


Original Research Article

A study on fasting insulin levels in non-diabetic carcinoma breast patients

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Abstract

Background: With the advent of multimodality treatment approach, the number of cancer survivors is increasing which push us further to increase our knowledge on potential sites which could be exploited for the survival benefit of the patients. Insulin resistance has long been known to be a risk factor in various malignancies including breast, colon and endometrium. Insulin, a member of the family of growth factors that includes insulin-like growth factors IGF 1, IGF II, exerts mitogenic effects on normal and mitogenic breast epithelial cells acting via insulin and IGF 1 receptor. Insulin resistance leads to overexpression of the above-mentioned receptors and malignant transformation of cells.

Aim of the study: To assess the prevalence of insulin resistance in non-diabetic carcinoma breast patients and to document fasting insulin levels in the same cohort of patients.

Materials and methods: This was a prospective study conducted in the Department of General Surgery, Government Stanley Medical College in 2018. This study included all patients diagnosed as carcinoma breast, who was a non-diabetic. The relevant details collected included a clinical, radiological, pathological and biochemical profile of patients with carcinoma breast.

Results: In our study, the majority of the patients had T3 lesion, with an almost equal incidence of T2. The incidence of T1 lesion was almost nil, which might indirectly indicate the lack of identification of carcinoma breast at an earlier stage in spite of widespread screening tests and campaign. In our study, the prevalence of insulin resistance was 17.2%. Five patients out of 29 of our study group had fasting insulin levels > 25µIU/L and found to have insulin resistance, with blood glucose levels within normal range.

Conclusion: The study stated that insulin resistance which is considered a risk factor for many cancers, including carcinoma breast, might be prevalent in patients with normal glucose levels and in the absence of any symptoms. Screening them may be useful in identifying this cohort of patients and

treating them with tailored insulin resistance lowering agents like metformin which was found to have anti tumourigenic activity, as well as complete pathological response.

Key words

Breast Carcinoma, Insulin Resistance, Sex hormones, Fasting blood glucose level.

Introduction

Humans have known breast cancer for a very long time. For those who think, Breast cancer is a modern disease, they would be surprised to know that the disease can be tracked right back to 3000 – 2500 BC where medical texts made by Edwin Smith Papyrus describes cases of breast cancer. And Hippocrates described the stages of breast cancer as early as 400 BC [1]. In the first century AD, doctors experimented with surgical incisions to destroy tumors. They thought breast cancer was due to the end of menstruation and thus came the concept of attributing malignancies to old age. The Renaissance saw the revival of surgery & doctors began exploring human bodies [2]. John Hunter was the one who identified lymph as a cause of breast cancer spread. It's both ironical and tragical that an exposed organ with easy access to self-examination and clinical diagnosis continues to exhort such a heavy toll [3]. The frequency of this disease in women has prompted an intensive study of risk factors that develop breast cancer to gain cues to its etiology as well as to identify risk factors that would be helpful for prevention strategies [4]. With the advent of multimodality treatment approach, the number of cancer survivors is increasing which push us further to increase our knowledge on potential sites which could be exploited for the survival benefit of the patients [5]. Insulin resistance has long been known to be a risk factor in various malignancies including breast, colon and endometrium. Insulin, a member of a family of growth factors that includes insulin-like growth factors IGF 1, IGF II, exerts mitogenic effects on normal and mitogenic breast epithelial cells acting via insulin and IGF 1 receptor. Insulin resistance leads to overexpression of the above-mentioned receptors and malignant transformation of cells [6]. Recent studies have shown that treatment with

metformin reduces insulin resistance and showed complete pathological response and less local recurrence and distant metastasis. Reliable data on insulin resistance in our population is scarce and its association with breast cancer is still a matter of debate which needs further analysis. Hence we felt the need for the study in our setting [7].

Materials and methods

This was a prospective study conducted in the Department of General Surgery, Government Stanley Medical College in 2018. This study included all patients diagnosed as carcinoma breast, who was a non-diabetic. The relevant details collected included a clinical, radiological, pathological and biochemical profile of patients with carcinoma breast.

Inclusion criteria: Patients with pathologically proven carcinoma breast.

Exclusion criteria:

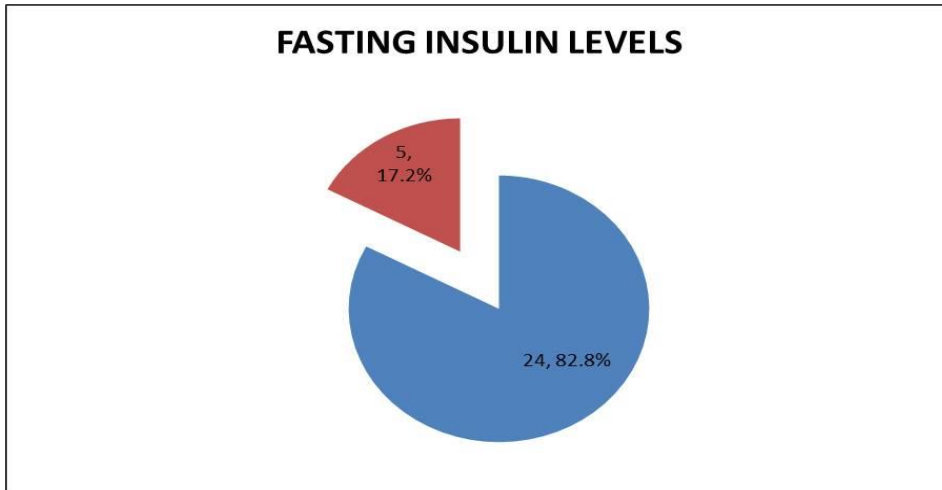
- Excluded were patients who have known a case of diabetes mellitus and found to be diabetic during the course of the evaluation.
- Male patients with carcinoma breast.

Statistical analysis: The collected data were analyzed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis was used for categorical variables and the mean and S.D were used for continuous variables.

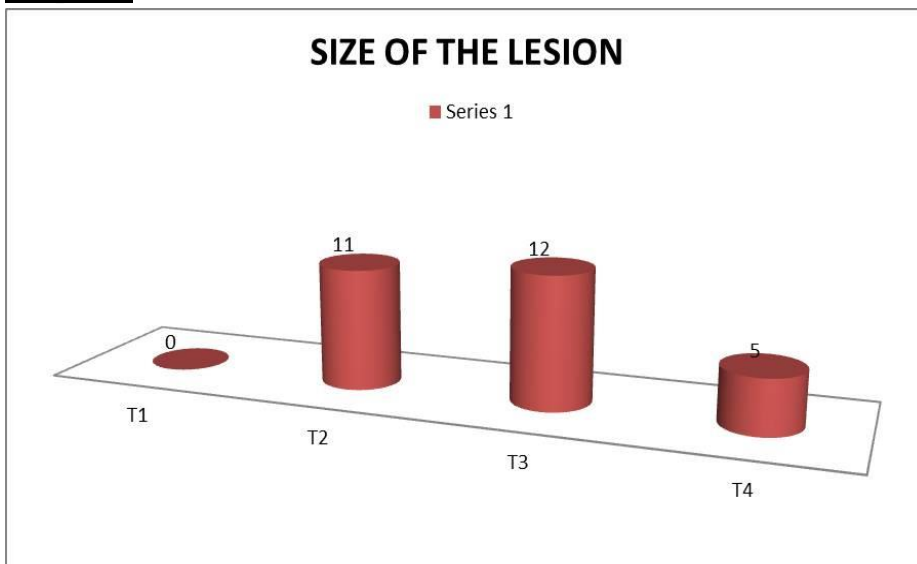
Results

In our study, the prevalence of insulin resistance was 17.2%. Five patients out of 29 of our study group have fasting insulin levels $> 25\mu\text{IU/L}$ and found to have insulin resistance, with blood glucose levels within normal range (**Graph – 1**). Size of lesion was as per **Graph – 2**.

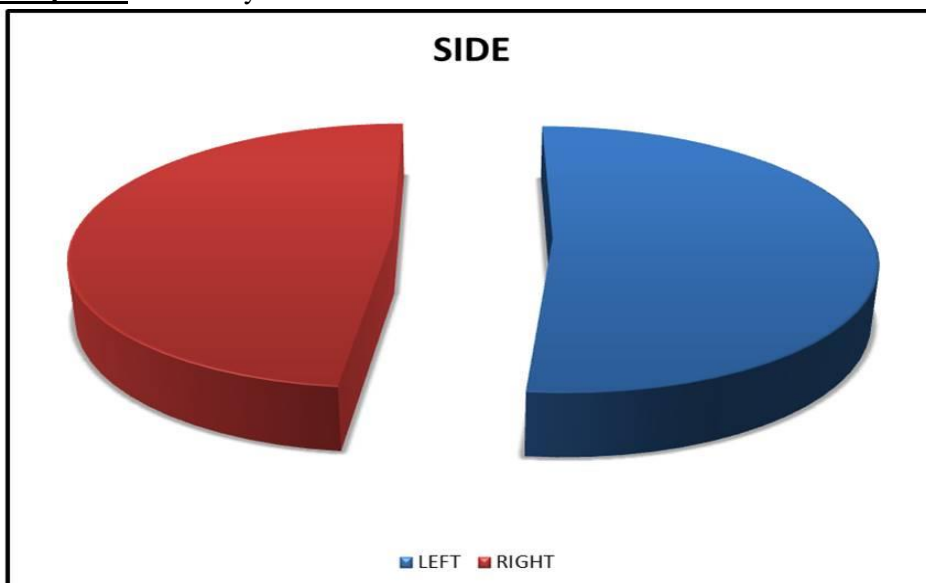
Graph – 1: Fasting insulin resistance.



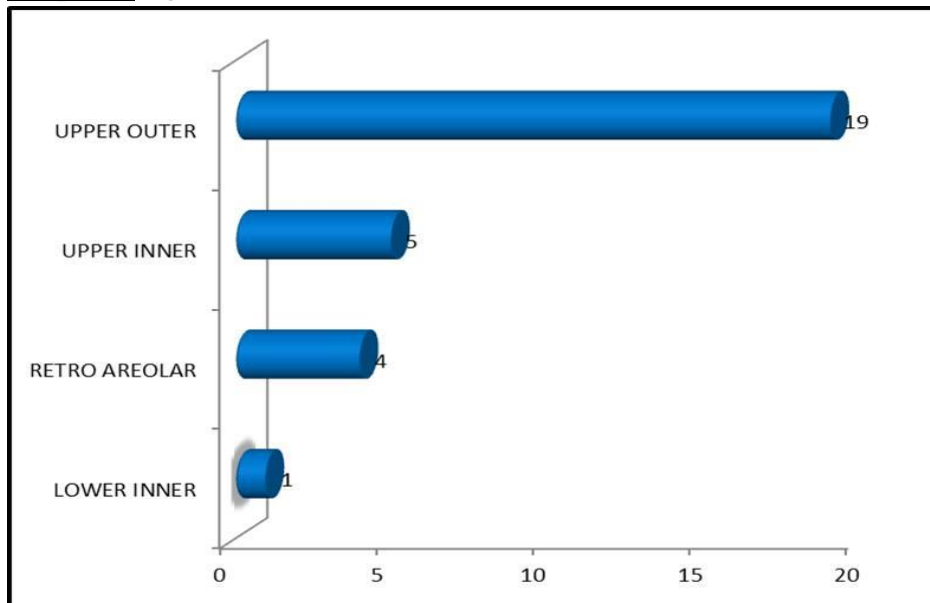
Graph – 2: Size of the lesion.



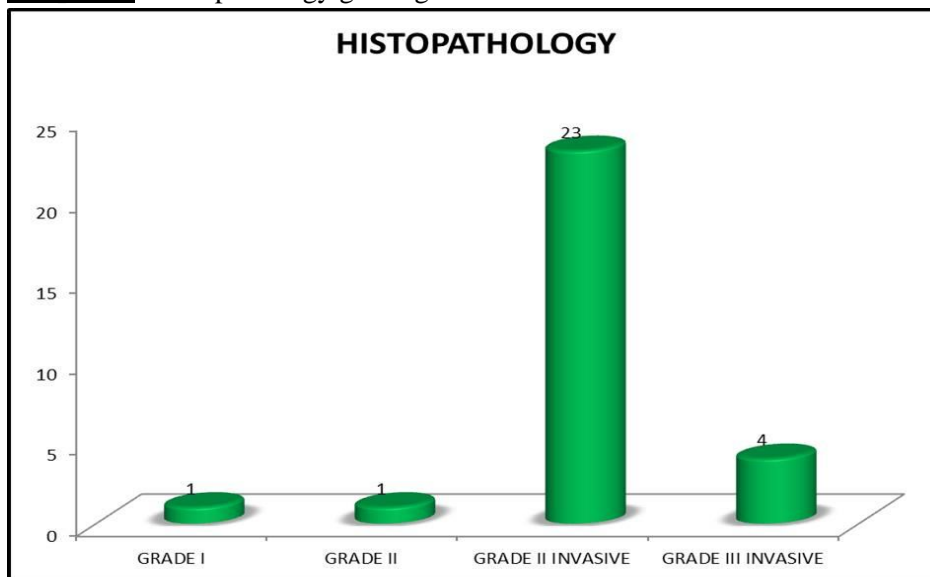
Graph – 3: Laterality.



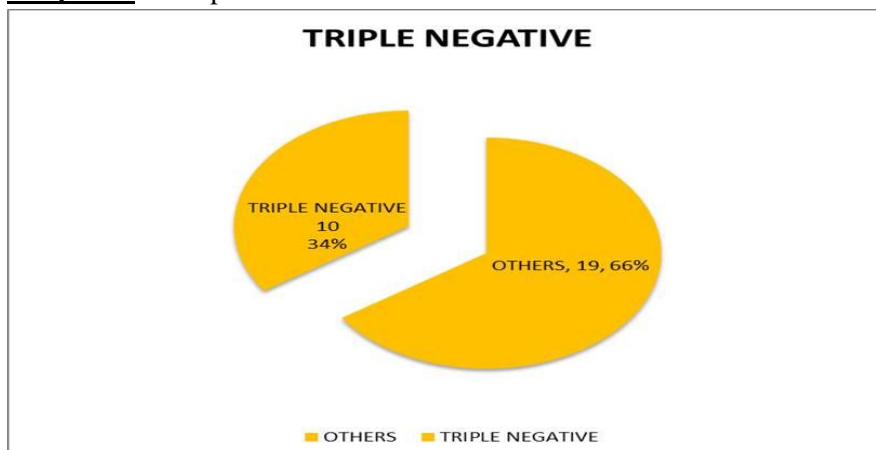
Graph – 4: Quadrant involved.



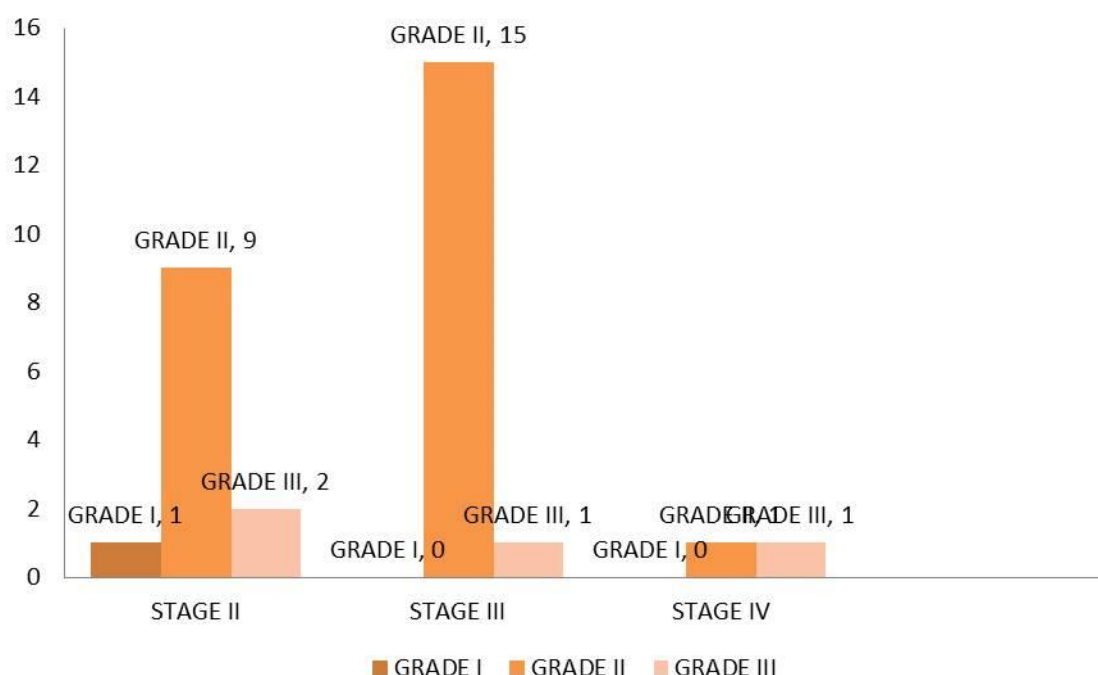
Graph – 5: Histopathology grading.



Graph – 6: Receptor status.



Graph – 7: Stage with grade of the tumor.



Laterality was found to be almost equal between both sides, with a slight increase in left-sided lesion (**Graph – 3**).

Upper outer quadrant was found to be the commonest involved quadrant (65.5%) as per **Graph – 4**.

23 out of 29 patients had GRADE II invasive cancer accounting to almost 80% (**Graph – 5**).

In our study, the incidence of triple-negative breast cancers was found to be 34%, which was higher when compared to other studies (**Graph – 6**).

Grade II appears to be common in all stages of a breast as per **Graph – 7**.

Discussion

Despite the availability of a large amount of data on the presence of a causal link between IGT or T2D and BC risk the role of sustained hyperglycemia, hyperinsulinemia, or IR in BC prognosis is far less investigated especially in non-diabetic BC patients [8]. Indeed, only a few studies - mostly from a single research group -

have been performed in cohorts of BC patients with metabolic characteristics comparable to those of the general population, while the majority of the articles available in the international literature have focused on the association between BC and glucose metabolism in patients with clinical features belonging to metabolic syndrome obesity or dyslipidemia, all of which recognize IR as a common factor [9]. Despite the observed differences, the results of our study are in agreement with, and extend, those reported by Goodwin, et al. suggesting that pretreatment insulin levels might have a prognostic role not only in early BC but also in advanced stages of the disease, thus reinforcing the rationale for lifestyle or insulin targeting pharmacologic interventions as a means of improving breast cancer outcomes [10]. In this light, it is worth mentioning an in vitro study on BC cells showing how insulin pricing potentially contributes to the estradiol-induced cancer growth by modulating estradiol-insulin signaling crosstalk. Insulin resistance as documented by increased fasting insulin levels was found in 5 out of 29 patients, which accounts to 17 %, which is slightly lower than a study conducted at Korea, which showed 26.4% prevalence of

insulin resistance and was associated with larger tumors [11]. Another study from Italy shows 46.95 % resistance with advanced breast cancers and with poor survival rates. This insists on the need for this study in mass populations to screen for insulin resistance [12]. The incidence of triple negative breast cancer is 34% present which is slightly higher when compared to other studies. The incidence of carcinoma breast is found to be most common in the age group of 41-50, with an almost equal incidence in 31-40 years. There seems to be a shifting trend of carcinoma breast in younger patients. The earliest age being 32 years and the other extreme being 76 years. Mean age group is 49.66. Insulin resistance was found more in women < 50 years of age (3 /5), in the analyzed cohort of patients. Its prevalence was more in postmenopausal women, with an almost equal incidence in premenopausal women [13]. It was associated with > 2 cm lesion. Patients with insulin resistance (5/29) had the node-positive disease. Insulin resistance is found in patients with ER negative, PR negative disease. Prevalence of HER 2 neu positivity is found more in patients with insulin resistance [14]. Three out of five patients who had insulin resistance had neoadjuvant chemotherapy prior to modified radical mastectomy. Stage III breast cancer is common among all age groups (55.12%) Grade II is found to be common in all stages of the tumor [15].

Conclusion

The study stated that insulin resistance which is considered a risk factor for many cancers, including carcinoma breast, might be prevalent in patients with normal glucose levels and in the absence of any symptoms. Screening them may be useful in identifying this cohort of patients and treating them with tailored insulin resistance lowering agents like metformin which was found to have anti tumourigenic activity, as well as complete pathological response.

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