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ORIGINAL ARTICLE

Smoking Effects on Serum Hepcidin Levels in Breast Cancer Patients: A Cross-Sectional Study

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Abstract

Background: Breast cancer remains a leading cause of cancer-related morbidity and mortality among women worldwide. Hepcidin, a central regulator of iron metabolism, has emerged as a potential biomarker in cancer biology and a predictive agent of recurrence. As smoking represents a risk factor in developing many types of cancer, this article discusses the possibility of the effect of smoking on hepcidin levels in women diagnosed with breast cancer.

Aim: To investigate the effect of smoking on hepcidin levels in breast cancer patients, and to assess the association with recurrence rate.

Materials and methods: The present cross sectional study comprises of 39 breast cancer patients across Stages (I, II, III), who were newly diagnosed and histologically confirmed. Serum Hepcidin levels were measured using ELISA before ongoing with any type of treatment. Patients were categorized based on smoking status. The chi-square test was used to evaluate the associations between smoking and hepcidin levels with recurrence.

Results: The sample concluded 39 women who were diagnosed with breast cancer. 23 patients were smoker with (58.97%). No statistically significant association was found between smoking status and serum hepcidin levels (p value = 0.43). Similarly, smoking status was not significantly associated with cancer relapse (*P* value = 0.15).

Conclusion: Smoking may not significantly impacts hepcidin regulation or the risk of recurrence in breast cancer patients.

Keywords

Hepcidin, Breast cancer, Relapse, Smoking

Introduction

Breast cancer is one of the most common malignancies in women, with significant implications for public health globally [1]. The etiology of breast cancer involves a complex interplay of genetic, hormonal, and environmental factors. Advances in early detection and treatment have improved survival rates, but challenges remain in understanding the factors influencing disease progression and recurrence [2].

Hepcidin is a peptide hormone produced by the liver that regulates iron homeostasis by inhibiting ferroportin [3], the iron exporter. Its role in cancer biology has garnered attention due to its regulatory function on iron, which is crucial for cell proliferation and metabolism [4]. Elevated hepcidin levels have been observed in various cancers, suggesting a potential role in tumor growth and progression [5].

Smoking is a well-established risk factor for many cancers, including breast cancer [6,7]. The carcinogens in tobacco smoke can induce genetic mutations and promote a pro-inflammatory environment, contributing to cancer development and progression [7]. However, the relationship between smoking and hepcidin levels in breast cancer patients remains underexplored.

Several studies have attempted to elucidate the impact of smoking on hepcidin levels, yielding mixed results. Some research suggests that smoking may elevate hepcidin levels due to increased inflammatory markers, while other studies report no significant effect [8-10]. Understanding the interaction between smoking

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and hepcidin levels in breast cancer patients could provide valuable insights into disease mechanisms and potential therapeutic targets.

Objectives

This study aims to explore the association between smoking status and serum hepcidin levels in breast cancer patients. Additionally, it seeks to determine whether smoking influences the likelihood of cancer relapse. By investigating these relationships, this study hopes to contribute to the broader understanding of breast cancer progression and the role of lifestyle factors in patient outcomes.

Materials and Methods

Study sample

This cross-sectional study included 39 breast cancer patients recruited from a single oncology center (Oncology Centre at Tishreen University Hospital). The patients were evenly distributed across three stages of breast cancer: 13 patients in Stage I, 13 in Stage II, and 13 in Stage III.

Place of the study

Oncology Centre, Tishreen University Hospital (TUH), Lattakia, Syria.

Inclusion criteria

All women who were admitted to the Oncology Centre and diagnosed with breast cancer before ongiong any type of treatments (surgical, chemical or radiological).

Exclusion criteria

1. Chronic breast diseases
2. Disorders of iron metabolism
3. Acute/chronic hemolytic lesions
4. Acute/chronic inflammatory or septic diseases
5. Severe nutritional deficiency

Sample collection

Blood samples were taken from each participant when confirming diagnosis with histological study and before undergoing any type of treatment. The samples were processed and stored at -20 °C until analysis.

Hepcidin measurement

Serum hepcidin levels were quantified using a commercially available enzyme-linked immunosorbent assay (ELISA) kit according to the manufacturer's instructions. Patients were categorized into low and high hepcidin groups based on the median hepcidin level.

Smoking status

Smoking status was determined through patient self-reporting and categorized as either smoker or non-smoker. Patients were not classified on the amount of cigarettes.

Statistical analysis

Chi-square tests were conducted to assess the relationship between smoking status and serum hepcidin levels, as well as between smoking status and cancer relapse. A *p*-value of less than 0.05 was considered statistically significant.

Results

Table 1 shows the correlation between hepcidin levels and smoking status, 23 patients of 39 were smokers. 13 patients of whom had increased levels of hepcidin. Chi-square analysis indicated no significant association between smoking status and serum hepcidin levels ($p = 0.43$).

Table 2 shows the distribution of patients by smoking status and the recurrence rate in patients with breast cancer. 15 patients of 39 were relapsed with (38.46%), 11 patients of whom were smokers. After analyzing this data, we found that 11 patients diagnosed with relapsed breast cancer were smokers and had high levels of Hepcidin (28.2%). Chi-square analysis showed no significant association between smoking status and cancer relapse ($p = 0.15$).

Discussion

This study aimed to elucidate the relationship between smoking status and serum hepcidin levels in breast cancer patients, as well as to explore the potential impact of smoking on cancer relapse. Our findings indicate no significant association between smoking status and serum hepcidin levels. Similarly, smoking was not significantly associated with an increased risk of cancer relapse.

The lack of association between smoking and hepcidin levels suggests that, in this cohort, smoking may not significantly influence hepcidin regulation. This

Table 1: Hepcidin levels and smoking status.

Smoking Status	Low Hepcidin N (%)	High Hepcidin N (%)	Total
No	9	7	16 (41.03%)
Yes	10	13	23 (58.97)
Total	**19 (48.7%)**	**20 (51.3%)**	**39 (100%)**

Table 2: Distribution of patients by smoking and cancer relapse.

Smoking Status	Low Hepcidin	High Hepcidin	Total
	Non-Relapse	Relapse	
No	12	4	16
Yes	12	**11 (28.2%)**	23
Total	24	15	39

finding is consistent with some previous studies but contrasts with others that reported elevated hepcidin levels in smokers [11-15]. The variability in results across studies may be attributed to differences in study populations, methodologies, and sample sizes.

Regarding cancer relapse, our results indicate that smoking status does not significantly affect the likelihood of relapse in breast cancer patients. This is in line with some literature suggesting that while smoking is a risk factor for the initial development of various cancers, its impact on relapse may be less pronounced and influenced by a multitude of other factors, including treatment protocols, genetic predispositions, and overall health status [16-20].

Several limitations should be considered when interpreting these results. The sample size of this study was relatively small, which may limit the generalizability of the findings. Additionally, self-reported smoking status may be subject to reporting biases. Future studies with larger sample sizes and more rigorous verification of smoking status could provide more definitive conclusions.

Despite these limitations, this study contributes to the understanding of the complex interplay between lifestyle factors and cancer biology. The findings suggest that while smoking is a critical factor in cancer development, its role in modulating serum hepcidin levels and influencing relapse may be limited. Further research is warranted to explore the underlying mechanisms and to identify other potential biomarkers that may interact with smoking in breast cancer progression.

Conclusion

This study found no significant relationship between smoking status and serum hepcidin levels or cancer relapse in breast cancer patients. These findings suggest that smoking may not significantly impact hepcidin regulation or relapse risk in this patient population. Future research should focus on larger, longitudinal studies to confirm these findings and to explore other factors influencing hepcidin levels and cancer outcomes.

Statement & Declarations

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Competing interests

The authors have no relevant financial or non-financial interests to disclose.

Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis. All authors read and approved the final manuscript.

Ethical approval

This research received approval from the scientific research ethics committee at Tishreen University and Tishreen University Hospital.

Consent to participate

Written informed consent was obtained from all individual participants included in the study.

Consent to publish

The authors affirm that human research participants provided informed consent for publication of this manuscript.

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References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataramet I, et al. (2021) Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 71: 209-249.
2. Tao Z, Shi A, Lu C, Song T, Zhang Z, et al. (2015) Breast cancer: Epidemiology and etiology. Cell Biochem Biophys 72: 333-338.
3. Nemeth E, Ganz T (2009) The role of hepcidin in iron metabolism. Acta Haematol 122: 78-86.
4. Vela D, Vela-Gaxha Z (2018) Differential regulation of hepcidin in cancer and non-cancer tissues and its clinical implications. Experimental & Molecular Medicine 50: e436.
5. Tesfay L, Clausen KA, Kim JW, Hegde P, Wang X, et al. (2015) Hepcidin regulation in prostate and its disruption in prostate cancer. Cancer Res 75: 2254-2263.
6. Gaudet MM, Gapstur SM, Sun J, Diver WR, Hannan LM, et al. (2013) Active smoking and breast cancer risk: original cohort data and meta-analysis. J Natl Cancer Inst 105: 515-525.
7. Reynolds P (2013) Smoking and breast cancer. J Mammary Gland Biol Neoplasia 18: 15-23.
8. Mustafa AJ, Jalil PJ, Ade JH, Mustafa J Anjam, et al. (2023) Serum iron, ferritin, erythroferrone and their inter-correlation in adult cigarette smokers: A case-control study. Iraqi Journal of Science 64: 5491-5500.
9. Chełchowska M, Maciejewski TM, Mazur J, Gajewska J, Zasimovich A, et al. (2019) Active tobacco smoke exposure in utero and concentrations of hepcidin and selected iron parameters in newborns. Int J Environ Res Public Health 16: 1996.
10. Chełchowska M, Ambroszkiewicz J, Gajewska J, Jabłońska-Głąb E, Maciejewski TM, et al. (2016) Hepcidin and iron

metabolism in pregnancy: Correlation with smoking and birth weight and length. Biol Trace Elem Res 173: 14-20.

11. Zhang WZ, Butler JJ, Cloonan SM (2019) Smoking-induced iron dysregulation in the lung. Free Radic Biol Med 133: 238-247.
12. Galesloot TE, Vermeulen SH, Geurts-Moespot AJ, Klaver SM, Kroot JJ, et al. (2011) Serum hepcidin: Reference ranges and biochemical correlates in the general population. Blood 117: e218-e225.
13. Wadowska K, Błasiak P, Rzechonek A, Bil-Lula I, Śliwińska-Mossoń M (2022) Hepcidin as a diagnostic biomarker in anaemic lung cancer patients. Cancers (Basel) 15: 224.
14. Vadhan-Raj S, Abonour R, Goldman JW, Smith DA, Slapak CA, et al. (2017) A first-in-human phase 1 study of a hepcidin monoclonal antibody, LY2787106, in cancer-associated anemia. J Hematol Oncol 10: 73.
15. Toshiyama R, Konno M, Eguchi H, Asai A, Noda T, et al. (2018) Association of iron metabolic enzyme hepcidin expression levels with the prognosis of patients with pancreatic cancer. Oncol Lett 15: 8125-8133.
16. Bérubé S, Lemieux J, Moore L, Maunsell E, Brisson J (2014) Smoking at time of diagnosis and breast cancer-specific survival: new findings and systematic review with meta-analysis. Breast Cancer Res 16: 1-11.
17. Alkhaifi M, Clayton A, Kishibe T, Simpson JS (2022) The association between smoking status and breast cancer recurrence: A systematic review. J Breast Cancer 25: 278-287.
18. Wong G, Lam E, Karam I, Yee C, Drost L, et al. (2020) The impact of smoking on adjuvant breast cancer radiation treatment: A systematic review. Cancer Treatment and Research Communications 24: 100185.
19. Bishop JD, Killelea BK, Chagpar AB, Horowitz NR, Lannin DR (2014) Smoking and breast cancer recurrence after breast conservation therapy. Int J Breast Cancer 2014: 327081.
20. Takada K, Kashiwagi S, Asano Y, Goto W, Kouhashi R, et al. (2020) The effect of smoking on biological change of recurrent breast cancer. J Transl Med 18: 153.