

**Original article:**

## **Serum ischemia modified albumin in Type 2 Diabetes patients attending tertiary care Teaching Hospital in Pune**

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### **Abstract**

**Introduction:** Diabetes mellitus (DM) is one of the most challenging health problems in 21<sup>st</sup> century and is leading among various causes of adult mortality and morbidity worldwide. Myocardial infarction, stroke and peripheral artery disease are most common causes of death in DM patients. Recent studies have highlighted the importance of ischemia modified albumin (IMA) as an ideal and sensitive biomarker for ischemia and oxidative stress but its role in type II DM without vascular complications is still largely unknown. Therefore, the present study was conducted with an aim to estimate serum ischemia modified albumin in type II diabetes mellitus patients.

**Material and methods:** A total of 70 newly diagnosed diabetic patients aged between 40-60 years having blood glucose level >126 mg/dl in fasting and >200 mg/dl random blood glucose load were included in the study. A total of 70 age and sex matched healthy individual without any major illness and not on any medication willing to give consent were included as controls. IMA level of subjects and controls were estimated.

**Results:** The mean IMA the mean IMA in control group was  $0.33 \pm 0.032$  ABSU and in diabetic group  $0.40 \pm 0.026$  ABSU. The IMA values were highly significantly raised in diabetic (case group) as compared to control group (Paired t test,  $p$ value < 0.0108).

**Conclusion:** As IMA levels were significantly high in diabetes patients, it can be concluded that IMA can be considered as an important biomarker in type II diabetes mellitus patients to prevent the complications and if this parameter is automated, it could be a useful method for extensive population based studies.

**Keywords:** Biomarkers, diabetes mellitus, Human serum albumin, ischemia modified albumin

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### **Introduction**

Diabetes mellitus (DM) is a clinical syndrome characterized by hyperglycemia, glycosuria due to absolute or relative insulin deficiency.<sup>1</sup> Hyperlipidaemia and sometimes ketonaemia may be seen in this metabolic disorder.<sup>1</sup> The chronic hyperglycemia in DM may lead to dysfunctioning and failure of various organs like eyes, kidneys, nerves, heart and blood vessels.<sup>2</sup>

DM is one of the most challenging health problems in 21<sup>st</sup> century and is leading among various causes of adult mortality and morbidity worldwide.<sup>2</sup> Myocardial infarction (MI), stroke and peripheral artery disease are most common causes of death in DM patients.<sup>2</sup>

Recent studies have highlighted the importance of ischemia modified albumin (IMA) as an ideal and sensitive biomarker for ischemia and oxidative stress.<sup>3, 4, 5</sup> IMA is also known as cobalt-binding albumin and is secreted in response to serum flowing through ischemic tissues.<sup>6</sup> The IMA serum levels increases in many diseases accompanied by ischemia.<sup>7</sup> IMA is a proven biomarker for the early diagnosis of myocardial ischemia but its

role in type II DM without vascular complications is still largely unknown. Therefore, the present study was conducted in a tertiary care academic hospital of Maharashtra with an aim to estimate serum ischemia modified albumin in type II diabetes mellitus patients.

### **Material and methods**

The present study was carried in the Department of Biochemistry, B J Government Medical College and Sassoon General Hospitals, Pune from December 2015 to June 2017. A total of 70 newly diagnosed diabetic patients aged between 40-60 years having blood glucose level >126 mg/dl in fasting and >200 mg/dl random blood glucose load were included in the study. A signed informed consent was obtained as per the proforma from all the subjects or their legally responsible attendant. The protocol of the study was approved by Institutional Ethics Committee. Following were the exclusion criteria:

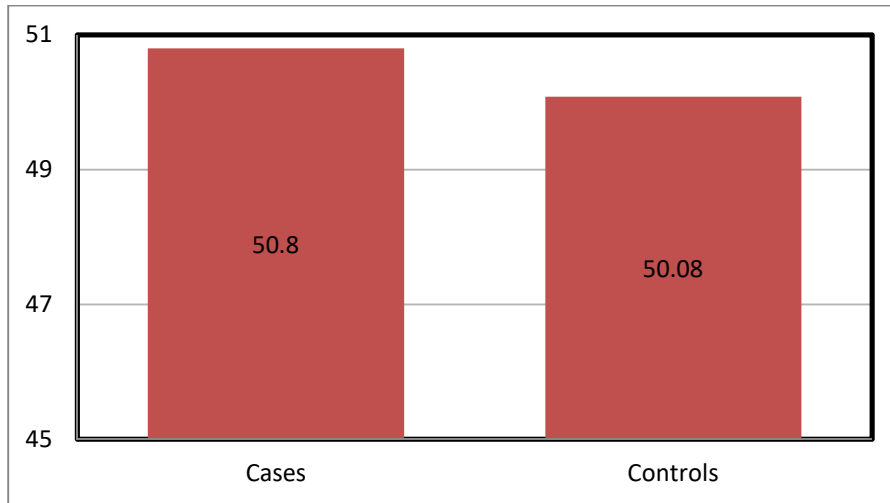
1. Patients with recent clinical infection, chronic inflammatory condition or neoplastic diseases.
2. Bleeding disorders, cerebral haemorrhage of any etiology, autoimmune disorders.
3. Conditions mimicking stroke.
4. Patients with recent surgery or major trauma.
5. Patients with any major renal or hepatic disease.
6. Ongoing cardiac ischemia and known peripheral vascular disease.

A total of 70 age and sex matched healthy individual without any major illness and not on any medication willing to give consent were included as controls. About 2 ml of blood samples were obtained from the ante-cubital vein of each subjects and control. The blood sample was transferred to a clean dry sterile plain vacutainer and allowed to clot for 30 minutes and then centrifuged. The serum samples were stored in aliquots till the time of estimation of IMA.

IMA level was estimated as per the method described by Micalet *al* (1998).<sup>8</sup> In brief, 50 µl of 0.1% cobalt chloride solution was added to 200 µl of serum and gently mixed. The mixture was allowed to stand for 10 min for adequate cobalt albumin binding. 50 µl of 0.15% Dithiothreitol (DTT) solution was added as a coloring agent and the reaction was quenched 2 minutes later by adding 1 ml of 0.9% NaCl. In a spectrophotometer color development was compared to a serum blank without DTT at 470 nm. The results were expressed as absorbance units (ABSU).

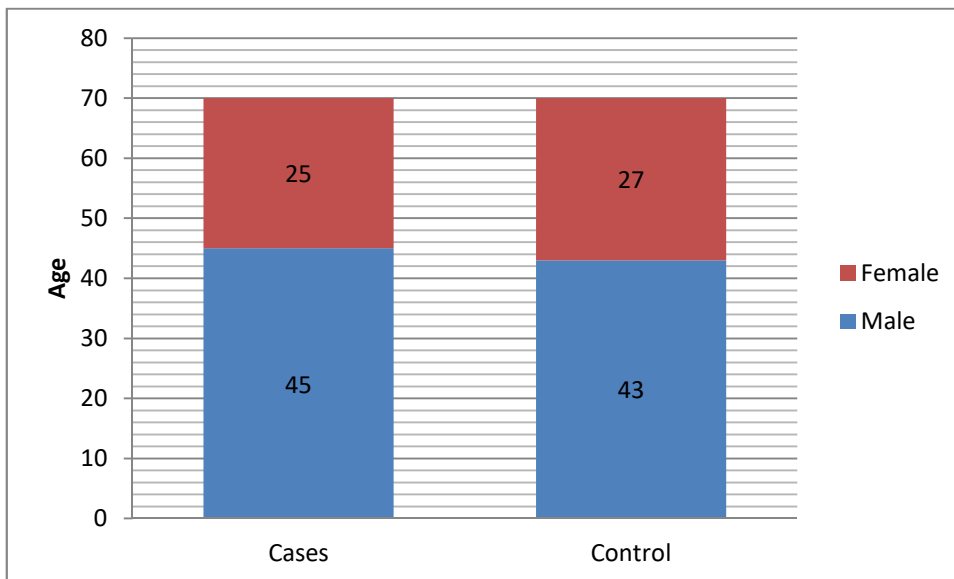
## Results

As shown in figure 1, the mean age of distribution was 50.08 years in control group and 50.8 years in is the case group.



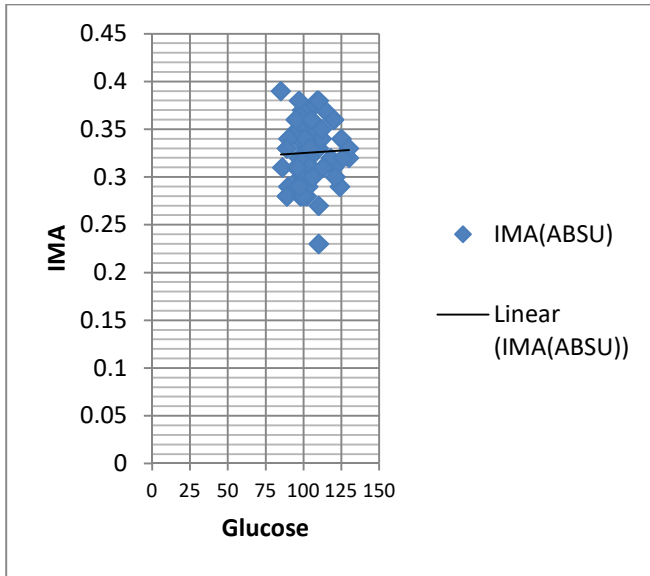
**Figure1: Mean average age distribution in case and control.**

The gender wise distribution of case and control group is shown in figure 2. Male predominance was noted in both the groups.

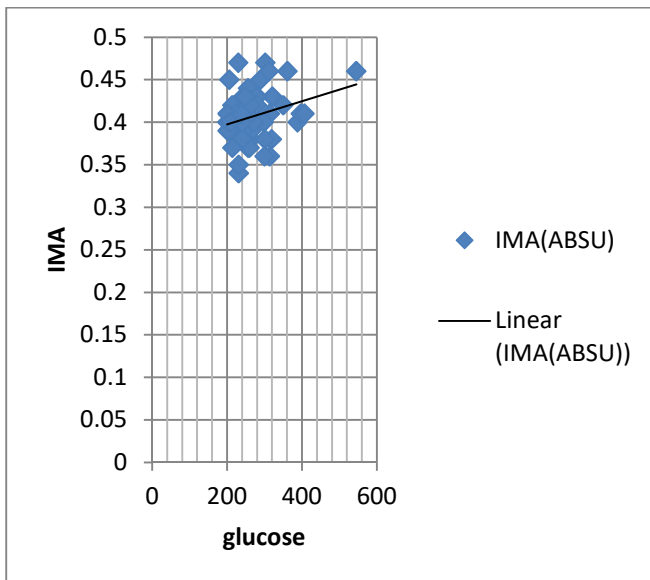


**Figure 2: Gender wise distribution in study group**

The comparison of IMA in control and case is shown in figure 3. The mean IMA the mean IMA in control group was  $0.33 \pm 0.032$  ABSU and in diabetic group  $0.40 \pm 0.026$  ABSU. The IMA values were highly significantly raised in diabetic (case group) as compared to control group (Paired t test,  $p$ value  $< 0.0108$ ).



1) IMA (ABSU) control



2) IMA (ABSU) cases

**Figure 3: Comparison of IMA in Control and cases.**

**Discussion**

Diabetes mellitus pose as a serious medical, socio-economic and rehabilitation problem worldwide. It is associated with various types of complications like retinopathy, nephropathy, and peripheral and autonomic neuropathy.<sup>2</sup> Incidence of atherosclerotic cardiovascular, peripheral arterial and cerebrovascular disease is high in diabetic patients.<sup>2</sup> Early diagnosis and detection of various complications in diabetic patients is very important for effective monitoring and treatment. Several novel biomarkers of inflammation related to pathophysiology of diabetes can be applied for diagnosis, assessment of therapy and prognosis.

In the present study, 70 diagnosed cases falling into category of diabetic group (case) attending Medicine out patients department were studied along with age and gender matched 70 healthy controls. The age distribution of the patients in this study was between 40 and 60 years. Average mean age was 50.8 in case group 50.08 years

in control respectively. The risk of Type II diabetes mellitus increased with increasing age. Type II DM is most common type of diabetes and usually goes undiagnosed for many years due to gradual hyperglycemia development. However, type II patients are at higher risk of developing macro and microvascular complications. In this study, IMA levels were studied in Type II DM patients. Human serum albumin (HSA) is the most abundant circulating plasma protein containing 585 amino acid residues.<sup>3</sup> Hippocrates in 400 BC was first to report the role HSA in human disease.<sup>9</sup> In *Aphrorismhe* he reported that foamy urine that is likelihood to be caused by the presence of HSA is indicator of renal disease.<sup>9</sup>

Exposure of HSA to ischemic tissue modifies the N-terminus and decreases metal binding capacity of HSA resulting in the formation of IMA.<sup>10</sup> Studies indicate that mechanisms involved in ischemia induced changes to albumin may include exposure to endothelial and extracellular hypoxia, acidosis, damage of free radicals, disruptions in membrane energy-dependent sodium and calcium pump and free iron and copper ion exposure.<sup>9, 11</sup>

IMA has been as a sensitive marker of myocardial ischemia, skeletal muscle ischemia, pulmonary embolism and mesenteric ischemia.<sup>8, 12</sup> Recently, this biomarker was also found to be useful for early identification of acute stroke.<sup>13</sup> However, until now, only few studies have evaluated IMA levels in newly diagnosed type II DM patients. In the present study the IMA levels were significantly elevated in type II DM cases compared to control and the mean levels were 0.33 ABSU in normal control and 0.40 ABSU in type II DM cases. On comparison between two groups, the IMA levels were significantly raised in case group than control group ( $p < 0.0108$ ). Similar findings were reported in the study of Sowjanya *et al* (2015).<sup>14</sup> They reported that plasma IMA can be used as an auxiliary marker for severity in type II DM patients.<sup>14</sup>

### Conclusion

In the present study as IMA levels were significantly high in diabetes patients, it can be concluded that IMA can be considered as an important biomarker in type II diabetes mellitus patients to prevent the complications and if this parameter is automated, it could be a useful method for extensive population based studies.

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