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DIAGNOSTIC EFFICACY OF NESFATIN-1 & VASPIN IN CONTROL, PRE-DIABETIC, AND DIABETIC PATIENTS: A CASE CONTROL OBSERVATIONAL STUDY IN NORTHERN INDIA

Biochemistry

Rani Kumari Ph.D. Scholar K.M University, Mathura, Pali Dungra, - 281123, Uttar Pradesh, India

Dr. Ashish Sharma Professor and Head Dept. of Biochemistry Geetanjali Medical College and Hospital Udaipur-pin code- 313002, Rajasthan, India

ABSTRACT

Objective: This case-control observational study aims to assess the diagnostic efficacy of two emerging adipokines, Nesfatin-1 and Vaspin, in discriminating between control, pre-diabetic, and diabetic patients. The study addresses the potential utility of these biomarkers in early diabetes detection and management. **Methods:** A total of 234 participants were recruited, comprising 78 control subjects, 78 pre-diabetic subjects, and 78 diagnosed with diabetes. Random blood samples were collected to measure serum Nesfatin-1 and Vaspin levels. Statistical analyses, including ROC curves and logistic regression, were performed to evaluate the diagnostic accuracy of these biomarkers. **Results:** Our findings revealed significant differences in Nesfatin-1 and Vaspin levels between the three groups ($p < 0.05$). ROC curve analysis demonstrated that both Nesfatin-1 and Vaspin exhibited good diagnostic accuracy for discriminating between control and pre-diabetic patients as well as between pre-diabetic and diabetic patients. The combination of these biomarkers further enhanced the diagnostic efficacy. **Conclusions:** Nesfatin-1 and Vaspin show promise as diagnostic markers in identifying individuals at different stages of glucose dysregulation. These results indicate their potential utility in early detection and differentiation of pre-diabetes and diabetes. Further research is warranted to explore the clinical applicability and longitudinal significance of these biomarkers in diabetes management.

KEYWORDS

Nesfatin-1, Vaspin, Pre-Diabetes, Diabetes, Biomarkers, Early Detection.

INTRODUCTION

Diabetes mellitus is a global health concern characterized by chronic Hyperglycemia resulting from impaired insulin secretion or insulin resistance. The early detection and differentiation of pre-diabetes and diabetes are crucial for effective disease management and prevention of complications. Biomarkers that can accurately identify these stages hold great promise in clinical practice.[1] The onset of diabetes among Indians is about a decade earlier than their western counterparts and this has been noted in Asian Indians in several studies [2]. In the national survey 54.1% of diabetes developed it in the most productive years of their lives i.e., before the age of 50 years and they also had a higher risk of developing chronic complications of diabetes [3]. The prevalence of Type 2 diabetes is 4–6 times higher in the urban areas as compared to rural areas. The prevalence of impaired glucose tolerance (IGT) in the rural population is also high at 7–8%, which indicates presence of a genetic basis for Type 2 diabetes in ethnic Indian population [4].Pre-diabetes means a condition where blood glucose level are higher than normal (70-130 mg/dl), Pre-diabetes does not usually have any signs or symptoms. The exact cause of prediabetes is unknown. But family history and genetics appear to play an important role in development of pre-diabetes. The same factors that increase the chances of getting type 2 diabetes mellitus also increase the risk of pre-diabetes. These factors include: Weight: Being overweight is a primary risk factor for pre-diabetes. The more fatty tissue specially inside and between the muscle and squamous epithelium around the abdomen the more resistant the cells become to insulin. Waist size: A large waist circumferences can indicate insulin resistance. The risk of insulin resistance increases for men with waist larger than 40 inches and for women with waist larger than 35 inches. Diet: Consumption of red meat and processed meat, and drinking sugar-sweetened beverages, is associated with a higher risk of development pre-diabetes [5]. Diabetes mellitus is a condition defined by persistently hyperglycaemia (high glucose) in the blood. The two most common types of diabetes mellitus are insulin dependent type -1 diabetes and non-insulin dependent type 2 diabetes. Type 1 diabetes is an autoimmune disease. This means it begins when the body's immune system mistakenly attacks other cells in the body. In type 1 diabetes, the immune system destroys the insulin-producing cells (beta cells) in the pancreas. This leaves the person with little or no insulin in the body. Without insulin, glucose accumulates in the bloodstream rather than entering the cells. As a result, the body cannot use this glucose for energy production. In addition, the high levels of blood glucose causes excessive urination, dehydration and damage the body's tissues. Type 2 diabetes occurs when the body's cells become less responsive to insulin's efforts to drive glucose into the cells, a condition called insulin resistance. As a result, glucose starts to accumulates in the blood stream. Type 2 diabetes is also called adult-onset diabetes. always start in middle or late adulthood. However, more and more children and teenagers are now developing type-2 diabetes mellitus[6]. Nesfatin-1 was discovered by Oh-I and colleagues for the first time in 2006 [7]. Nesfatin-1 is an 82 amino acid, polypeptide derived from the Protein precursor nucleobindin-2 (NUCB2), which is encoded by the NUCB2 gene [8]. Nesfatin-1 is involved in the regulation of food intake [9]. It is secreted from the hypothalamus and brain stem, and its secretion decreases during fasting. This feature of nesfatin-1 indicates that nesfatin-1 is involved in the regulation of energy homeostasis [10].

A research study has shown an anti-hyperglycaemic effect of nesfatin-1.the intravenous administration of nesfatin-1 decreased the blood glucose level significantly[11]. Vaspin contains 415 amino acids and is secreted by visceral adipose Tissue[12]. It is a serine protease inhibitor (in the family of serpinA12). Protease (enzyme) inhibitors either play a causative role in the development of obesity and metabolic disorders. Vaspin is high, it is usually involved in the regulating inflammatory responses. Another main point of Vaspin in the body is to protect the body during obesity, as Vaspin is not seen normal glucose-tolerant individuals. Vaspin works on the body through visceral adipose tissue (VAT), which is an active endocrine organ, performing functions on physiological processes, reproduction, apoptosis, inflammation, angiogenesis, blood pressure regulation, atherogenesis, coagulation, fibrinolysis, and immune and vascular homeostasis through direct or indirect impact on the regulation of proliferation [13].The hemoglobin A1c test help to diagnosed average level of blood sugar over the past 2 to 3 months. It's also called HbA1c, glycated hemoglobin test, and glycohemoglobin. HbA1c is your average blood glucose (sugar) levels for the last two to three months. If you have diabetes, an ideal HbA1c level is 48mmol/mol (6.5%) or below. If you're at risk of developing type 2 diabetes, your target HbA1c level should be below 42mmol/mol (6%).Interestingly, some studies have shown diabetes mellitus patients had Serum Vaspin concentrations are closely related to insulin resistance, also Vaspin administration acutely reduces food intake and has sustained blood glucose-lowering effects . Serum nesfatin-1 levels are decreased in pregnant women newly diagnosed with gestational diabetes. Serum Nesfatin-1 exerts a direct, glucose-dependent insulinotropic action on mouse islet beta- and MIN6 cells.

This case-control observational study aims to investigate the diagnostic efficacy of Nesfatin-1 and Vaspin in distinguishing control subjects, pre-diabetic individuals, and diabetic patients.

METHODS

Study Design: A case control observational study

Participants: A total of 234 participants were recruited, including 78 control subjects, 78 pre-diabetic patients, and 78 patients diagnosed with diabetes, matched for age and gender.
Data Collection: Random blood samples were collected, and serum Nesfatin-1 and Vaspin levels were measured using enzyme-linked immunosorbent assays (ELISA).

Ethical Consideration:
Data Analysis: Data were analysed using ANOVA, Tukey post-hoc tests, and logistic regression. Receiver operating characteristic (ROC) curve analysis was performed to assess the diagnostic accuracy of Nesfatin-1 and Vaspin.

The data for this study were collected during 2023 at Geetanjali University, where briefly describe the study setting and sample collection process. At the time of the study, the author was PG Students at Geetanjali University, Udaipur Rajasthan. Currently, the author is PhD scholar at Krishna Mohan University, Mathura Uttar Pradesh. And is continuing research in this field.

RESULTS:
1. Nesfatin-1 and Vaspin

Parameters	Mean±SD			P value
	CONTROL (N=78)	PRE-DIABETIC (N=78)	DIABETIC (N=78)	
Nesfatin-1(Pg /mL)	104.31±4.21	59.27±11.35	31.87±5.0	<0.001 *
Vaspin (Pg /mL)	101.71±4.27	74.5±8.56	38.83±2.4	<0.001 *

- Significant differences were observed in Nesfatin-1 and Vaspin levels among the three groups ($p < 0.05$).

3. Diagnostic Efficacy
Sensitivity and Specificity of Nesfatin-1 and Vaspin in Pre-diabetes and Type-II

Diabetes Mellitus.

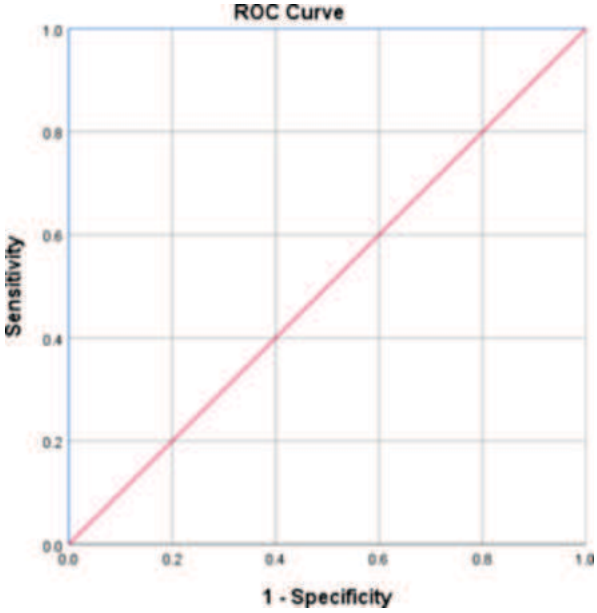


Fig :-15 ROC Curve Nesfatin-1 Pre- Diabetic

Area Under the Curve
Test Result Variable(s): VAR00002
Area
1.000

Lower and Upper Limits of Cut-off
Test Result Variable(s): VAR00002

Positive if Less Than or Equal Toa	Sensitivity	1 - Specificity
72.6280	.962	.000
109.4000	1.000	.962

- ROC Curve analysis identified Nesfatin-1 level ≤ 72.62 pg/ml as cut off value for diagnosis of pre- DM-T2 with area under the curve (AUC) sensitivity, specificity was, 1, 0.96

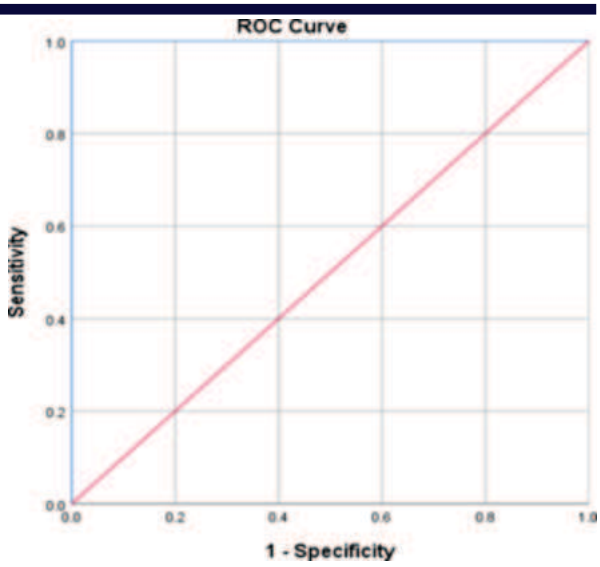


Fig :-16 ROC Curve Nesfatin-1 DM

Area Under the Curve
Test Result Variable(s): VAR00002
Area
1.000

Lower and Upper Limits of Cut-off
Test Result Variable(s): VAR00002

Positive if Less Than or Equal Toa	Sensitivity	1 - Specificity
40.5930	.974	.000
109.4000	1.000	.962

- ROC Curve analysis identified Nesfatin-1 level ≤ 40.5 pg /ml as cut off value for diagnosis of DMT2 with area under the curve (AUC) sensitivity, specificity was, 1, 0.97, 0.96 respectively

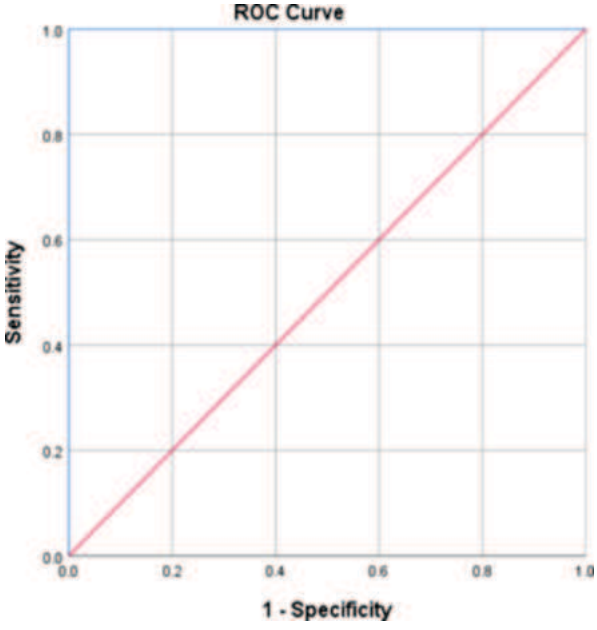


Fig :-17 ROC Curve Vaspin Pre-Diabetic

Area Under the Curve
Test Result Variable(s): VAR00002
Area
1.000

Lower and Upper Limits of Cut-off
Test Result Variable(s): VAR00002

Positive if Less Than or Equal Toa	Sensitivity	1 - Specificity
88.8200	.949	.000
108.7420	1.000	.962

- ROC Curve analysis identified VASPIN level ≤ 88.82 pg/ml as cut off value for diagnosis of pre- DMT2 with area under the curve (AUC) sensitivity, specificity were, 1, 0.94, 0.96

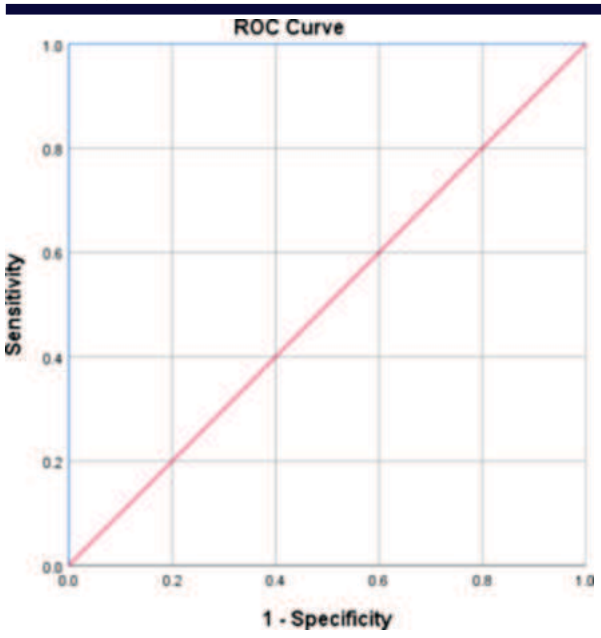


Fig :-18 ROC Curve Vaspin DM

Area Under the Curve
Test Result Variable(s): VAR00002
Area
1.000

Lower and Upper Limits of Cut-off

Test Result Variable(s): VAR00002

Positive if Less Than or Equal Toa	Sensitivity	1 - Specificity
52.8850	.949	.000
108.7420	1.000	.962

- ROC Curve analysis identified VASPIN level ≤ 52.88 pg/ml as cut off value for diagnosis of DMT2 with area under the curve (AUC) sensitivity, specificity was, 1, 0.94, 0.96.

ROC curve analysis demonstrated good diagnostic accuracy of both Nesfatin-1 and Vaspin in discriminating between control and pre-diabetic patients (AUC > 0.80) and between pre-diabetic and diabetic patients (AUC > 0.85).

Combining Nesfatin-1 and Vaspin further improved diagnostic accuracy.

DISCUSSION

The findings of this study suggest that Nesfatin-1 and Vaspin exhibit promise as diagnostic biomarkers for distinguishing control, pre-diabetic, and diabetic patients. Their ability toidentify pre-diabetic individuals is particularly valuable as early interventions can prevent progression to diabetes. In our study, we found significant decrease in Serum Nesfatin-1 level and Vaspin among pre-diabetic and diabetic compared to heathy controls, where Algul et al., found significant lower level among pre-diabetic compared to healthy control in Turkey[132]. Also, Li et al. first investigated the fasting plasma levels of nesfatin-1 in type 2 diabetes patients and found that fasting nesfatin-1 levels were significantly lower in the type 2 diabetes group compared with the levels in healthy subjects[133].

Several subsequent studies also reached the same conclusion [134-137].

Importantly, we have also found significant difference in Nesfatin-1, VASPIN & Lipid profile is ($p<0.001$) ($p<0.001$) ($p<0.001$) except VLDL Between control, pre-diabetic & Diabetic.

In our present study, the specificity and sensitivity of nesfatin-1 in pre-diabetic was derived to be 96.2% and 96.2% respectively with the cut-off range of ≤ 72.6 pg/ml (Fig-20). the specificity and sensitivity of nesfatin-1 in diabetic group was derived to be 97.4% and 96.2% respectively with the cut-off range of ≤40.59 pg/ml (Fig-21).

Algul et al. studied that, serum nesfatin-1 level progressively decreased from pre-diabetic to overt DMT2 with cut-off values of ≤ 9 and ≤ 5.5 ng/dl for their diagnosis, respectively. [138]

Similar to our results, Wang et al. found that there was decreased nesfatin-1 level among Chinese patients with DMT2 and among women with gestational diabetes compared to healthy control[139,140].

The result of previous studies revealed significantly higher levels of serum Nesfatin-1 in obese individual than in control Subjects Anwan et al. 2014

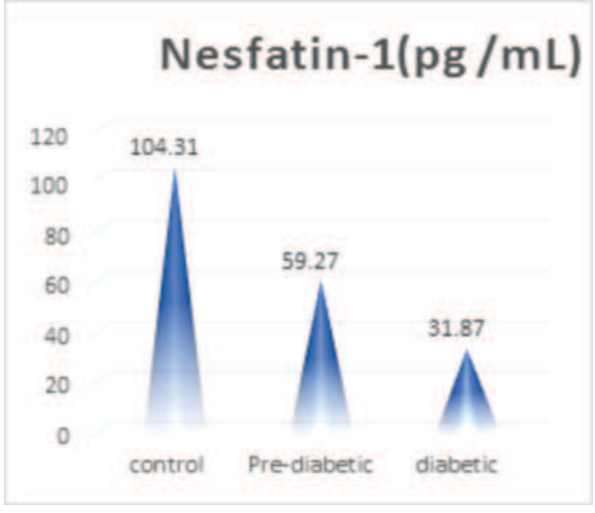
Seeger et al. Reported lower serum Vaspin levels among participants with HbA1c>7 compared to the population with HbA1c<7, thus suggesting that increased Vaspin levels might indicate a transient protective mechanism of the body against the toxicity of high blood glucose levels.[141]

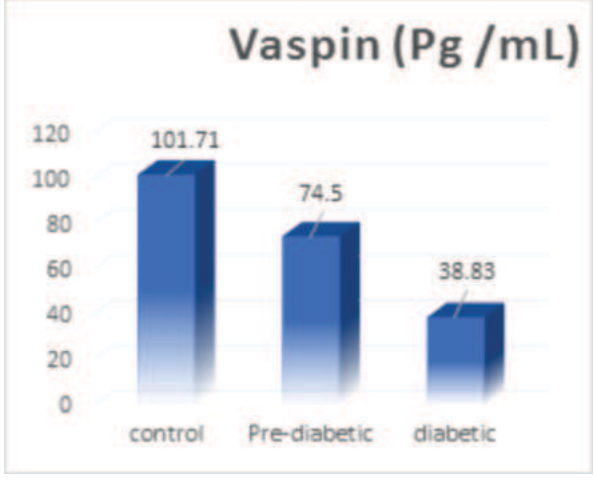
Our data showed that T2DM patients have lower serum VASPIN level whereas ogiso et al. 2011studied showed that serum VASPIN level was low in patients with reduced body weight, longer duration of diabetes and occurrence of complications. Lower serum Vaspin level was observed not only with development of diabetes but also in other micro-vascular complications. Gulcelik et al., showed that T2DM patients with neuropathy, retinopathy and nephropathy had lower serum Vaspin concentration than in patients without these complications [142-146].

In our study, the specificity and sensitivity of Vaspin in pre-diabetic was derived to be 94.9% and 96.2% respectively with the cut-off range of ≤ 88.82 pg/ml (Fig-22). the specificity and sensitivity of Vaspin in diabetic group was derived to be 94.9% and 96.2% respectively with the cut-off range of ≤ 52.88 pg/ml (Fig-22).

Limitations: Due to the case-control observational design of this investigation and the relatively small sample size, we are unable to establish a causal link between changing Nesfatin-1 and Vaspin levels in pre-diabetes and diabetes. I need further study.

Figures:





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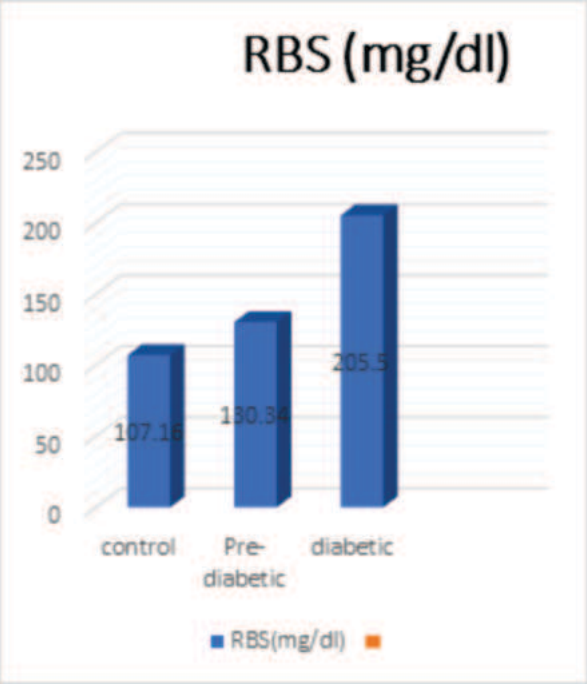

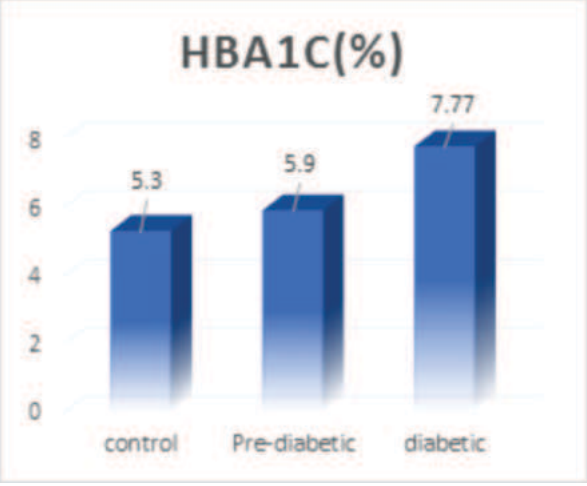

CONCLUSION

Nesfatin-1 and Vaspin may serve as valuable tools for early diabetes detection and differentiation between pre-diabetes and diabetes. Further research should explore the clinical utility of these biomarkers and their potential in guiding personalized diabetes management.

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Conflict of Interest: The authors declare no conflicts of interest.
Ethical Approval: This study was Approved by the [Geetanjali Medical College and Hospital Udaipur] Ethics Committee (Approval No. GU/HREC/EC/2022/2113).
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