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Original Research Article

Homocysteine level and venous stasis

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ABSTRACT

BACKGROUND: Venous stasis is a common vascular disorder with an incidence of 5,00,000 cases per years.

AIM AND OBJECTIVES: To study the levels of homocysteine in patients with Venous stasis.

MATERIAL AND METHODS: This prospective non-randomized case controlled study was conducted on 100 patients. The patients were divided into two groups. Group A included 50 patients who had clinical features suggestive of Venous stasis and diagnosis confirmed on color doppler. Group B included 50 patients who did not have clinical features suggestive of any venous or arterial disorder. The informed consent was obtained from every participating patient.

RESULTS: In group A commonest age involved was 21-30 years with mean age of 37.32 years. Male patient of venous stasis as compared to females in group A and male to female ratio was 1.27:1. BMI range in group A was 18.5-24.99 kg/m2 with a mean of 22.61±3.47. In group A, there were 28 patients of left leg venous stasis as compared to 18 patients of right leg venous stasis with a ratio of 1.56:1. Four patients in group A had bilateral venous stasis. Commonest presenting symptoms were swelling and pain of the lower limb presenting in 100% and 98% of the patients, respectively. 48% patients in group A had symptoms for duration of 1 to 5 days. 46% patients who were not having any of the risk factors present and 54% patients had one or more than one risk factors. Swelling of the lower limbs was present in all cases of group A while calf tenderness and Homan's sign were present in 82% and 80% of the patients respectively. Seventy two percent of patients had proximal venous stasis. In group A mean homocysteine level was 20.33±14.73 while in group B, it was 1.14±19.9 showing significant difference that serum homocysteine levels raised in venous stasis patients in group A as compared to group B. In group A, the venous stasis prevalence of hyperhomocysteinemia was 58% as compared to 16% in group B control patients with statistically significant association. There were 23 patients of idiopathic venous stasis out of 50 patients in group A. The prevalence of hyperhomocysteinemia in these patients was 65.22% while it was 51.85% in patients of secondary venous stasis and statistically found to be significant.

CONCLUSION: The prevalence of hyperhomocysteinemia in cases of venous stasis in present study was 58% as compared to 16% in control group which was statistically significant. In patients with idiopathic venous stasis, the prevalence of hyperhomocysteinemia was higher as compared to patients of secondary venous stasis. Hence, we suggest the measurements of serum homocysteine levels in all cases of Venous stasis especially in cases where no predisposing risk factor is present and patients of Venous stasis in younger population so that the necessary measures required to reduce the levels of serum homocysteine can be taken.

Keywords: Homocysteine, Venous Stasis

INTRODUCTION

Venous stasis is a common vascular disorder.[1] It has an incidence of 5,00.000 cases per year.[2] Approximately 1 million patients annually undergo investigations for suspected Venous stasis in North America.[3] It is characterized by the formation of a semi solid coagulum or thrombus or a blood clot in the lumen of the deep veins.[2] Venous stasis occurs in 20-30% of patients after major surgical operations.[2] When prophylactic measures are not used, it

may occur in 40-50% of patients after major gynaecological and orthopaedic especially pelvic surgeries.[4] Data from a study, published since 1976 with a combined population of about 19 million persons, showed an incidence of 50 per 1,00,000 for the primary cases of venous stasis for whole of the population. Venous stasis occurred rarely below 20 years but the incidence increased with age, so that in people over 70 years, the rate was 200 per 1,00,000.[1-4] Incidence was same in men and women.[5] The causes of venous stasis were cancer or previous hospital admission for about quarter to a third of cases respectively.[5] More than 90% of patients who develop pulmonary embolism have mortality rate of 18% to 30% without treatment.[6]

In a population of general surgery patients who did not receive prophylaxis and who mostly had undergone elective abdominal surgery, there was a 19% incidence of Venous stasis, a 7% incidence of proximal venous stasis and 1.6% incidence of pulmonary embolism (PE) with 0.9% of patients experiencing fatal PE.[2] The factors which predispose to venous thromboembolism were initially described by Virchow in 1856 and include a triad of hypercoagulability, endothelial damage or intimal changes and reduced blood flow or stasis. However factors relating to platelet activity and fibrinolytic potential of blood are also associated with venous stasis. The consequences like pulmonary thrombosis and chronic venous insufficiency following venous stasis make the accurate and timely diagnosis of venous stasis important.

Venous stasis effect the leg veins usually. Occasionally veins of the arms are affected. If it occurs spontaneously, this condition is known as Paget Schrotter disease.[7] Bernstein reported that clinical diagnosis of ileofemoral venous thrombosis could generally be made from the clinical presentation. The most marked features include unilateral lower extremity pain, oedema and discolouration associated with tenderness in the calf and muscles along the saphenous or femoral vein. Positive Homan's sign also adds to the clinical diagnosis but during eliciting the Homan's sign, thrombus may break off and may lead on to pulmonary embolism. So its usage is limited nowadays. Classically, chief complaint in a patient with venous stasis is painful swollen leg. Location of the swelling is determined by the location of the thrombus. Pathologic states that clinically mimic Venous stasis include cellulitis, osteomyelitis, haematoma, postphlebitic syndrome, lymph nodes enlargement causing extrinsic compression of veins, venous and arterial aneurysm, rupture of inflamed popliteal (Baker's) cyst and heterotrophic ossification.[8]

Early diagnosis of Venous stasis is extremely important since the clot propagation and pulmonary embolism may be prevented to some extent by early anticoagulant therapy which can reduce overall morbidity and mortality and at the same time unnecessary anticoagulant therapy may be prevented.

Various diagnostic tools used for diagnosing venous stasis include venography, colour Doppler, d-dimer assay etc. Venography has traditionally been referred to as gold standard in the diagnosis of Venous stasis because of its ability to demonstrate the whole venous system. But it is an invasive technique and has many drawbacks, such as painful, contrast associated reactions/complications, radiation exposure and cannot be repeated. In the last 20 years colour Doppler has replaced contrast venography as the diagnostic modality of choice in venous stasis. Colour Doppler is noninvasive and highly accurate in diagnosing venous stasis and carries essentially no risk to the patients. For these reasons its usage has increased exponentially over the last decade.

There are a lot of risk factors known for causing venous thromboembolism which include patient related factors like age, obesity, varicose veins, immobility, pregnancy, puerperium, high-dose oestrogen therapy, previous Venous stasis or pulmonary embolism and presence of thrombophilic factors or factors related to diseases or surgical procedures like trauma, surgery (especially procedure on pelvis, hip and lower limb), malignancy (especially pelvic, abdominal or metastatic), heart failure, recent myocardial infarction, paralysis of lower limbs, infection, inflammatory bowel disease, nephrotic syndrome, polycythaemia, paraproteinaemia, paroxysmal nocturnal haemoglobinuria, lupus anticoagulant, Behchet's disease, homocysteinemia.[9] Various thrombophilic factors known to cause venous stasis are: deficiency of anti-thrombin III, protein C or protein S, antiphospholipid antibody or lupus anticoagulant, factor V Leiden gene defect or activated protein C resistance, dysfibrinogenaemias and homocysteinemia.[10]

The most important factor out of above all is a hospital admission for the treatment of a medical or surgical condition. Injury, especially fractures of the lower limbs and pelvis, pregnancy and the oral contraceptive pills are other well-recognised predisposing factors. Endothelial damage is now recognised to be increasingly important. The interaction of the endothelium with inflammatory cells or previous deep vein endothelium damage may render the endothelial surface hypercoagulable and less fibrinolytic. Hyperhomocysteinemia is a known risk factor for development of atherosclerosis and other vascular complications like venous stasis.[11] Thromboembolism of the veins and arteries and premature arteriosclerosis are common causes of death in patients with the inherited disorder like homocystinuria. Vascular episodes may occur in early adolescence and even in childhood. Ten to twenty percent of women and men who suffer a venous stasis have high homocysteine levels, compared to about 5% of people who have not suffered from venous stasis.[12] The higher the homocysteine level, the higher the risk: one analysis of 24 studies found that each 50% increase in homocysteine raised the risk of venous stasis or pulmonary embolism by 60%.[13]

Homocysteine is a sulphur containing amino acid and it is derived from dietary methionine. Its metabolism stands at the intersection of two pathways and its remethylation requires two key enzymes: methionine synthase (MS) and methylenetetrahydrofolate reductase (MTHFR). The MS uses vitamin B_{12} as a cofactor and 5-methyltetrahydrofolate as a methyl donor. When there is an excess of protein or methionine, a larger proportion of homocysteine is metabolized by irreversible transsulfuration pathway, which degrades homocysteine to cysteine. In this, homocysteine is first conjugated to cystathionine by cytathionine beta-synthase (CBS). Cystathionine is further cleaved into cysteine by cystathionine γ-lyase. Both enzymes need Vitamin B6 as a cofactor. Hyperhomocysteinemia acts via various mechanisms: such as increased tissue factor expression, attenuated anticoagulant processes, enhanced platelet reactivity, increased thrombin generation, augmented factor V activity, impaired fibrinolytic potential via impairing with the synthesis of collagen and flbrillin and vascular injury including endothelial dysfunction which lead on to increased potential for venous thrombosis. Molecular mechanisms undergoing prothrombotic actions of homocysteine are incompletely understood and include oxidative stress, DNA hypomethylation and pro inflammatory effects.[14] Thus, the present study was conducted to study the levels of homocysteine in patients with Venous stasis and to compare with normal population.

MATERIAL AND METHODS

This prospective non-randomized case controlled study was conducted in the Department of Biochemistry, Lady Hardinge Medical College, New Delhi. A total of 100 patients were studied. The patients were divided into two groups. Group A included 50 patients who had clinical features suggestive of Venous stasis and diagnosis confirmed on color doppler. Group B included 50 patients who did not have clinical features suggestive of any venous or arterial disorder. The informed consent was obtained from every participating patient.

Group A: In group A patients, a detailed history was taken including the history of predisposing factors like pregnancy / puerperium, oral contraceptive pills intake, history of prolonged immobilization, trauma or any surgery etc. and duration and severity of the illness was recorded. Then a thorough physical examination was carried out. The clinical diagnosis of Venous stasis of lower limbs was suspected on the basis of findings described by Bernstein which included pain in the lower extremity, swelling, skin discoloration, calf tenderness and positive Homan's sign. Doppler ultrasound of Venous stasis was done in all the patients to confirm the diagnosis.

Group B: In group B patients, a detailed history was taken including the predisposing factors and regarding any chronic comorbid conditions like obesity, diabetes mellitus, hypertension and patients having these factors were excluded from group B. Physical examination was done to rule out any venous or arterial disorder in group B patients.

All the patients were subjected to laboratory investigations like haemoglobin, bleeding time, clotting time, urine examination, prothrombin time and index and activated partial thromboplasmin time.

Treatment

All the patients of group A were treated with conventional treatment of Venous stasis by low molecular weight heparin for 7 days followed by oral anticoagulants for a period of 6 months. Dose of heparin and oral anticoagulants was titrated as per activated partial thromboplastin time and prothrombin time and international normalized ratio (INR) levels, respectively. International Normalised Ratio (INR) levels were kept between 2.5 to 3.5.[15] All the patients fulfilling the inclusion criteria were explained about the study and written consent was taken regarding the testing of serum homocysteine levels.

Estimation of homocysteine:

Homocysteine was estimated by immuno assay technology.[16]

Specimen collection and handling

Homocysteine was measured through a routine blood test in all the patients in both groups. After overnight fasting for 12 hours, two ml of venous blood sample was taken.

The following recommendations for handling and storing blood samples were followed by us as given by the Clinical and Laboratory Standards Institute (CLSI).[17]

* All blood samples were collected following universal precautions for venipuncture.
* Blood samples were collected in vaccutainers without any preservations and sent to Department of Biochemistry. There, the vacutainer tubes containing blood samples were kept capped and upright all the time.
* Serum samples were allowed to clot adequately before centrifugation

* Samples were frozen only once and then mixed thoroughly after thawing.

The following additional recommendations were followed for handling and storing blood samples for homocysteine assay:

* Samples were centrifuged to remove serum or plasma from red blood cells at the earliest to ensure accurate measurements. Samples that were not separated soon after collection were stored on ice until centrifugation.

Reagents

All primary reagent pack was mixed by hand before loading them onto the system. Visually inspect the bottom of the reagent pack was inspected to ensure that all particles are dispersed and re-suspended.

	Reagent	**Ingredients**
Primary reagent pack	Lite Reagent	Monoclonal mouse anti-SAH antibody (~0.4µg/mL) labeled with acridinium ester in phosphate buffer with bovine serum albumin and preservatives.
	Solid Phase	SAH (~2.1µg/mL) covalently coupled to paramagnetic particles in phosphate buffer with bovine serum albumin and preservatives
	Enzyme Reagent	Bovine derived S-adenosylhomocysteine hydrolase enzyme (~60 mU/mL) in TRIS buffer with preservatives
Ancillary reagent	Reducing Reagent	Dithiothreitol (~1.5 mg/mL) in citrate buffer with preservatives
	Homocysteine Diluent	Phosphate buffer with bovine gamma globulin and preservatives

Assay Principle

Homocysteine assay is a competitive immunoassay using direct, chemiluminescent technology. The different forms of homocysteine in the patient sample are reduced to free homocysteine by the Reducing Reagent. Free homocysteine is then converted to S-adenosylhomocysteine (SAH) by the Enzyme Reagent. Converted SAH from the patient sample competes with SAH covalently coupled to paramagnetic particles in the Solid Phase for a limited amount of acridinium ester-labelled anti-SAH in the Lite Reagent.

The system automatically performs the following steps:

- Dispenses 20 µL of sample into a cuvette
- Dispenses 50 µL of Reducing Reagent and incubates for 4.7 minutes at 37°C
- Dispenses 50 µL of Enzyme Reagent and incubates for 3.0 minutes at 37°C
- Dispenses 250 µL of Solid Phase and incubates for 3.0 minutes at 37°C
- Dispenses 100 µL of Lite Reagent and incubates for 3.0 minutes at 37°C
- Separates, aspirates, and washes the cuvettes with Wash 1

- Dispenses 300 µL each of Acid Reagent (R1) and Base Reagent (R2) to initiate the chemiluminescent reaction.
- Reports results according to the selected option.

An inverse relationship exists between the amount of Hcy present in the patient sample and the amount of relative light units (RLUs) detected by the system.

Sample volume

This assay requires 20 µL of sample for a single determination. The system reports tHcy results in µmol/L.

Reference value:

Homocysteine normal value = 3.7-13.3µmol/L

Vit. B12 normal value = 200-900 pg/ml

Folic acid normal value = 2-20 ng/ml

In group A patients serum homocysteine levels and B_{12} and folic acid levels were estimated in all the samples by immuno assay. All the patients were given vitamin B_{12}, 1500 µg once a day and folic acid 5 mg once a day along with standard treatment of venous stasis. After 12 weeks of B_{12} and folic acid therapy the homocysteine levels were again estimated. In group B (control group) only homocysteine levels was studied.

Statistical analysis

The collected records and data was analysed statistically by using Student t-test and Chi-square test. A p value of <0.05 was considered statistically significant.

RESULTS

The mean age was 37.32 years with age range of 13 to 65 years in group A while in group B, it was 40.01 years with a range of 17 to 70 years (p>0.05). A total of 28(56%) out of 50 patients of venous stasis in group A and 26(52%) patients in group B were males as compared to 22(44%) and 24(48%) female patients in these groups respectively (p >0.05).

In group A, BMI of the patients ranged from 17.48 to 36.11 with mean BMI of 22.61±3.47. Majority of the patients were in BMI range of 18.5-24.99 in both the groups. There was only 1 case of obesity (BMI >30) in group A patients of venous stasis (p>0.05). In group A, out of 46 patients with unilateral venous stasis, there were 28 patients (56%) with left leg venous stasis and 18 patients (36%) with right leg venous stasis. Upper limb was not involved in any patient. Four patients (8%) in group A had bilateral venous stasis.

In group A, pain and swelling were the most consistent presenting symptoms with a prevalence of 98% and 100% respectively. Skin discoloration was seen in 24% (12 out of 50) patients and fever was present in 4%(2 out of 50) patients. In group A, the duration of symptoms ranged from 2 days to 20 days. There were 24(48%) patients presenting in 1-5 days, 16 (32%) patients in 6-10 days, 6 (12%) patients in 11-15 days and 4(8%) patients presenting very late with more than 15 days duration of symptoms.

A total of 23(46%) were having no risk factor present in the history while there were 22 patients (44%) who were having one risk factor in their presentation and there were 5 patients (10%) who were having >2 risks factors.

Table 1: Distribution of patients in group A with respect to clinical signs

Clinical signs	No. of patients in group A (n=50)	Percentage
Calf tenderness	41	82
Homan's sign	40	80
Difference in calf circumference >3 cm	33	66
Swelling of limb	50	100
Skin discoloration	12	24
Asymmetrical pitting oedema	4	8
Localized tenderness	36	72
Superficial collateral veins	5	10

In group A, 14 patients (28%) were having swelling up to below knee region while 36(72%) were having swelling extending above knee region.

Table 2: Distribution of patients in group A with respect to colour Doppler findings

Colour Doppler showing thrombus	No. of patients in group A (n=50)	Percentage
Upto calf veins	1	2%
Upto popliteal veins	7	14%
Upto femoral veins	28	56%
Upto iliac veins	11	22%
Upto IVC	3	6%

In group B, there was 14 patients (28%) of cholelithasis, 13 patients (26%) of hernia, 5 patients (10%) of benign breast diseases, 4 patients (8%) of lipoma, 3 patients (6%) each of fistula in ano and thyroid diseases, 2 patients (4%) each of hydrocele, varicocele and stoma closure, 1 patient (2%) each of piles and sialadenitis.

Table 3: Serum homocysteine concentration in both the groups

Parameters	Group A (n=50)	Group B (n=50)
Serum homcysteine levels (µmol/L)	20.33±14.73*	8.49±4.48
Range (µmol/L)	2.41-70.54	1.14-19.9

*p <0.001 when compared to group B

Table 4: Prevalence of hyper-homocysteinemia among both groups

Parameters	Group A (n=50)	Group B (n=50)
Hyper homocysteinemia present	29	8
Hyper homocysteinemia absent	21`	42
Prevalence	58%	16%

(Hyper Hcy >13.3 (µmol/L) Odds ratio 7.25, CI 95% 2.827-18.594

In group A, the number of patients having hyperhomocysteinemia was maximum in the age grup of 21-30 years i.e. 11 out of 18(61.11%) patients. The prevalence of hyperhomocysteinemia was 60.46% (26 out of 43) in patients aged less than 60 years as compared to 42.86% (3 out of 7) in patients aged more than 60 years and this difference was not significant statistically (p >0.05). Homocysteinememia was present in 17 out of 28 (60.71%) male patients as compared to 12 out of 22 female patients (54.55%) of venous stasis (>0.05). There were 5 out of 14 patients (35.71%) with venous stasis in below knee region and 24 out of 36 patients (66.67%) with venous stasis extending above knee region were having hyperhomocysteinemia and this difference was statistically significant (p=0.04) showing that hyperhomocysteinemia is associated more with above knee swellings i.e. proximal venous stasis. In patients with no risk factor present (idiopathic cases), 15 out of 23 patients (65.22%) were having hyperhomocysteinemia; while in patients with risk factors present, 14 out of 27 (51.85%) patients were having hyperhomocysteinemia and this difference was statistically significant (p 0.04).

DISCUSSION

Many studies in the literature are available regarding levels and prevalence of hyperhomocysteinemia in western countries. But there are only few studies or literature available regarding the levels of homocysteine and prevalence of hyperhomocysteinemia in venous stasis patients in Indian population. So this study was conducted to measure the serum homocysteine levels in venous stasis patients in this region of India. Various studies that had been done in patients with venous stasis showing a mean age in the range of 50-60 years.[18,19] In the present study, the mean age of the patients with venous stasis was 37.32 years while in control group the mean age was 40.01 years. Many patients in the present study were in younger age group with age less than 30 years, mainly because of more of female patients who were pregnant or in puerperium. Most of these women were below the age of 30 years. Moreover there are regional differences in age related incidence of venous stasis. In the literature most of the studies from western countries have reported a higher incidence of venous stasis in female patients as compared to male patients.[7] But the study conducted by Gautam et al in India has reported that female to male ratio is only 0.32 indicating that venous stasis is more common in male patients.[20] In the present study, the female to male ratio was 0.79:1. It might be due to increased awareness and early mobility in pregnant patients and patients in puerperium de to better antenatal and postnatal care or due to less smoking in females in India population. In might also be in the regional differences in the incidence of venous stasis in respect to sex.

Obesity (BMI >30) is a risk factor for development of venous stasis. In the present study, mean weight in study group was 22.61±3.47 kgs and 22.71±2.55 kgs in control group. Guan et al had reported a mean BMI of 25.88 in a group of 95 patients showing an increased potential for venous stasis with increase in the BMI.[21] Tsai et al reported a mean BMI of 29.1 kg/m^2 as compared to 27.7 kg/m^2 in controls.[22] These studies indicate that an increase

in BMI is a potential risk factor for venous stasis. In the present study, BMI of the patients were comparatively less due to more number of young females belonging to rural areas who were having less body weight in comparison to urban population. Incidence of thrombosis in left leg is more than thrombosis in right leg. The factors responsible are compression of left side vein by right iliac artery, an over distended bladder, gravid uterus and congenital webs within the veins. In present study, ratio of left leg to right leg involvement in venous stasis ranged was 1.56:1. Vashist et al found the ratio of left to right leg involvement in venous stasis as 1.5:1.[23] Chan et al had studied 96 patients of venous stasis and found the involvement of the left leg in 84 patients (88%) with a ratio of 7:1.[24] In various clinical studies conducted, ratio of left to right leg involvement in venous stasis ranged from 1.2 to 4.3:1.[24]

In the present study, pain was present in 98% of patients, swelling of the limbs in all the patients (100%), skin discolouration in 24% and fever in 4% patients with venous stasis. Villa et al had reported pain, swelling, skin discolouration and fever as the presenting symptoms in 86%, 72%, 24% and 15% of patients respectively.[25] In a study done by Diamond et al, presenting symptoms included leg pain in 42.6% of patients, leg swelling in 53.4% of patients, skin discoloration in 40% of patients and fever in 15% of patients with venous stasis.[26] These findings show that the pain and swelling are the cardinal features of venous thrombosis of legs. There should be a higher degree of clinical suspicion in patients presenting with pain and swelling of leg along with the presence of any of the predisposing risk factors.

In the present study, there were 54% patients with one or more predisposing risk factors, these included 12 (24%) patients who were either pregnant or had given birth to a child recently, 7 patients (14%) who had undergone major surgical procedure recently, 2 patients (4%) were taking oral contraceptive pills, 4 patients (8%) had recent history of trauma, 3 patients (6%) were having history of severe infections, 2 patients (4%) had history of smoking, 1 patient (2%) each of epilepsy and PIVD. There were 5 patients (10%) who were having >2 risk factors present. In a study done by Diamond et al, there were 51% patients who had known risk factors for venous stasis which included previous history of venous stasis in 11% patients, cancer in 11% patients, recent surgery or trauma in 12% patients, paresis in 2% patients and oral contraceptive pills usage in 3% of patients.[26] In this study, there were 10% patients who had no risk factors present. In study done by Villa et al, 63% patients were classified as having predisposing risk factors when the following circumstances or disorders were present: 22% patients subjected to immobilization due to medical or surgical conditions, 27% had cancer, 24% had severe venous insufficiency with previous history of venous stasis.[25]

In present study, the mean levels of serum homocysteine was 20.33±14.73 in patients with venous stasis as compared to levels of controls with a mean of 8.49±4.48. The difference was significant showing that the serum homocysteine levels were significantly raised in venous stasis patients (group A) as compared to group B patients and the p value was <0.001. Falcon et al found the mean serum homocysteine levels in patients with venous stasis to be 10.3±5.1 as compared to 8.3±3.4 in control group.[27] However, a few studies like Ravari et al and Mehdi et al have shown higher mean values of serum homocysteine in venous stasis patients as compared to controls but they found no significant association between serum homocysteine levels and venous stasis.[28,29]

In the present study, we studied 50 patients of venous stasis and 50 control subjects. The prevalence of hyperhomocysteinemia in patients with venous stasis was 58% as compared to 16% in the controls showing a strong

association between the development of venous stasis and hyperhomocysteinemia. Falcon et al found the prevalence of hyperhomocysteinemia to be 8.8% in venous stasis patients as compared to 0 in control subjects.[27] Fermo et al found moderate hyperhomocysteinemia in 13.1% with venous stasis and concluded that moderate hyperhomocysteinemia has a pathogenic significance in venous stasis.[30]

However, few studies done by Brattstrom et al, Amundsen et al and Mehdi et al had not shown any relation between the hyperhomocysteinemia and the development of venous stasis.[33,32,29] This higher prevalence values of hyperhomocysteinemia may be due to regional or racial differences showing a high prevalence in Indian population as compared to western population. In present study, the hyperhomocysteinemia was more common in patients of age 21-30 years (11 patients out of 18 patients i.e. 61.11%) and the prevalence of hypoerhomocysteinemia was 60.46% in patients aged less than 60 years as compared to 42.86% in patients aged more than 60 years and showed an association of hyperhomocysteinemia and development of venous stasis in younger population, though this difference was not statistically significant. Falcon et al[27] found that homocysteine levels were significantly higher in patients with venous stasis before the age of 40 years compared with age and sex matched controls. Tsai et al[22] found a significant association between hyperhomocysteinemia and adults aged 45-64 years of venous stasis and an inverse association in those >65 years of age in patients of venous stasis.

In the present study, the prevalence of hyperhomocysteinemia in male patients was 60.71% as compared to 54.55% in female patients of venous stasis although this difference was not statistically significant. Other study done by Ravari et al[28] found the prevalence of hyperhomocysteinemia to be higher in both male patients as well as in male controls as compared to female patients and controls respectively. Hence, the present study shows that hyperhomocysteinaemia is a risk factor for Venous stasis.

CONCLUSION:

The prevalence of hyperhomocysteinemia in cases of venous stasis in present study was 58% as compared to 16% in control group which was statistically significant. In patients with idiopathic venous stasis, the prevalence of hyperhomocysteinemia was higher as compared to patients of secondary venous stasis. Hence, we suggest the measurements of serum homocysteine levels in all cases of Venous stasis especially in cases where no predisposing risk factor is present and patients of Venous stasis in younger population so that the necessary measures required to reduce the levels of serum homocysteine can be taken.

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