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Original Article

Comparison of Serum Visfatin Levels in Post-Menopausal Pakistani Women with and Without Breast Carcinoma

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ABSTRACT

Objective: To compare serum Visfatin levels in Pakistani post-menopausal women having breast carcinoma with healthy women.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Physiology Department, Army Medical College, in collaboration with Armed Forces Institute of Pathology, Rawalpindi, Pakistan, from Dec 2019 to Dec 2020.

Methodology: Eighty post-menopausal Pakistani women were included, out of which forty women were post-menopausal newly diagnosed and histologically confirmed cases of breast carcinoma awaiting their treatment. Menopause was confirmed through interviews and relevant history. Serum Visfatin levels were determined using an enzyme-linked immunosorbent assay (ELISA).

Result: Mean serum Visfatin levels were significantly higher in the Breast Carcinoma-Group (28.14±8.17 ng/ml) compared to the Healthy Control-Group (13.64±1.07 ng/ml). Moreover, serum Visfatin levels correlated positively with weight (r=0.735), body mass index (r=0.678), waist circumference(r=0.295) and waist-to-hip ratio (r=0.220).

Conclusion: Serum Visfatin levels were markedly elevated in post-menopausal women with breast carcinoma as compared to Healthy Controls. Higher serum Visfatin may be regarded as a potential risk factor in the development of breast carcinoma.

Keywords: Breast Carcinoma, Menopause, Obesity, Visfatin.

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INTRODUCTION

Breast carcinoma is the most prevalent cancer among females, with a high mortality rate and varying survival rates.[1] Disease awareness and early detection remain the foundation of breast carcinoma regulation.[2] Studies indicate the association of hormone receptor-positive breast carcinoma with obesity.[3] The role of adipose tissue as an endocrine organ and the association of adipokines secreted from the adipose tissue in the development of breast carcinoma is vastly being studied.[4]

Visfatin, also known as Nampt (nicotinamide phosphoribosyl transferase), was discovered in 1994 with a gene isolated from leucocytes.[5] Studies have shown the positive association of serum Visfatin with breast carcinoma in post-menopausal females who are obese.[6] Elevated Visfatin expression is also associated with malignant behaviour and an adverse prognosis of breast carcinoma. It also promotes metastasis through gene expression of tumour angiogenesis.[7] One such product is a signal protein named vascular endothelial growth factor (VEGF) that promotes angiogenesis. Tumor progression and invasion are promoted through matrix metalloproteinases (MMP 2/9). Breast carcinoma patients with high levels of serum Visfatin have a poor prognosis, advanced stage, metastatic tendency and lymph node involvement along with large-sized tumours. Studies on animal models have also revealed Visfatin to be associated with tumour growth and metastasis into the lungs, and suppression of these effects is observed when inhibitors of c-Abl and STAT3 are given to animal models.[8,9] After menopause, increased adiposity increases the risk of breast carcinoma because the visceral adipose tissue secretes Visfatin and other adipokines.[10] Early diagnosis can lead to improved patient survival. In this study, we have compared serum Visfatin levels in post-menopausal healthy women with those having breast carcinoma to establish its association with breast carcinoma as a novel diagnostic/prognostic biomarker.

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METHODOLOGY

The study was conducted at the Department of Physiology, Army Medical College/National

University of Health Sciences in collaboration with the Armed Forces Institute of Pathology, Rawalpindi Pakistan, from December 2019 to December 2020 after approval from the Ethics Review Committee (ERC/ID/90). The sample size was calculated by using a G power sample size calculator based on the prevalence of breast carcinoma in post-menopausal women.[10]

Inclusion Criteria: Post-menopausal women aged 45-65 years with newly diagnosed and histologically confirmed cases of breast carcinoma and post-menopausal healthy women (Controls) were included.

Exclusion Criteria: Subjects with any other carcinoma, distant metastasis at the time of diagnosis, suffering from inflammatory diseases and users of anti-inflammatory drugs were excluded.

Diagnosis of breast carcinoma was made on histopathology done at the Armed Forces Institute of Pathology, Rawalpindi, and only newly diagnosed cases awaiting treatment were selected. A non-probability convenience sampling technique was used for sample selection. The basic demographic data and relevant history and physical examination were recorded for all subjects.

Blood sampling was done under strict aseptic conditions. Samples for the determination of Visfatin were collected in serum-separating tubes. They were allowed to clot, then centrifuged and stored at -70 Celsius. Analysis was performed by an automated EMP analyzer machine that worked on the principle of Enzyme-linked immunosorbent assay (ELISA). Anthropometric parameters were measured, including age, weight, height, BMI, waist circumference and waist-to-hip ratio.

Statistical Package for Social Sciences (SPSS) version 22.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Independent sample t-test was applied to explore the inferential statistics. Pearson correlation coefficient was used to assess the correlation of serum Visfatin with other study variables. The *p*-value of ≤0.05 was considered significant.

RESULTS

A total of eighty participants were included in the study, which included forty newly diagnosed post-menopausal breast carcinoma patients and forty post-menopausal healthy women. Serum Visfatin was measured for all study participants.

All anthropometric parameters significantly differed between the two groups, including weight, height, body mass index (BMI), waist circumference and waist-to-hip ratio (Table-I).A comparison of serum Visfatin between the two groups showed that serum Visfatin levels were higher, with a mean value of 28.14±8.17 ng/ml in the Breast Carcinoma Group compared to the Control Group, 64±1.07 ng/ml (*p*-value of <0.001) (Table-II).

Table-I: Comparison of Age and Anthropometric Parameters between Breast Carcinoma Group and Healthy Control Group (n=80)

Anthropometric Parameter	Breast Carcinoma Group n=40 Mean±SD	Control Group n=40 Mean±SD	*p*-value
Age (Years)	60.38±7.33	62±6.17	0.288
Weight (Kg)	71.5±12.35	66.6±7	0.008*
Height (cm)	153.6±7.34	157.9±6.2	<0.001*
Body mass index (BMI)	30.8±4.78	26.9±3.11	<0.001*
Waist Circumference (cm)	94.8±12.76	87±9.7	0.003*
Waist to Hip Ratio	0.86±0.042	0.84±04	0.02*

Table-II: Comparison of Serum Visfatin Levels between Study Groups (n=80)

Serum Visfatin	Breast Carcinoma Group n=40 Mean±SD	Control Group n=40 Mean±SD	*p*-value
Serum Visfatin (ng/ml)	28.14±8.17	13.64±1.07	<0.00*

Moreover, serum Visfatin had a significant positive correlation with weight (r-value of 0.735 and *p*-value of <0.001), body mass index (r-value of 0.678 and *p*-value of <0.001), waist circumference (r-value of 0.295 and *p*-value of 0.008) and waist to hip ratio (r-value of 0.220 and *p*-value of 0.05) (Table-III).

Table-III: Correlation between serum visfatin and anthropometric parameters of metabolic syndrome

Anthropometric parameters of metabolic syndrome	Serum Visfatin	
	r-value	*p*-value
Age (years)	0.047	0.774
Weight (kg)	0.735**	<0.001*
Height (cm)	0.105	0.517
BMI	0.678**	<0.001*
Waist Circumference (cm)	0.295**	0.008*
Waist to Hip Ratio	0.220**	0.050*

DISCUSSION

Carcinoma is becoming a major cause of death worldwide. Among females, breast carcinoma is one of the most prevented carcinomas, and it is implicated as the leading cause of oncology-induced deaths worldwide.[11,12] Pakistan has the highest age-standardized incidence and mortality rate from this disease.[13]

In our study, the serum Visfatin levels were significantly higher in the breast carcinoma group (28.14±8.17 ng/ml) compared to the healthy control group (13.64±1.07 ng/ml). A study conducted in Makkah by Assiri et al. in 2016 had similar results.[6] Their study showed that the breast carcinoma group had higher serum Visfatin levels (18.36±3.92 ng/ml) than healthy controls (15.6±2.66 ng/ml) with a *p*-value of <0.05.[6]

A longitudinal case-control study with 258 new cases of invasive ductal carcinoma and 100 controls was carried out in Taiwan by Hung *et al*.[9] and this study also showed significantly increased serum Visfatin levels in breast carcinoma patients (40.87±13.86 ng/ml) as compared to controls (32.20±17.42 ng/ml) with a *p*-value of <0.001. Another study used an enzyme-linked immunosorbent assay to detect serum Visfatin levels and had results similar to our study.[14] In agreement with our findings for Visfatin, this study also reported higher mean serum Visfatin levels in breast carcinoma patients than in controls. However, this study was carried out on a bigger sample size, and patients were followed through their course of treatment for ten years. Therefore, this study also concluded that raised serum Visfatin levels were associated with poor survival. Visfatin promotes the proliferation and the rate of DNA synthesis in breast carcinoma cells. Another study showed that Visfatin-treated cells had increased cell survival mainly by activating c-Abl (cellular-Abelson tyrosine kinase) and STAT3 pathways.[15]

Another previous study demonstrated similar results of high mean serum Visfatin levels in post-menopausal women suffering from breast carcinoma. They also used ELISA, like our study, to detect serum Visfatin serum levels.[16] The inclusion and exclusion criteria were almost similar to our study, and they took blood samples from patients a night before surgery; serum Visfatin levels were significantly higher in the breast carcinoma group (65.6±16.9 ng/ml) as compared to healthy controls (37.2±9.6ng/ml) with a *p*-value of <0.001. These values were higher compared to our study, and the possible cause for this difference could be that they took blood samples from pre-operative breast carcinoma patients a night before surgery. So apparently, they had larger tumour masses that required surgery, and it is known that serum Visfatin levels are associated with tumour size. At the same time, we took breast carcinoma patients at the start of their disease when they came for histopathology and were awaiting treatment. In addition, the same patient sample was tested twice in this study, and the mean value was used in the final results. Unlike our study, the patients were followed for the next three years to see the outcome, disease-free survival and overall survival. They tried to establish the prognostic role of Visfatin in breast carcinoma.

A case-control study on 102 post-menopausal breast carcinoma patients and 102 age-matched healthy controls; researchers studied various other adipokines besides Visfatin.[17] Like our study, they found higher mean serum Visfatin levels in breast carcinoma patients (57.9±31.2 ng/ml) compared to healthy controls (43.6±28.1 ng/ml) with a *p*-value of <0.001. In contrast to our study, they showed no association of Visfatin with anthropometric and metabolic parameters. Our study had a significant positive association of anthropometric and some metabolic parameters with serum Visfatin. In this study, the post-menopausal women with the highest quartile of serum Visfatin and who were obese with a raised BMI had an elevated risk of developing breast carcinoma. This suggests that altered secretion of serum Visfatin might be the cause of the association between post-menopausal breast carcinoma and obesity. Another contrast to our study was that we included post-menopausal women up to 65 years of age, whereas they included women up to 85 years of age. Therefore, old age group might also be a factor because this age group has various other health issues that can affect anthropometric and metabolic parameters.[18]

CONCLUSION

Serum Visfatin levels were markedly higher in the post-menopausal women having breast carcinoma as compared to their healthy controls. Elevated serum Visfatin may be regarded as a potential risk factor in the development of breast carcinoma.

Conflict of Interest: None.

Authors Contribution:

Following authors have made substantial contributions to the manuscript as under:

LG & UA: Conception, study design, drafting the manuscript, approval of the final version to be published.

NZ & MW: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

SA & SJ: Critical review, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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