, A 26-year-old young adult showing a superior sagittal sinus CVT with an extended falx cerebri thickening. The non-enhanced axial CT image shows a hyper attenuated the SSS and region of interest (2.2mm ,66.2HU)

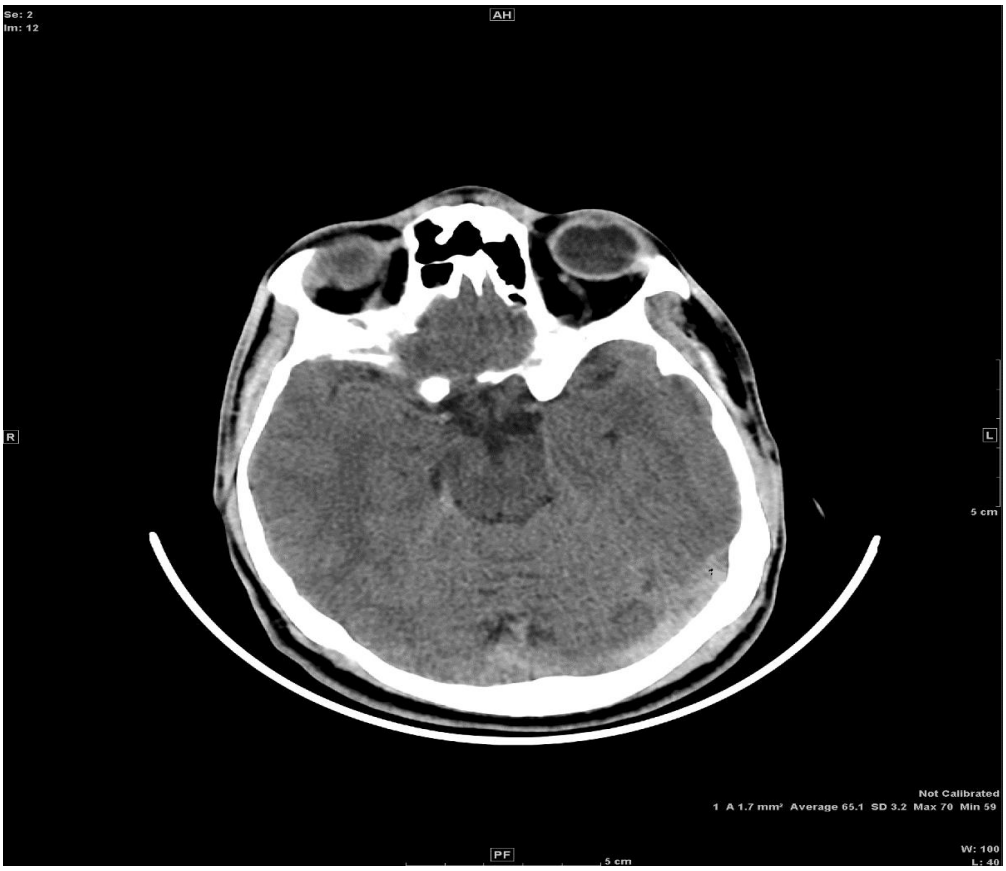


Fig 10, Axial non-enhanced CT images show areas of abnormal hyper attenuation indicative of CVT in the left transverse sinus region of interest (1.7mm 65.1HU).

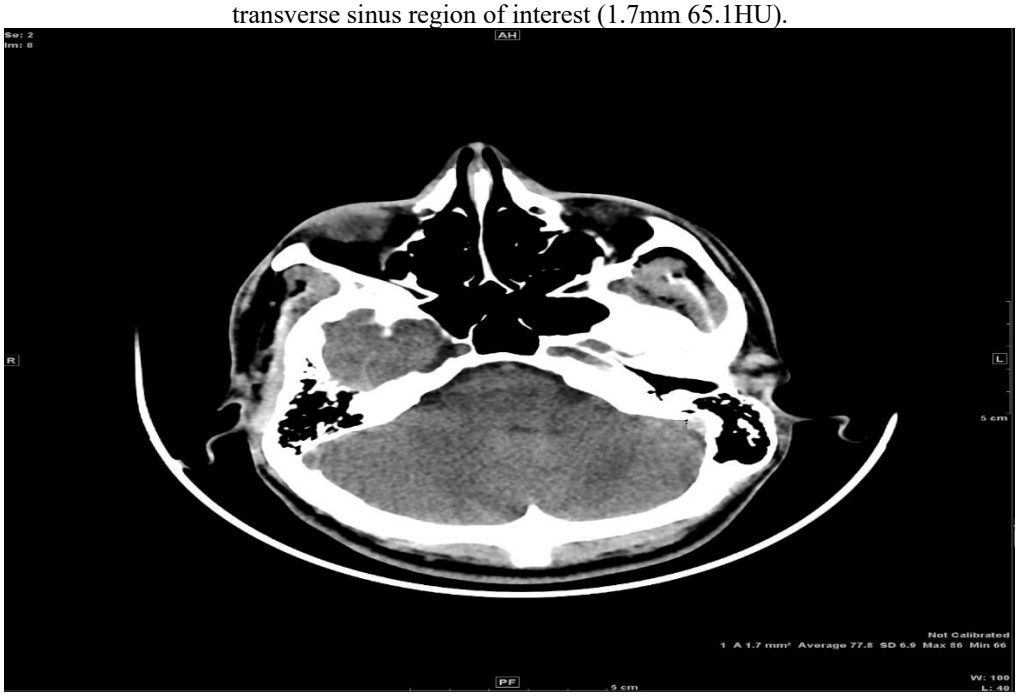


Fig11, Left sigmoid sinus thrombus. Axial non-enhanced CT image reveals a hyperattention of the left sigmoid sinus (region of interest, 1.7mm ,77.8 HU)

According to (Canakci et al., 2021), the most common presentation was headache, observed in 56% of patients. Also, I got most frequently reported symptom was headache, which was reported at presentation in (60.5%) of patients. Uluduz et al. (Uluduz et al., 2020) found nausea and vomiting (33%) patients. In our study, we had 9.5% of patients followed by seizures, whereas Canakci et al. (Canakci et al., 2021) observed 34% of patients, and Uluduz et al. (Uluduz et al., 2020) point out 34% of patients. I detect seizure was reported in (10%) of the patients. Canakci et al. (Canakci et al., 2021) found that the sign of CVT such as focal motor deficits 27% while I got 10% of patients, papilledema 9.9% patients. (AlSheef et al., 2020) spotted those oral contraceptive pills (OCP) were the most frequently reported risk factor, while I observed 6.5% of them impacted by OCP. I found the highest risk factor was OCP. It was eight patients, 7.9% for the control group and five patients, 5.1% for the CVT group. There was no significant difference in the reported risk factors between the control and CVT groups due to insufficiently documented history or incomplete investigation of potential risk factors during hospitalization or outpatient follow-up Table 5 figure 4. Shayganfar et al. (Shayganfar et al., 2019) spotted in attenuation >60.4, HU was the best-optimized cut-off with an AUC of 0.918 (0.848–0.962) that had 71.4% sensitivity and 100% specificity for detecting the CVT. Canakci et al. (Canakci et al., 2021) establish 66 HU as a cut-off value, the attenuation had an AUC of 0.89 ($p < 0.0001$), resulting in a sensitivity of 93% and a specificity of 98%. (ROC) analysis showed that a cut-off value of 63 HU enables the identification of segments with thrombosis with 52% sensitivity and 88% specificity (Bonatti et al., 2021). In our study, We observed the CVT optimal cut off attenuation value for all Dural or superficial sinuses was 62 HU with a sensitivity of 66.82%, a specificity of 89.45%, and an AUC of 0.831.

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CONCLUSION:

CVT is a common cause of cerebrovascular events, but it is difficult to diagnose due to its highly variable and non-specific presentation. Such as headaches and seizures. In emergency cases, non-enhanced head CT is still the most appropriate test for screening patients with non-specific neurological symptoms. This retrospective study is being conducted to identify appropriate HU for NCCT and laboratory predictors such as hematocrit, blood urea nitrogen, creatinine, and INR for the accurate and rapid diagnosis of CVT. Our study noticed that most patients with CVT were females, and there was a significant difference in gender and age. Patients with CVT had a median age of 40.7. Our results showed a mean hematocrit for positive patients of 37. In comparing laboratory findings with attenuation values and making a final decision on whether to confirm CVT, radiologists should consider the patient's age. We determined that the optimal CVT cut-off attenuation value for all Dural or superficial sinuses was 62 HU with a sensitivity of 66.82%, a specificity of 89.45%, a positive predictive value (PPV) of 64.5%, a negative predictive value (NPV) of 90.38%, and an AUC of 0.831. Our study suggests the (H: H ratio) was calculated for CVT group 1.6 and the correlation between hematocrit and attenuation levels was significant, but the correlation was weak ($r = 0.13$). The BUN reading was 3.8 and the creatinine 59.0, too. The differences between the two studied groups for creatinine and BUN levels were not statistically significant ($p > 0.05$). Most of the CVT patients had an INR of 1.1, and we did not find a correlation between INR and CVT. The superior sagittal sinus was thrombosed in 21.9% of patients, followed by the right transverse sinus (20.9%) and the right sigmoid

(19.5%). Headache was most frequently reported as a symptom. Patients with focal motor deficits of 10% and papilledema of 9.9% showed signs of CVT. The most-reported risk factor was OCP. The values of Hounsfield units are affected by a variety of factors, including thrombosis location, hydration status, and etiology. By measuring the Dural or superficial sinus attenuation, it is possible to obtain more reliable findings and to utilize any brain NCCT better, and take into consideration age, laboratory results, and any factors affecting the Dural sinus. The Hounsfield measurement unit in non-enhanced CT helps the radiologist be confident in the decision-making in the diagnosis of the patient and helps the clinician with rapid treatment.

Abbreviations:

HU Hounsfield Unit
CVT Cerebral venous thrombosis
NCCT Non-enhanced computed tomography
CTV Computed Tomography venogram
SSS Superior sagittal sinus
TS Transverse sinuses
SS Sigmoid sinuses
BUN Blood urea nitrogen
HCT Hematocrit
INR International normalized ratio
Cr Creatinine
H:H ratio Hounsfield Unit: hematocrit ratio

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