



## HISTOMORPHOLOGICAL FEATURES OF VARICOSE VEINS IN YOUNG MALE POPULATION: A PROSPECTIVE CASE CONTROL STUDY IN SOUTH INDIA

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### ABSTRACT

Varicose veins are tortuous, widened veins in the subcutaneous tissues of lower limbs and are often easily visible. The primary cause of varicose vein formation is not clear. Previous histological studies of varicose veins demonstrate the disorganization of the venous wall. This is because of varying degrees of intimal thickening, infiltration of fibrous tissue in the muscular layers, accumulation of collagen and fragmentation of elastic fibres. The aim of the study was to compare the histological changes in varicose veins with normal veins. Materials and methods: Patients of 18-35 years undergoing stripping surgery for varicose veins were selected for the study and compared with normal veins extracted from similar group undergoing herniorrhaphy for groin hernia. Biopsies received were subjected for histological examination using haematoxylin & eosin, van- giesen and verhoff stains. Histological examination showed changes in intima, media, adventitia and smooth muscle. Intima & adventitia showed accumulation of collagen fibers. There was disturbed architecture of smooth muscle fibres arranged in media. Changes were present in all the layers including the adjacent areas of the affected varicose veins. This suggests primary weakness in vein wall as cause of varicosity. However more studies have to be carried out to obtain results than can lead to generalizations.

**Key words:** Varicose vein, histological changes



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## INTRODUCTION

Varicose veins (VV) are complex venous disease commonly affecting the lower extremities. The exact etiology and pathophysiology remains unclear. Risk factors include family history, increasing age, female gender, pregnancy, obesity, standing occupations or history of previous deep venous thrombosis<sup>(1)</sup>. There is abnormal distensibility of connective tissue in the vein wall. Earlier work has suggested that veins from patients with varicosities are more distensible than normal veins indicating a probable systemic basis for the abnormality<sup>(2)</sup>. Our study was to establish the cause of development of VV in young males of 18-35 years. Very few studies have been done especially in this age group. So, we examined histological features of varicose veins and compared with normal saphenous veins of inguinal hernia patients which served as control.

## MATERIALS AND METHODS

50 male patients aged 18-35 years to K.S.Hegde Charitable Hospital, Mangalore undergoing surgery for varicose veins and similar group undergoing surgery for groin hernia were respectively selected as cases and controls for the study. Informed written consent was taken. We excluded those who were < 18 years or > 35 years of age, those who had inability to give informed written consent and those who had undergone prior interventions for varicose veins like surgery or sclerotherapy.

## RESULTS

Thickening of Histopathological examination of both normal (control) and varicose veins were studied using routine H&E and special stains like van-gieson and verrhoff's stains (FIG 1A & 1B). Tunica intima showed thickening with increased accumulation of collagen, degenerated elastic fibres and smooth muscle cell proliferation (FIG 1C). Media showed irregular thickening with loss of polarity, focal atrophy of muscle fibres and splitting of smooth muscles by collagenous tissue.

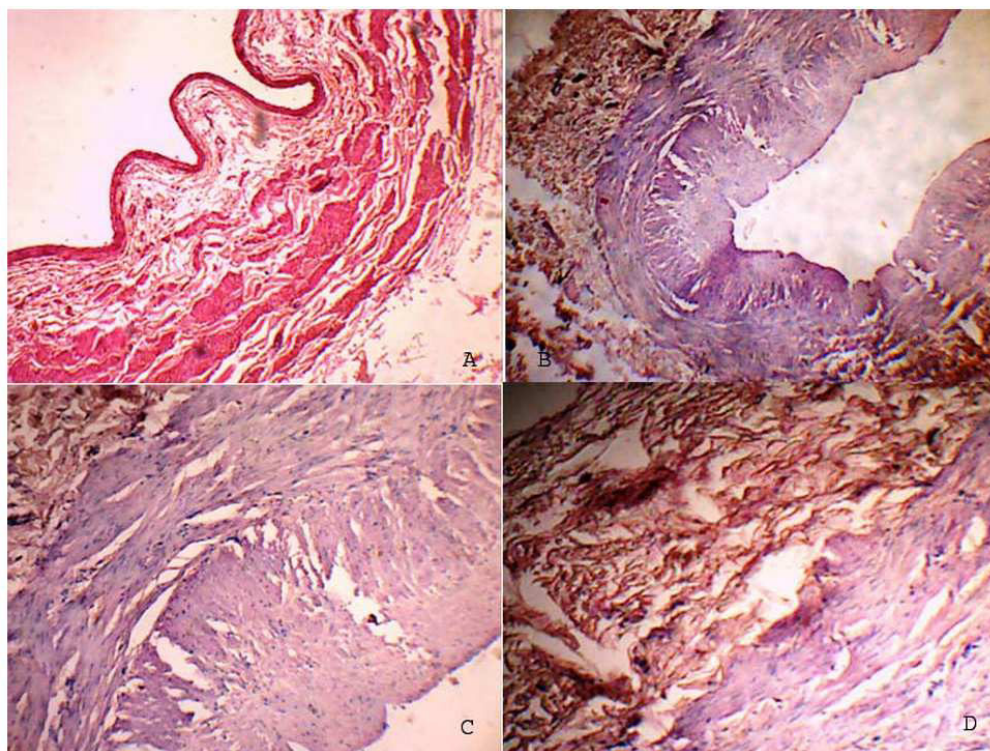
Adventitia showed increased accumulation of collagen with vasa vasorum (FIG 1D). Special stain (Van giesen) confirmed the above findings which was observed in routine H & E stain (FIG 2A-2D).

## DISCUSSION

The cause of development of varicose veins is not clear. Hirai and colleagues reported a positive family history in 42% of Japanese patients with varicose veins<sup>(3)</sup>. Several studies have shown that prevalence of varicose vein increases with age and is common in women<sup>(4,5)</sup>. However, the occurrence of varicose veins in young men is also fairly common. Our study was to investigate the cause of development of varicose veins in this population: Normal saphenous vein has three layers tunica intima, media and adventitia. The intima consists of a single layer of endothelium that lies on a poorly defined internal elastic membrane. The innermost portion of media consists of longitudinally dispersed smooth muscle fibres and elastic fibres. The outer muscle layer is thicker and consists of circular smooth muscle fibres. More peripheral to this is the adventitia which consists largely of collagen and smooth muscle fibres<sup>(6)</sup>. The main objective of our study was to analyze the cause and morphology of VV in young male population. So, we compared the morphology of both VV and normal veins (controls). Both these specimens were fixed with 10% formalin, carefully grossed and longitudinal and cross sections were taken. The tissues were processed, 5  $\mu$  sections were taken, stained (H&E and special stains) and analyzed under the microscope. The special stains done were van-gieson and verrhoffs to highlight the collagen and elastic fibres respectively. Histologically, varicose veins are characterized by significant disruption of the regular architectural pattern observed in normal veins. These were demonstrated by the studies conducted by London NJ et al., and Milroy et al.,<sup>(7,8)</sup>. These findings appear as skip or alternate lesions and may not involve the entire circumference of the venous wall. The intima

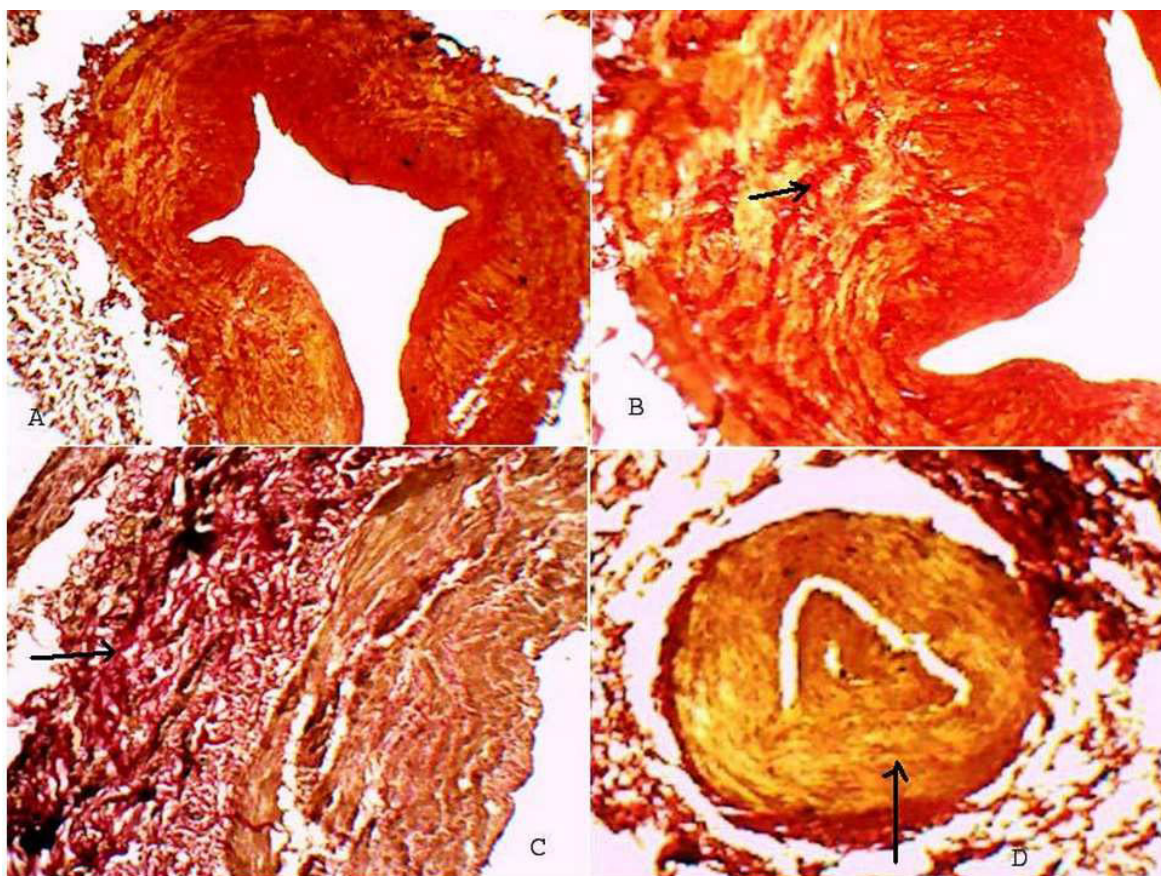
may be intact, but asymmetric areas of intimal thickening or fibrosis interspersed with areas of normal appearing intima are not uncommon. These intimal changes are associated with increased collagen deposition and plaques below the endothelial lining<sup>[10,11]</sup>. In the media, remodeling of the components of the extracellular matrix scaffold results in disruption of the longitudinal and circular muscle fiber bundle arrangement.<sup>(12)</sup> Smooth muscle cells (SMC) appear enlarged and have lost their elongated morphology, suggesting a phenotypic change from their contractile to a synthetic state<sup>(13)</sup>. Transmission electron microscopic evaluation of varicose veins shows that the SMC bundles in the media are separated within a matrix of disorganized collagen fibers. Areas of thinning or blowout lack SMCs and are composed mostly of collagen fibres and atrophic adventitia due to

thickening of vasa vesorum causing ischemia of the wall.(FIG 2D) These morphologic changes may not be uniformly distributed along the entire circumference of the vein; however it is not uncommon to find normal venous segments interspersed with abnormal varicose veins<sup>(14)</sup>. These findings suggest primary weakness in vein wall, hence causing varicosity. However, more studies are required to obtain results that can lead to generalizations. We hereby conclude that, distinct morphological changes in the venous wall cause weakening, dilatation and tortuosity; which in turn leads to valvular incompetence in varicose veins. So, young population especially who have strong family history of VV's, should be given awareness with respect to risk factors like prolonged standing, obesity etc., to have good quality of life.



**Figure 1**

- A) Microphotograph of the normal vein showing tunica intima, media, adventitia with thin internal elastic lamina.(H& E Stain x10X)**  
**B) Low power view of VV displaying irregular thickening of the intima and media with replacement by collagen tissue. (H& E Stain x 10X)**  
**C) High power view of the intima and media displaying thickening and collagen deposition in the intima associated with splitting of inner longitudinal muscle layers of the media. (H& E Stain x 40X)**  
**D) High power view of the adventitia displaying increased collagen deposition in the adventitia (H& E Stain x 40X)**



**Figure 2**

- A) Van giesen stain, low power view of VV displaying irregular thickening and narrowing of the lumen. (Van giesen stain x10X)*  
*B) High power view of the same confirming the collagen accumulation in the intima and splitting of the media by it (arrow) (Van giesen stain x40X)*  
*C) High power view confirming the collagen accumulation in the adventitia (arrow) (Van giesen stain x40X)*  
*D) High power view of the adventitia displaying thickening of the vasa vesorum. (arrow) (Van giesen stain x40X).*

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