DOI: https://doi.org/10.54393/pjhs.v6i7.3116

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 6, Issue 07 (July 2025)

Original Article

OPEN ACCESS

Association of Serum Asprosin with the Risk Assessment of Diabetic Retinopathy

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ARTICLE INFO

Keywords:
Diabetic Retinopathy, Asprosin, Diabetes, Serum

How to Cite:
Sarwer, A., Atif, A., Saeed, S., Perveen, S., Sabir, A., & Iqbal, M. U. N. (2025). Association of Serum Asprosin with the Risk Assessment of Diabetic Retinopathy: Association of Serum Asprosin with the Risk Assessment. Pakistan Journal of Health Sciences, 6(7), 268-272. https://doi.org/10.54393/pjhs.v6i7.3116

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Received Date: 30th April, 2025
Revised Date: 21st July, 2025
Acceptance Date: 27th July, 2025
Published Date: 31st July, 2025

ABSTRACT

Diabetic retinopathy (DR) is a microvascular complication of uncontrolled diabetes, resulting from impaired retinal blood circulation. Asprosin, a recently identified adipokine, exacerbates this condition by inducing inflammatory cytokines that enhance retinal inflammation and vascular permeability. **Objectives:** To investigate the association of serum Asprosin levels with the progression of diabetic retinopathy and its potential role as a biomarker for early diagnosis and disease monitoring. **Methods:** This cross-sectional analytical study was conducted from January to December 2023, involving 255 participants divided into three groups: diabetics with no retinopathy, diabetics with retinopathy, and non-diabetic controls (85 each). Serum Asprosin, fasting glucose, insulin, lipid profiles, and other relevant clinical features were evaluated. Statistical analyses were conducted using SPSS version 26, including One-Way ANOVA, the Bonferroni test, and Pearson's correlation. **Results:** The group with retinopathy showed the highest levels of Asprosin, insulin, fasting glucose, triglycerides, and LDL, while HDL was lowest in this group. The diabetic group showed intermediate levels, and controls showed the lowest levels across these variables. A strong positive correlation was observed between Asprosin and insulin resistance indicators such as HOMA-IR. **Conclusions:** Elevated serum Asprosin correlates with the presence and severity of diabetic retinopathy and aligns with dysregulated lipid and glycemic profiles. These findings support the potential of Asprosin as an early biomarker for DR risk and progression. Future longitudinal studies are necessary to determine its causal role and clinical applicability in diabetes-related retinal complications.

INTRODUCTION

Diabetes mellitus (DM) is one of the biggest health challenges we face today, marked by issues with insulin production or function that result in high blood sugar levels [1]. To date, most attention has been placed on Type 2 DM because of its increasing incidence and associated complications. If not controlled, high blood sugar can cause serious issues, including damage to the eyes, kidneys, and harm to the blood vessels and nerves [2]. One such major long-range complication is Diabetic Retinopathy (DR), which arises from blood flow inadequacy to the retina and can eventually result in impaired vision and even blindness [3]. DR is the leading cause of global blindness, and the good news is that it is largely preventable with early detection and treatment [4]. It is important to manage this condition to enable blood sugar levels, hypertension, and cholesterol to stay under control [5]. While blood sugar levels remain elevated, it creates advanced glycation end products (AGEs) that damage the tiny blood vessels in the retina and lead to leaks, vitreous hemorrhage, and retinal detachment [6]. The diabetes-associated increased permeability of blood vessels, inflammation, endothelial cell damage, and high

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concentration of inflammatory cytokines are responsible for DR in its advanced stages [7]. Asprosin, a peptide hormone discovered in 2016, has a significant role in regulating blood glucose through interactions with OLFR734 receptors in various organs [8]. It is negatively associated with HOMA-B and positively with HOMA-IR, indicating its link with insulin resistance [9]. When Asprosin is high, as in diabetes, it leads to insulin resistance and persistent hyperglycemia, which worsens DR [10]. By increasing oxidative stress and inflammation in the retinal tissue, asprosin makes the situation worse by hastening the destruction to the retina's blood vessels and cells. Inflammatory cytokines are produced in response to it, and this can exacerbate retinal inflammation and increase vascular permeability [11]. As a result, the blood-retinal barrier breaks down, allowing fluids and blood to seep into the retina and resulting in macular edema [9]. Additionally, asprosin affects angiogenesis by modifying the expression of VEGF (vascular endothelial growth factor), which results in aberrant and delicate angiogenesis. These vessels are prone to bleeding, contributing to retinal hemorrhages and further visual impairment. Through enhanced oxidative stress and inflammation in the retinal tissues, Asprosin accelerates the devastation of retinal blood vessels and cells, weakening the blood retinal barrier. This leads to macular edema and eventual vision loss [10]. Given these multifaceted roles, asprosin represents a potential therapeutic target for treating diabetic retinopathy. Interventions aimed at reducing asprosin levels or blocking its activity may offer new avenues for preventing or slowing the progression of this vision-threatening condition [12].

This study aimed to investigate the connection between Asprosin levels and diabetic retinopathy (DR) in a varied group of participants.

METHODS

This cross-sectional analytical study was conducted in the Outpatient Departments of Diabetes and Ophthalmology between January and December 2023, after obtaining ethical approval from the IRB of Al-Ibrahim Eye Hospital, Isra Postgraduate Institute of Ophthalmology, Karachi, Pakistan (Letter No. REC/IPIO/2023/067). A total of 255 participants were enrolled and divided equally into three groups of 85 each: diabetics with diabetic retinopathy (DR), diabetics without DR, and healthy individuals. Patients with DR were diagnosed through fundus examination, following international clinical retinopathy guidelines. A purposive sampling method was employed with specific inclusion and exclusion criteria. Individuals with non-diabetic eye diseases, active inflammation, chronic infections, steroid use, or conditions affecting glucose metabolism and obesity were excluded. The minimum sample size was calculated using the online software OpenEpi, referencing a previous study ("Frequency of Diabetic Retinopathy in Karachi, Pakistan: A Hospital-Based Study," 2015). The prevalence of DR was taken as 6.5%, with a 95% confidence level, 5% margin of error, population size (N) of 100,000, and a design effect (DEFF) of 1. The formula applied was:

$$n = \frac{DEFF \times N \times p(1-p)}{\left(\frac{d^2}{Z^2_{1-\alpha/2}} \times (N-1)\right) + p(1-p)}$$

where Z1−α/2=1.96Z_{1-\alpha/2} = 1.96Z1−α/2=1.96. This yielded a minimum required sample size of 93. However, we recruited 255 participants to improve statistical power and subgroup analyses. All participants provided informed consent in their native language. A self-designed, pre-tested questionnaire was used to collect demographic details, lifestyle and dietary habits, medical history, and current or past treatments. Anthropometric measurements (including BMI) were recorded, along with blood pressure, pulse, respiratory rate, and pulse pressure. A fasting venous blood sample (5 ml) was collected, centrifuged, and the serum was stored at −20 °C for analysis. Fasting blood glucose was measured using sodium fluoride vacutainers, while serum Asprosin and insulin levels were quantified using a human ELISA kit (Cat. No. E4095, sensitivity: 0.23 ng/ml; [Manufacturer, Country]). Data were analyzed using SPSS version 26.0. For normally distributed continuous data, one-way ANOVA with a Bonferroni post hoc test was applied. Pearson's correlation was used to evaluate relationships between anthropometric and biochemical parameters, with a particular focus on serum Asprosin levels.

RESULTS

Study results demonstrate significant differences in demographic measurements (age, weight, height, BMI, systolic and diastolic blood pressure, and pulse rate) across the control, diabetic, and retinopathy groups, with p-values around or close to .000. These variations indicate distinct physiological profiles among the groups (Table 1).

Table 1: Demographic and General Physical Parameter Analysis of the Study Groups

Variables	Controls (N=85) Mean ± SD	Diabetics (N=85) Mean ± SD	Retinopathy (N=85) Mean ± SD	F-Value	p-Value
Age	40.37 ± 9.599	50.98 ± 7.543	51.84 ± 6.469	54.155	0.000
Weight (kg)	67.65 ± 8.35	65.36 ± 8.76	67.64 ± 7.54	2.164	0.117
Height (cm)	167.35 ± 7.68	162.64 ± 10.27	165.64 ± 8.36	6.148	0.002
BMI (kg/m^2)	24.38 ± 2.62	25.05 ± 3.35	25.07 ± 2.72	1.513	0.222
Systolic BP (mmHg)	118.51 ± 7.67	117.88 ± 7.57	116.00 ± 8.27	2.350	0.097
Diastolic BP (mmHg)	75.10 ± 8.61	76.59 ± 6.82	74.47 ± 6.86	1.802	0.167

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Pulse rate (b/min)	74.07 ± 3.73	75.29 ± 4.17	77.96 ± 5.33	16.828	0.000
Pulse Pressure	42.74 ± 5.98	41.18 ± 3.75	41.82 ± 6.76	1.632	0.198
R/R (Breaths/min)	15.57 ± 2.17	16.06 ± 2.16	14.62 ± 2.16	9.651	0.000

The analysis of biochemical markers demonstrated significant disparities among the groups. Lipid parameters (cholesterol, triglycerides, HDL, LDL, and VLDL), fasting blood sugar (FBS), fasting insulin, HOMA-IR, and serum Asprosin all had highly significant p-values of .000, suggesting notable differences in metabolic and lipid profiles between the groups. The biochemical analysis of serum Asprosin revealed significant differences between groups. Specifically, the Retinopathy group exhibited the highest Asprosin levels, followed by the Diabetic and Control groups (Table 2).

Table 2: Biochemical Analysis of the Study Groups

Variables	Controls (N=85) Mean ± SD	Diabetics (N=85) Mean ± SD	Retinopathy (N=85) Mean ± SD	F-Value	p-Value
Cholesterol	152.69 ± 9.59	177.32 ± 8.62	331.38 ± 4.35	85.90	0.000
Triglycerides	157.25 ± 6.38	219.25 ± 1.27	449.10 ± 5.63	67.24	0.000
HDL	63.42 ± 5.57	56.74 ± 18.33	33.79 ± 8.06	95.39	0.000
LDL	70.19 ± 9.46	67.40 ± 34.77	207.89 ± 2.43	49.78	0.000
VLDL	31.45 ± 13.28	43.85 ± 28.85	89.82 ± 50.53	67.24	0.000
FBS	94.75 ± 7.10	124.34 ± 37.37	146.85 ± 7.90	48.48	0.000
Fasting Insulin	0.71 ± 2.48	2.39 ± 9.29	7.02 ± 3.85	8.61	0.000
HOMA-IR	0.17 ± 0.58	68 ± 2.69	2.70 ± 5.80	11.01	0.000
Asprosin	19.99 ± 7.83	26.79 ± 8.67	47.30 ± 11.59	189.423	0.000

Asprosin positively correlates with age, hypertension, diabetes status, and pulse rate, indicating higher levels in older individuals. A negative correlation with gender suggests lower levels in males. Weak negative correlations were found with systolic and diastolic blood pressure, but no significant correlation was observed with weight, height, BMI, or pulse pressure. These findings suggest Asprosin's potential as a biomarker for age-related changes, hypertension, and diabetes (Table 3).

Table 3: Correlation of Asprosin with Demographic and General Physical Parameters

Variables	Pearson Correlation	p-Value
Age (in years)	0.317**	0.000
Gender	-0.178**	0.004
Hypertension	0.222**	0.000
Diabetes	0.581**	0.000
Weight (kg)	0.006	0.930
Height (cm)	-0.019	0.759
BMI (kg/m^2)	0.036	0.570
Systolic BP (mmHg)	-0.128*	0.041
Diastolic BP (mmHg)	-0.136*	0.030
Pulse rate (beats/min)	0.279**	0.000
Pulse pressure	-0.005	0.935
R/R (breaths/min)	-.187**	0.003

**Correlation is significant at the 0.01 level (2-tailed). At a 95% confidence interval

*Correlation is significant at the 0.05 level (2-tailed). At a 95% confidence interval

BMI body mass index, blood pressure/R respiratory rate

The study found significant positive linear correlations between Asprosin and FBS, fasting insulin, HOMA-IR, cholesterol, triglycerides, LDL, and VLDL, indicating that higher Asprosin levels were associated with adverse metabolic profiles. In contrast, a significant negative correlation was observed between Asprosin and HDL, suggesting that elevated Asprosin levels may be linked to lower HDL levels, which are critical for cardiovascular and overall health (Table 4).

Table 4: Correlation of Asprosin with Biochemical Factors

Variables	Pearson Correlation (r)	p-Value
Cholesterol	0.481**	0.000
Triglycerides	0.431**	0.000
HDL	-0.586**	0.000
LDL	0.483**	0.000
VLDL	0.431**	0.000
FBS	0.501**	0.000
Fasting Insulin	0.315**	0.000
HOMA-IR	0.321**	0.000

**. Correlation is significant at the 0.01 level (2-tailed)

**. Correlation is significant at the 0.01 level (2-tailed).

HDL high high-density lipoprotein; LDL low density lipoprotein; VLDL: very low-density lipoprotein; FBS: fasting blood sugar; HOMA-IR: homeostatic assessment model of insulin resistance

DISCUSSIONS

When we compared the demographic and physical parameters, we noticed some significant differences among the groups we studied. The participants in the retinopathy group were older than those in the diabetic group, while the control group was notably younger than both. Ongoing hyperglycemia gradually weakens the retinal blood vessels, which play a role in diabetic retinopathy (DR), a condition that tends to be more severe in older individuals [13]. Previous research has also found a positive link between the prevalence of DR and the duration of diabetes, likely due to age-related changes in the retina that diminish macular blood flow and increase metabolic alterations. In comparison to the control group, both the diabetic and retinopathy groups showed higher BMI values, highlighting

DOI: https://doi.org/10.54393/pjhs.v6i7.3116

the connection between obesity, diabetes, and related complications. Earlier studies have similarly confirmed that a higher BMI is associated with diabetes, as excess body fat disrupts insulin metabolism through hormones and inflammatory markers, leading to insulin resistance and increased blood sugar levels [14]. The retinopathy group exhibited significantly altered lipid profiles compared to the diabetic group, while the control group maintained normal levels. Dyslipidemia can result in cholesterol buildup in the retina, which may lead to crystallization and contribute to DR, a finding that aligns with previous studies [15]. Current research revealed that the retinopathy group had higher levels of fasting blood sugar (FBS), fasting insulin (FI), and HOMA-IR compared to the other groups. In contrast, these parameters were within the normal range for the control group. Long-term high blood sugar can lead to various complications, including tissue inflammation, fluid imbalances, and damage to the retinal blood vessels, which aligns with findings from previous studies [16]. In the current study, serum Asprosin levels differed among the groups, peaking in the retinopathy group, followed by the diabetic group, and being the lowest in the control group. This peptide hormone is known to play a role in insulin sensitivity, appetite control, and energy balance, as highlighted in earlier research [17]. Interestingly, serum Asprosin levels tend to rise with age and prolonged diabetes, hinting at a link to metabolic issues like obesity and insulin resistance, which are more prevalent in older individuals. We observed some gender differences too, with females showing higher serum Asprosin levels than males, a finding that previous studies have also supported. This difference could be attributed to hormonal variations, body composition, and metabolic needs [18]. For instance, estrogen might boost Asprosin production, while testosterone could have the opposite effect, explaining these discrepancies. The severity of diabetes also plays a role in serum Asprosin levels, with those experiencing poorly controlled diabetes showing higher levels compared to those with better control. Elevated Asprosin levels were positively correlated with fasting insulin, fasting blood glucose, HOMA-IR, LDL, and triglycerides, underscoring its involvement in disrupted glucose metabolism and diabetic complications [19]. Conversely, we found a negative correlation between Asprosin and HDL. Previous studies have further reinforced these connections, indicating that uncontrolled blood sugar levels can lead to complications like diabetic retinopathy [20]. The cross-sectional study design is one of the limitations of the study, as the patient sample was taken only once in the study. It was carried out at a single center setting, which may limit its generalizability to other clinical settings. Several factors, like the stage and severity of diabetic retinopathy (DR), duration of illness, medication usage, or patient compliance, were not accounted for in this study, which may limit the findings. Future studies should be conducted in compliance with the above limitations may produce profound effects on findings.

CONCLUSIONS

Higher levels of Asprosin might act as both diagnostic and prognostic indicators for DR, highlighting metabolic stress and inadequate glycemic control. This biomarker could be instrumental in pinpointing patients who are at a greater risk for DR, potentially allowing for timely interventions to prevent or slow down its progression. Asprosin shows great potential as a means for early detection and focused treatment of complications related to diabetic retinopathy. As it was a cross-sectional study, future longitudinal studies are needed to establish causality and determine its clinical utility.

Authors Contribution

Conceptualization: AA, MUNI
Methodology: AS, MUNI
Formal analysis: AA, MUNI
Writing review and editing: SS, SP, AS

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

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