**Table: 1 Risk factors and etiology22**

**Genetic thrombophilias**

Antithrombin III deficiency

Protein C and S deficiency

Factor V Leiden mutation (FVR506Q)

Prothrombin gene mutation (G20210A)

Hereditary homocyteinemia / homocysteinuria

Factor XII gene polymorphism

**Acquired thrombophilias**

Antiphospholipid antibodies

Hyperhomocysteinemia

Nephrotic syndrome

Pregnancy and puerperium

Increased Factor VIII concentration

**Hematological disorders**

Primary and secondary polycytemia

Essential thrombocytosis

Leukemias, Lymphomas

Anemias (iron deficiency, Sickle cell, thalassemia, and others)

Paroxysmal nocturnal hemoglobinuria

Use of erythropoietin

High altitude

**Infections**

Meningitis and brain abscess

Otitis, mastoiditis, sinusitis, tonsillitis, and dental infections

Sepsis

**Systemic inflammatory diseases**

Systemic lupus erythematosis

Sarcoidosis, Wegener’s granulomatosis

Behcet’s disease

Inflammatory bowel disease (ulcerative colitis, Crohn’s disease)

**Drugs and natural products**

Oral contraceptives

Steroids

Cytostatics

Talidomide

Tamoxifen

L-Asparaginase

Estrogen-like substance including phytogenics

**Local and mechanical causes**

Brain tumors

Arteriovenous malformations

Neurosurgical operations

Lumbar puncture

Trauma to face, maxillary sinuses, and cervical veins

Catheterization of cervical veins

Hypoxia

**Others**

Spontaneous intracranial hypotension

Malignancies

Dehydration

Thyrotoxicosis

Down syndrome

**OBSEVATIONS AND RESULTS (Table no 2 to 21, Figures 1&2 in supplemental data)**

**Table 2: Distribution of patients according to duration of symptoms Mode of Onset and sex.**

|  |  |  |
| --- | --- | --- |
| **Sex** | **Duration of symptoms** | **Total** |
| **≤48 Hr** | **3-30 Days** | **≥30 Days** |
|   | Female | 15(37%) | 19(46%) | 7(17%) | 41 |
| Male | 4(13%) | 21(70%) | 5(17%) | 30 |
| Total | 19(27%) | 40(56%) | 12(17%) | 71 |

 Acute (≤48 hrs), Sub-acute (3-30 days), Chronic (≥30 days)

**Table 3: Predictors of seizure.**

|  |  |  |
| --- | --- | --- |
| **Risk factors** | **Odds Ratio** | **95% Confidence Interval** |
| Headache  | 2.567 | .712- 9.254 |
| Pregnancy, postpartum related  | 1.394 | .857-2.262 |
| Fever | 0.638 | .307-1.323 |
| red sensorium | 4.755 | 1.256-17.99 |
| Speech impairment | 4.754 | .727-31.093 |
| Focal neurological deficit | 3.78 | 1.286-11.113 |
| Raised ICT | 1.367 | .769-2.343 |
| mRS>2  | 3.11 | 1.231-7.878 |
| Anemia | 1.25 | .685-2.249 |
| Vomiting | 0.3 | .2-.5 |
| Parenchymal lesion in MRI | 11.1 | 3.3-41.8 |

**Table 04: Difference between male and female in clinical presentation.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Symptoms present** | **Male** | **Female** | **P-value** | **Odds ratio** | **95% Confidence Interval** |
|  | **Female** | **Male** | **Female** | **Male** |
| Fever | 2 | 18 | **0.001** | **1.966** | 0.182 | 1.42-2.79 | .048-.694 |
| Headache | 26 | 34 | 0.667 | 0.89 | **1.192** | .541-1.466 | .518-2.743 |
| Seizure  | 15 | 26 | 0.258 | 0.788 | **1.367** | .514-1.28 | .797-2.343 |
| Vomiting  | 12 | 18 | 0.742 | **1.07** | 0.911 | .718-1.593 | .521-1.592 |
| Altered sensorium  | 5 | 13 | 0.153 | 0.731 | **1.698** | .499-1.0730 | .765-3.770 |
| Psychiatry manifestation  | 2 | 2 | 0.741 | 0.859 | **1.196** | .316-2.33 | .431-3.318 |
| Blurring of vision | 10 | 20 | 0.193 | **1.302** | 0.683 | .880-1.925 | .377-1.239 |

**Table 5: Distribution of focal neurological deficit.**

|  |  |  |
| --- | --- | --- |
|  | **Frequency** | **Percent** |
| Normal on neurological examination | 37 | 52 |
| Unconscious | 13 | 18 |
| B/L weakness(asymmetrical) | 4 | 5.6 |
| Left side weakness | 7 | 9.9 |
| Paraparesis | 2 | 2.8 |
| Right side weakness | 8 | 11.3 |
| Total | 71 | 100 |

**Table 06: Hemoglobin, peripheral smear and sex distribution.**

|  |  |  |
| --- | --- | --- |
| **Sex** | **PBF(Peripheral blood film)** | **Total** |
| **Dimorphic** | **Macrocytic** | **Microcytic hypochromic** | **Normocytic normochromic** |
| Female | HB | <11(P) | 3 | 0 | 19 | 3 | **25** |
| ≥11(P) | 2 | 0 | 0 | 2 | 4 |
| <12(NP) | 1 | 0 | 6 | 2 | **9** |
| ≥12(NP) | 0 | 1 | 0 | 2 | 3 |
| TOTAL | 6 | 1 | 25 | 9 | 41 |
| Male | HB | <10 | 0 | 0 | 1 | 0 | **1** |
| <11 | 1 | 0 | 0 | 1 | **2** |
| <12 | 0 | 0 | 0 | 1 | **1** |
| <13 | 0 | 2 | 1 | 2 | **5** |
| ≥13 | 0 | 2 | 0 | 10 | 12 |
| **≥16.5** | **0** | **0** | **0** | **9** | **9** |
| Total | 1 | 4 | 2 | 23 | 30 |
| Total | **7** | **5** | **27** | **32** | 71 |

Anemia was defined as hemoglobin level <13 g/dl in males (>15yrs) and <12 g/dl in non-pregnant women and < 11g/dl pregnant women (World Health Organization (2008). *Worldwide prevalence of anemia 1993–2005*).

**Table 07: Lipid profile of CVST Patients.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Lipid Profile Normal Value** | **Lipid profile** | **Number of pts** | **Percent (%)** |
|
| ·          Total Cholesterol(CH) >240mg/dL | Normal | 50 | 62 |
| ·          Triglycerides(TG) >200mg/dL | CH (↑)TG()↑ HDL(↓) | 2 | 2.8 |
| ·          Low-density lipoprotein(LDL) | CH(↑) TG(↑) | 4 | 5.6 |
| >160mg/dL | TG(↑) HDL(↓) | 1 | 1.4 |
| ·          High-density lipoprotein (HDL) <35(F), <45(M)mg/dl | CH(↑) HDL(↓) | 4 | 5.6 |
|  | HDL(↓) | 5 | 7 |
|   | TG(↑) | 3 | 4.2 |
|   | CH(↑) | 2 | 2.8 |

**Table 08: Rheumatology investigation.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Rheumatology investigation** | **No. of pts** | **Percent (%)** |
| CRP | Positive | 33 | 46.5 |
| Negative | 38 | 53.5 |
| RA | Positive | 5 | 7 |
| Negative | 66 | 93 |
| ANA/Anti ds-DNA | Positive | 2 | 2.8 |
| Negative | 67 | 94.4 |
| + C-ANCA | 1 | 1.4 |
| +Anti RO/LA | 1 | 1.4 |
| **Sex** | **CRP** | **Total** | **Chi-Square Tests** |
| Positive | Negative | .002 |
| Female | 26(63.4%) | 15(36.6%) | 41 |
| Male | 7(23.3%) | 23(76.7%) | 30 |
| Total | 33(46.5%) | 38(53.5%) | 71 |

**Table 09: Serum homocysteine and sex relationship.**

|  |  |
| --- | --- |
| **Homocystine and sex relationship** | **Chi-Square Tests** |
|   | SEX | Total (40/71) |   |
| F | M | 0.003 |
| Homocystine | <15 | 7 | 9 | 16(40%) |   |
| >15 | 9 | 15 | 24(60%) |   |

Hyperhomocysteinemia was defined as serum homocysteine >15 mg/100 ml in patients below 60 years.

Serum homocysteine level was done in 40 patients.

**Table 10: D-dimer and sex relationship.**

|  |  |
| --- | --- |
|  **D-dimer**  | **Chi-Square Tests** |
|   | SEX | Total(32/71) | 0.001 |
| F | M |
| D-DIMER | <500 | 2(18%) | 2(9%) | 4(12%) |
| >500 | 9(82%) | 19(90%) | 28(88% |

D-dimer was done only in 32 patient.

**Table 11: Prothrombotic conditions.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Prothrombotic conditions** | **Positive** | **Negative** | **Done in no. pts**  |
| Protein-C (%) deficiency | 6(25%)[5male,1female] | 18(75%) | 24 |
| Protein-S(%) deficiency | 1(4%)[male] | 23(96%) | 24 |
| Anti Cardiolipin (GPL/MPL) | 1(2.5%)Female | 39(97.5%) | 40 |
| Anti Phospholipid (U/ML) | 1(2.5%)Female | 39(97.5%) | 40 |
| β-2 Glycoprotein (U/ML) | 1(2.5%)Female | 39(97.5%) | 40 |
| Methylene tetrahydrofolate reductase (MTHFR) 677TT Mutation | 4(25%)(3 Hetrozygous,1 homozygous) [3 male+1 female] | 12(75%) | 16 |
|
| Prothrombin G20210A Mutation | 2(17%) (heterozygous) (17%) only male | 10(83%) | 12 (only male) |
| Von Willebrand factor (VWF) | 8(28.57%) [3 female + 5 male] | 28(71.45%) |   |
| Antithrombin III, Resistance to activated protein C, factor V Leiden gene mutation |  Not done due economic issue |

**Table 12: NCCT Head and parenchymal lesion.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Location of parenchymal lesion** | **Right** | **Left** | **Bilateral** | **Total** |
| Frontal | 5 | 8 | 7 | 20 |
| Parietal | 1 | 3 | 1 | 5 |
| Temporal | 2 | 0 | 0 | 2 |
| Fronto parietal | 2 | 4 | 3 | 9 |
| Fronto temporal parietal | 1 | 4 | 2 | 7 |
| Fronto temporal | 1 | 0 | 0 | 1 |
| Parieto temporal | 1 | 3 | 0 | 4 |
| Basal ganglia and thalamus with intra ventricular hemorrhage | 0 | 0 | 4 | 4 |
|   | 13 | 23 | 16 | 52 |
| Normal NCCT | 19 |   |

The secondary signs of CVST in NCCT head including cerebral swelling, edema, and/or hemorrhage or infarction and subarachnoid hemorrhage.

**Table 13: NCCT and direct sign of CVST.**

|  |  |
| --- | --- |
| Isolated superior sagittal sinus (dense triangle sign) | 8 |
| SSS (dense triangle sign) with right transverse sinus hyperdensity (RT TS) | 1 |
| SSS (dense triangle sign) with left transverse sinus hyperdensity (LT TS) | 5 |
| Lt transverse sinus hyperdensity (LT TS) | 3 |
| Rt transverse sinus hyperdensity (RT TS) | 3 |
| Total sinus involved | 26 |

Superior sagittal sinus was in 14 and transverse sinus was in 12 patients involved.

NCCT head and direct signs of CVST including hyper dense Dural sinus, dense triangle sign

**Figure 1: NCCT and direct sign of CVST.**

**Table 14: Distribution of parenchymal lesion on MRI.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Parenchymal lesion** | **Right** | **Left** | **Bilateral** | **Total** |
| Frontal | 1 | 5 | 6 | 12 |
| Parietal | 1 | 2 | 1 | 4 |
| Temporal | 2 | 3 | 0 | 5 |
| Fronto parietal | 1 | 4 | 4 | 9 |
| Parieto temporal | 3 | 3 | 0 | 6 |
| Fronto temporal | 1 | 2 | 0 | 3 |
| Fronto temporo parietal | 2 | 3 | 1 | 6 |
| Basal ganglia and thalamus  | 0 | 0 | 3 | 3 |
| Total parenchymal lsesion  | 11 | 22 | 15 | 49 |
| IIH  | 4 | 53 |

MRI Brain normal in 15 patients and not done in 3 patients.

MRI brain and secondary signs of CVST including cerebral swelling, edema, and/or hemorrhage, infarction and subarachnoid hemorrhage.

**Table 15: Direct signs of CVST on MRI brain.**

|  |  |  |
| --- | --- | --- |
| **Sinus** | **Number** | **Total sinus** |
| Isolated superior sagittal sinus(SSS) | 15 | Superior sagittal  | 28 |
| Superficial with deep system(all) | 2 | Lt transverse | 8 |
| Superior sagittal sinus with LT transverse sinus  | 6 | Rt transverse | 7 |
| Superior sagittal sinus with RT tranverse sinus | 2 | Sigmoid sinus | 3 |
| Superior sagittal sinus, LT transverse, sigmoid sinus and internal jugular vein  | 1 | Internal jugular vein | 2 |
| Superior sagittal sinus, RT transverse, sigmoid, internal jugular vein | 1 | Straight sinus | 1 |
| Superior sagittal sinus with bilateral transverse | 1 | 49 |
| LT transverse | 0 |
| R T transverse | 2 |
| Superior sagittal sinus with RT transverse sigmoid and straight sinus and deep system | 1 |

MRI brain and direct signs of CVST including absence of a flow void with alteration of signal intensity in the dural sinus.

**Figure 2: Direct signs of CVST on MRI brain.**

**Table 16: MRV BRAIN FINDING ACCORDING INVOLVED SINUS.**

|  |  |  |
| --- | --- | --- |
| **Sinus** | **Number** | **Total**  |
| **Isolated superior saggital sinus** | **21** | **Superior saggital sinus** | **58** |
| **Superior saggital sinus with LT transverse**  | **4** | **LT transverse** | **34** |
| **Superior saggital sinus with RT transverse** | **2** | **RT transverse**  | **24** |
| **Superior saggital sinus, LT transverse, sigmoid, internal jugular vein**  | **13** |  **RT sigmoid sinus with internal jugular vein** | **9** |
| **Superior saggital sinus, RT transverse, sigmoid, internal jugular vein** | **9** | **L T sigmoid sinus with internal jugular vein** | **13** |
| **Superior saggital sinus with bilateral transverse** | **6** | **Thrombosis with collateral**  | **9** |
|  **isolated LT transverse** | **8** | **Only cortical vein**  | **1** |
|  **isolated RT transverse** | **3** | **Cortical vein with other sinus** | **3** |
| **Superior saggital sinus with bilateral transverse, straight sinus with deep system** | **3** | **Superficial and deep both system** | **3** |

**MRV brain not done in one patient and one patient expired before MRV.**

**Table 17: Duration of warfarin in months.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Months** | **3-6months** | **12months** | **Continue** | **Total** | **Total** | **Death** |
| Female | 37 | 2 | 1 | 40 | 69 | 2 females |
| Male | 20 | 1 | 8 | 29 |

**Table 18: No. of antiepileptic in individual patients.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Single** | **Double** | **Three** | **Total no patients(40/41) 01patient expired during hospitalization** |
| 28 | 7 | 5 | 40 |

**Table 19: Follow up of MRV result.**

|  |  |  |
| --- | --- | --- |
|   | **Frequency** | **Percent** |
| Complete Recanalisation | 17 | 23.9 |
| Partial Recanalisation | 1 | 1.4 |
| Partial Recanalisation & collateral | 8 | 11.3 |
| **Not done** | **40** | **56.3** |
| Loss to follow up | 3 | 4.2 |
| Expired | 2 | 2.8 |
| Total | 71 | 100 |

**Table 20: mRS and GCS on follow up at 1 month, 3 month and 6 month.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **mRS** | **On admission** | **1 month** | **3 month** | **6 month** | **GCS** | **On admission** | **1 month** | **6** |
| **month** |
| 0 | 0 | 45 | 47 | 50 | **3** | 7 | 1 | 0 |
| 1 | 42 | 5 | 8 | 10 | **5** | 1 | 0 | 0 |
| 2 | 10 | 9 | 9 | 3 | **10** | 4 | 0 | 1 |
| 3 | 6 | 7 | 2 | 2 | **12** | 3 | 1 | 0 |
| 4 | 7 | 3 | 3 | 1 | **13** | 4 | 3 | 1 |
| 5 | 6 | 1 | 0 | 1 | **14** | 2 | 7 | 5 |
| 6 | 0 | 1 | 2 | 2 | **15** | 50 | 58 | 59 |
| Loss to follow up | 0 | 1 | 2 | 3 | 0 | 1 | 3 (2 died) |

**Table 21: Predictors of mRS & GCS on admission, 1 month, 3 month and 6 month.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Prognostic factor** | **mRS at admission** | **mRS at 1 month** | **mRS at 3 month** | **mRS at 6 month** | **GCS at admission** | **GCS at 1 month** | **GCS at 3 month** | **GCS at 6 month** |
| Sex(f) | **0.041** | 0.679 | 0.696 | 0.99 | 0.017 | 0.904 | 0.936 | 0.937 |
| Pregnancy related  | **0.058** | 0.77 | 0.91 | 0.677 | **0.058** | 0.791 | 0.682 | 0.574 |
| Headache | 0.742 | 0.466 | 0.244 | 0.296 | 0.548 | 0.396 | 0.137 | 0.83 |
| Fever | **0.047** | 0.823 | 0.994 | 0.773 | **0.033** | 0.156 | 0.306 | 0.66 |
| Vomiting | 0.326 | 0.679 | 0.377 | **0.023** | 0.141 | 0.66 | 0.171 | **0.049** |
| Altered sensorium | **0.0002** | 0.125 | **0.003** | **0.019** | **0.0003** | 0.223 | **0.043** | 0.162 |
| Blurring, of vision | **0.019** | 0.14 | 0.116 | 0.943 | 0.548 | 0.396 | 0.137 | 0.83 |
| Seizure | **0.003** | 0.699 | 0.452 | 0.577 | **0.006** | 0.635 | 0.171 | 0.306 |
| Speech | **0.0001** | **0.026** | **0.005** | **0.002** | **0.0007** | **0.004** | **0.021** | **0.016** |
| Pallor | **0.029** | **0.05** | **0.049** | 0.283 | **0.013** | 0.1 | 0.359 | 0.321 |
| Cranial nerve involvement | **0.0002** | 0.081 | 0.062 | 0.33 | **0.0003** | **0.014** | 0.184 | 0.026 |
| BMI | 0.073 | 0.162 | 0.073 | 0.64 | 0.07 | 0.954 | 0.109 | 0.583 |

**DISCUSSION: (Table no 22 to 24 in supplemental data)**

**Table 22: Comparison of clinical feature of our study with old Indian series.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Clinical finding** | **Bansal11** | **Srinivasan12** | **Nagaraja19** | **Present study** |
| **n=138(%)** | **n=135(%)** | **n=405(%)** | **N=71(%)** |
| 1. Fever | 62 | 16 |  | **28** |
| 2. Headache | 48 | 24 | 70.8 | 85 |
| 3. Vomiting | 36 | 24 | 38 | 42 |
| 4. Seizures |  |  |  |  |
| i.GTCS | 29 | 50 | 39.7 | 31 |
| ii.Focal | 17 | 22 | 30.1 | 25.3 |
| 5. Dysphasia | 25 | 5 | - | - |
| 6. Diplopia | 1 | - | - | 42 |
| 7. Nuchal rigidity | 3 | 10 | 13 | Na |
| 8. Deep leg vein thrombosis  | **10** | - | - | 7.04 |
| 9. Altered sensorium | 41 | 43 | 58 | 10 |
| 10. Papillodema | 35 | 16 | 18.5 | **42.7** |
| 11. Ocular palsy | - | 2 | 11 | 26.8 |
| 12. Motor deficit | 69 | 49 | 66.4 | 30 |

**Table 23: Comparison in relation to other studies of recanalization on follow up.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Study** | **No. of patients** | **Partial recanalization at 3 to 6 month, no.** | **Complete recanalization at 3 to 6month, no.** | **Partial recanalization at 1 yr or more, no.** | **Complete recanalization at 1 yrs or more, no.** |
| Stolz et al55 | 37 | 7 | 19 | 7 | 20 |
| Baugmatner et al,35 2003 | 33 | 15 | 18 | 15 | 18 |
| **Present study** | 26 | 8 with Collateral | 17 | 1 | na |

na=Not assessed

**Table 24: Comparison of mortality with other studies.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Study** | **Years** | **No. of patients** | **Mortality rate (%)** |
| Khealani BA7 | 2008 | 109 | 9 |
| Azin H41 | 2008 | 61 | 9 |
| Stolz E55 | 2005 | 79 | 15 |
| ISCVT22 | 2004 | 624 | 4 |
| Present study | **2015** | **71** | **2.8** |