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## Original Article

# Histomorphometric study of basilar artery in normal and suicide persons



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## ABSTRACT

**Background:** Depression in association with cerebro-vascular risk factors and white matter lesions is increasingly referred to as 'vascular depression'. There are several brain areas known for playing a role in patho-physiology of depression which may lead to suicidal tendencies, are fed by basilar artery. Therefore, the arterial histoarchitecture was studied in the normal and suicide individuals to establish a relationship between the vascular structural changes and depression.

**Methods:** 40 post-mortem samples (both sexes) of basilar artery have been collected and were grouped into normal and suicide groups. Samples were measured for arterial, lumen diameter and the thickness of tunica intima, media and adventitia using H & E stained sections. While, Orcein stained sections were used to estimate the volume fraction of elastic fibres, and Van Gieson stained sections to estimate the volume fraction of collagen fibres.

**Results:** The mean thickness of tunica media of basilar artery in suicide individuals (1.08 microns) showed a statistically significant decrease when compared to normal person (1.33 microns). Further, volume fraction of collagen ( $0.06 \text{ mm}^3/\text{mm}^3$ ) and elastic fibres ( $0.06 \text{ mm}^3/\text{mm}^3$ ) in suicide persons showed a statistically significant decrease when compared to normal person (collagen fibres  $0.08 \text{ mm}^3/\text{mm}^3$ ; elastic fibres  $0.09 \text{ mm}^3/\text{mm}^3$ ).

**Conclusions:** This study establishes a probable causative relationship between vascular structural abnormality and depression which may drive the individual to commit suicide.

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## At a glance commentary

### Scientific background

There are several brain areas known for playing a role in patho-physiology of depression which may lead to suicidal tendencies, are fed by basilar artery. Therefore, the arterial histoarchitecture was studied in the normal and suicide individuals to establish a relationship between the vascular structural changes and depression.

### What this study adds to the field

This study does establish a probable causative relationship between vascular structural abnormality and depression. Till now this relation was more of hypothetical concept than the evidential concept from a scientific study. This study shows the structural alteration in an artery of an individual which may be responsible for neurodegeneration at a later stage.

Over the past 50 years, relationships between stress and the neurobiological changes seen in depressive disorders have been well-documented. Also, the depressive individuals commit suicide because of their inability to bear the stress, cognitive thought depressive symptoms of having hopelessness, worthlessness and helplessness is a fact well known. A majority of investigations in this area are focused to evaluate the role of different areas of brain which are supposed to play significant role in several depressive disorders. The areas which are proven in their role in depression are pre-frontal cortex, temporal cortex, superior temporal gyrus, thalamus, hypothalamic-pituitary-adrenal (HPA) axis, limbic areas, including the hippocampus and amygdaloid body [1–6].

It is also proved with consistent evidences that dysfunction of these areas are associated with cerebro-vascular disturbances which in turn increases the vulnerability for developing the major depressive syndrome. The function of these areas of brain may also be impaired in individuals who show grey matter volumetric reductions, histopathological abnormalities, and altered haemodynamic responses [3]. Some of these abnormalities are mood state-dependent, and appear in regions where cerebral blood flow increases during normal and pathological emotional states. It has also been proved beyond any doubt that cerebral blood flow increases in the different brain areas involved in depression [7].

However, the status of the histoarchitecture of the artery involved in the supply to the regions of the brain implicated in the depression is untouched. So, the present study is designed to evaluate the structural changes of the basilar artery as it supplies to those areas of the brain which are proved to be playing definitive role in depression.

## Materials and methods

40 age matched post-mortem basilar artery samples were collected and grouped into two groups. One group (n = 20) of basilar artery is categorised as of normal persons which acted as control and another group (n = 20) of basilar artery as of suicidal persons with a history of depression. Cases with any type of head injuries were excluded.

The paraffin blocks of the basilar artery were processed by standard histological techniques [8]. 5 micron thick sections were cut using rotary microtome, 20–25 sections representing different regions of the artery were cut from each block and used for analysis.

Histological sections were stained with Hematoxylin–Eosin (H & E) for measuring arterial, lumen diameter and the thickness of tunica intima, media and adventitia. While, Orcein stained sections were used to estimate the volume fraction of elastic fibres and Van Gieson stained sections were used to estimate the volume fraction of collagen fibres. Histological evaluation was performed using a light microscope (Olympus Magnus – MLX) and digitized images of all the sections with various magnifications were obtained. The thicknesses of different layers of the artery were measured using commercial image analysis software (Digimizer image analysis software Version 3.6.0). Apart from this, volumes fraction of elastic and collagen fibres were estimated by point count method using eye piece graticule calibrated with the Digimizer image analysis software.

All the data was computed and the mean, standard error were calculated and Student's t-test were performed to know the level of significance using Microsoft excel (version MS office 2003). The  $p < 0.05$  is considered as statistically significant.

## Results

### Thickness of tunica intima, media and adventitia

The mean thickness of tunica intima of basilar artery of normal persons was found to be 0.12 microns, of tunica media was 1.33 microns and of tunica adventitia was 0.81 microns. While the mean thickness of the tunica intima of basilar artery of suicide persons was 0.11 microns, the tunica media was 1.08 microns and that of tunica adventitia was 0.77 microns. Though all the results were indicative of decreased trend in the thickness, the tunica media of the suicide persons showed statistically significant decrease ( $p < 0.05$ ) in thickness when compared to that of the tunica media of the normal persons [Table 1; Fig. 1].

### Arterial and lumen diameter

The mean value of arterial diameter of normal person's basilar artery was 15.81 microns and lumen diameter was 12.84 microns. Further, the arterial diameter was found to be 15.10 microns and lumen diameter was 12.34 microns in the suicide persons. These results also reveal the decreased

**Table 1 – Mean values of thickness of wall layers, arterial diameter, lumen diameter and volume fraction of collagen and elastic fibres in the basilar artery.**

Groups	Tunica intima (mean ± SE in μ)	Tunica media (mean ± SE in μ)	Tunica adventitia (mean ± SE in μ)	Arterial diameter (mean ± SE in μ)	Lumen diameter (mean ± SE in μ)	Volume fraction of collagen fibres (mean ± SE in mm <sup>3</sup> /mm <sup>3</sup> )	Volume fraction of elastic fibres (mean ± SE in mm <sup>3</sup> /mm <sup>3</sup> )
Normal	0.12 ± 0.009	1.33 ± 0.08	0.81 ± 0.05	15.81 ± 0.48	12.84 ± 0.43	0.08 ± 0.01	0.09 ± 0.02
Suicide	0.11 ± 0.009	1.08 ± 0.04*	0.77 ± 0.05	15.10 ± 0.47	12.34 ± 0.48	0.06 ± 0.01***	0.06 ± 0.01***

n = 20, \*p < 0.05 \*\*\*p < 0.001.

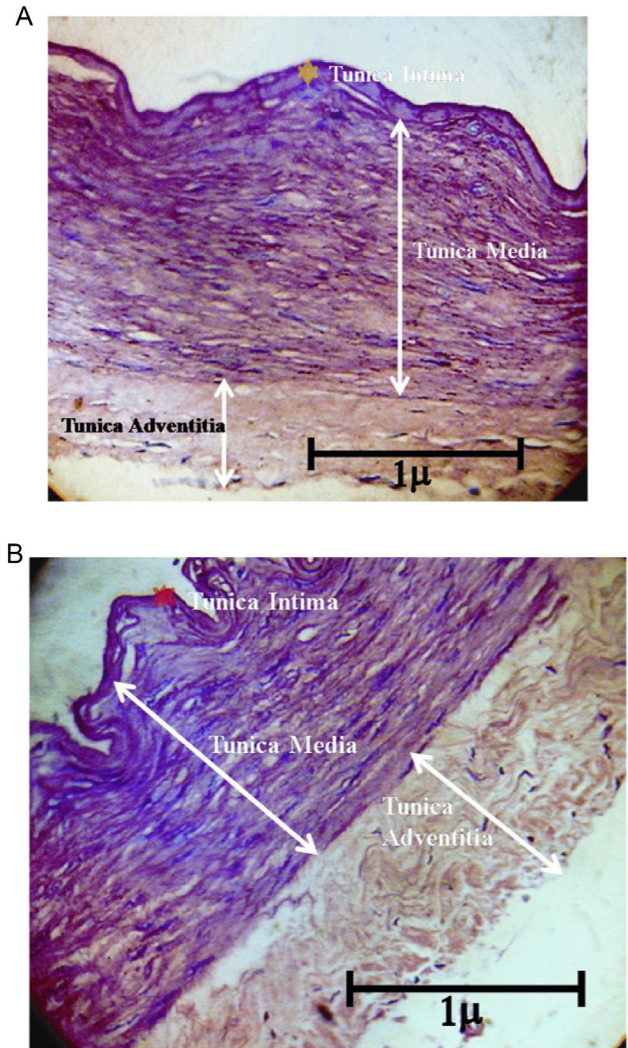


Fig. 1 – Photomicrographs showing the thickness of layers of basilar artery (A) normal person (B) suicide person (H & E stain, ×400).

lumen and arterial diameter in the suicide people but they were statistically non-significant (Table 1).

**Volume fraction of collagen and elastic fibres**

The mean value of volume fraction of collagen fibres of normal person's basilar artery was 0.08 mm<sup>3</sup>/mm<sup>3</sup> of tissue and volume fraction of elastic fibres was 0.09 mm<sup>3</sup>/mm<sup>3</sup> of tissue. While, volume fraction of collagen fibres was 0.06 mm<sup>3</sup>/mm<sup>3</sup> of tissue and elastic fibres was 0.06 mm<sup>3</sup>/mm<sup>3</sup> of tissue in the suicide individuals. The results indicate highly significant decrease in the values in suicide individuals when compared to the normal (p < 0.001) [Table 1; Figs. 2 and 3].

**Discussion**

Though vascular depression concept seems to have promising implications for understanding the pathogenesis,



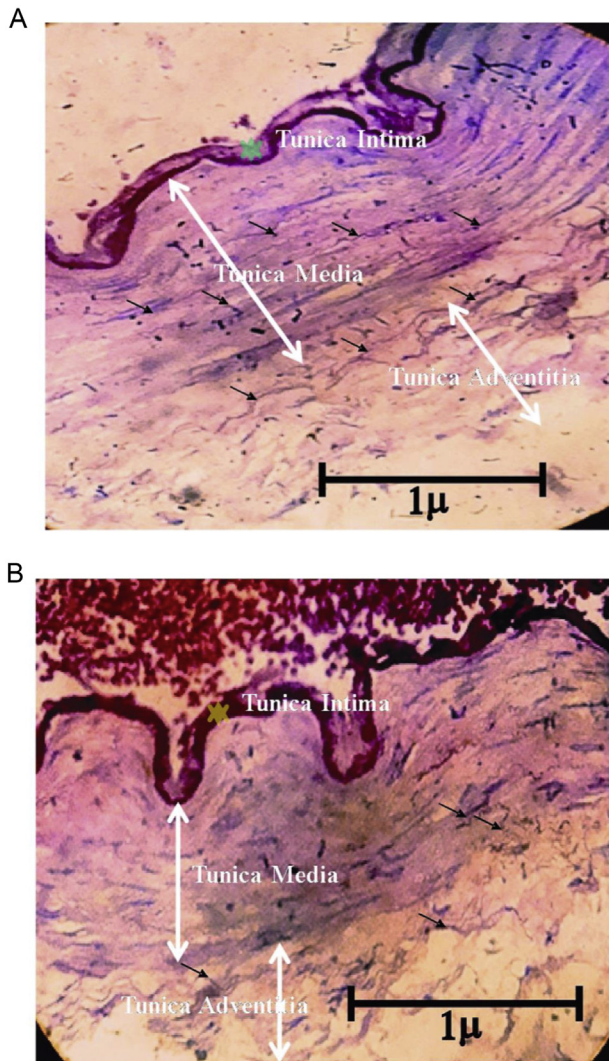


Fig. 2 – Photomicrographs showing the elastic fibres in the wall of basilar artery (A) normal person (B) suicide person (Orcein stain,  $\times 400$ ).

treatment and possibly aiding in the prevention of depressive disorder but much of the evidence supporting this concept is associative rather than casual.

The histomorphometric changes that were noticed in the present study are indicative of the functional impairment leading to the catastrophic events. Generally there will be decrease in the content of the tunica media as the age advances and this may be the probable cause for the rigidity of the arterial wall but it is neutralised by the increased arterial diameter which in turn maintain the functional integrity of the vessel [9,10]. But in the present study though we observed the decreased thickness of the tunica media which is predicted to be due to the altered composition of the same and may be the factor leading to the rigidity of the artery, there is no significant change in the arterial diameter. This is suggesting that the counter mechanism for the arterial rigidity in order to maintain the functional balance has failed. This has led to the loss of structural integrity of the artery resulting in

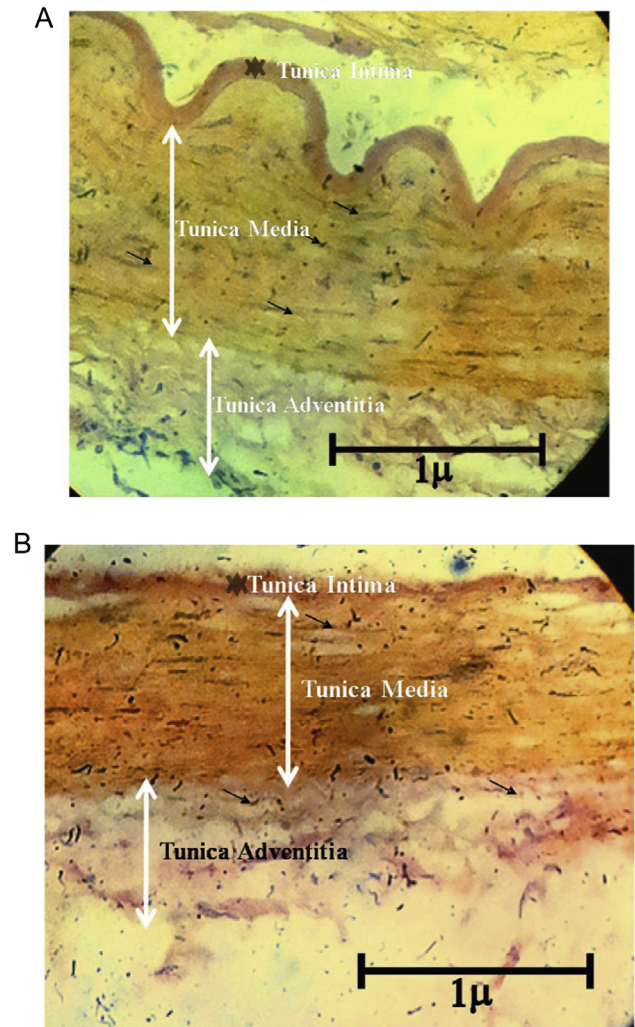


Fig. 3 – Photomicrographs showing the collagen fibres in the wall of basilar artery (A) normal Person (B) suicide person (Van Geison's stain,  $\times 400$ ).

the functional incompetence leading to the pathology of depression which is a driving force for the individual to commit suicide.

The results of the study also indicate the decreased volume fraction of the elastic and collagen fibres. This further confirms the hypothesis that the tunica media is decreased in thickness due to the change in its contents. The normal architecture of the artery suggests that the collagen and elastic fibres in the media are mainly having attachment to the smooth muscle fibres. Further, the collagen fibres are responsible for the spread of the muscle tension along the circumference while the elastic fibres bring about the uniform distribution of the muscle tension around the vessel [11]. So the decreased fibre content noticed in the present study may result in the failure of the distribution of the muscle tension and thereby the functional impairment. Normally the initial resistance of the artery to stiffness is taken up by the elastic fibre which is followed by the collagen fibres. The collagen fibres offer the higher resistance required by the artery in

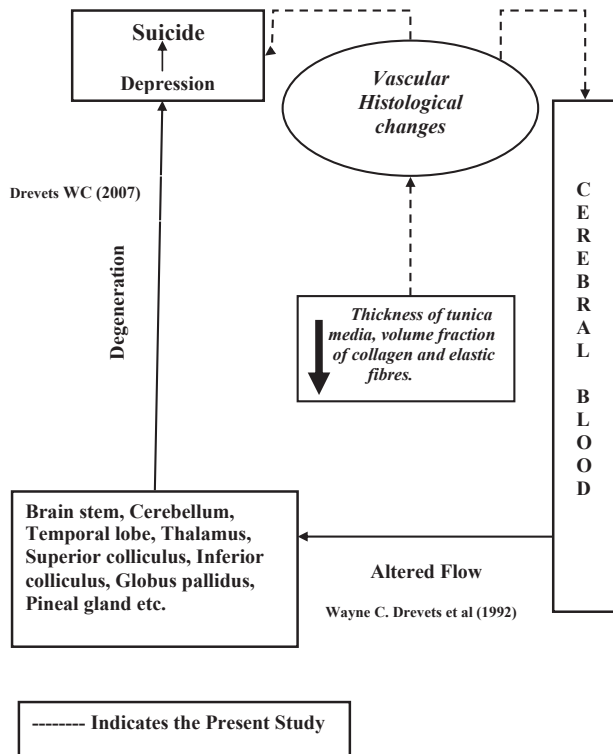


Fig. 4 – Mechanism of vascular induced depression leading to suicide.

order to bear the high strain of the increased pressure. Further, it is reported that the rigidity in the arterial wall as the age advances is not only correlated to the increased collagen but also to the failure of the elastic fibres which fail to function as the first stage mechanism in resisting the initial stiffness [12]. Ironically in our study the results are indicative of the failure of whole mechanism for counter acting the stiffness. The elastic fibres are decreased which has increased the workload on the collagen fibres. The decreased collagen fibres reveal that instead of taking up this extra workload, the collagen fibres are failed to protect the functional integrity. This probably has led to the failure of the normal protective mechanism of arterial wall thereby to the functional impairment. In addition the ratio of the volume fraction of the collagen to elastic fibres showed the increased trend in the suicide category substantiating the loss of elasticity of the artery and contributing to the stiffness of the artery. In total, all the changes noticed are indicative of the fact that the structural alterations of the arteries in the suicidal persons have an impact on the haemodynamics and the blood flow. These changes further may have an altered influence on the regions supplied by the basilar artery and it is some of these regions like pons, upper part of medulla, anterior and posterior thalamus, globus pallidus, lateral and medial geniculate body, colliculi, uncus, parahippocampal, medial and lateral occipitotemporal gyri which are implicated in the pathology of the depression. So the probable reason for the functional abnormality of these regions is the structural abnormality of the feeding vessel.

In conclusion, this study does establish a probable causative relationship between vascular structural abnormality and depression [Fig. 4]. Till now this relation was more of hypothetical concept than the evidential concept from a scientific study. Further, vascular depression provides a useful framework which reminds the clinician of important interactions between depression and vascular abnormality but conceptually it may be too restrictive. However, the vascular depression hypothesis, if substantiated through further research, potentially has much wider implications. This knowledge may allow the prevention of the physical consequences of depression like reducing the mortality rate. Also, may open doors for new treatment strategies for vascular remodelling, thereby curing depression and probably preventing neurodegeneration at a much later stage.

### Conflicts of interest

I declare that there are no conflicts of interest.

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