Journal Of Cardiovascular Disease Research
ISSN: 0975-3583,0976-2833 VOL15, ISSUE6, 2024

Original Research

Comparitive Study Of Biomarkers Ca 15.3, Ca 27.29, Ca125 And Cea In Diagnosed Cases Of Breast Cancer

[1]Dr. Jeetu Singh, [2]Dr. Sukhraj Kaur, [3]Dr. Tejinder Singh

[1]Junior Resident, Department of Biochemistry, Govt. Medical College, Amritsar
[2]Assistant Professor, Department of Biochemistry, Govt. Medical College, Amritsar
[3]Assistant Professor, Department of Biochemistry, Govt. Medical College, Amritsar

Corresponding Author:-
Dr. Tejinder Singh
Assistant Professor, Department of Biochemistry, Govt. Medical College, Amritsar
Email:- v_tajinder79@yahoo.com

Received: 16 May 2024 Accepted: 18 June 2024

Abstract
Background: The breast cancer is one of the most prevalent diagnosed cancer and 5th most common cause of cancer related deaths. The present study was conducted to compare the biomarkers CA 15.3, CA 27.29, CA 125 and CEA in diagnosed cases of breast cancer.
Material and methods: The present open observational comparative study was conducted among 100 diagnosed cases of breast cancer. In the present study 100 cases separated in to two groups-75 new cases those who were recently diagnosed cases of breast cancer by FNAC or Biopsy along with clinical history and 25 old cases, who were under treatment(Chemotherapy or Radiotherapy) attending OPD and admitted in department of Surgery Guru Nanak Dev Hospital, Government Medical College, Amritsar.100 normal healthy volunteers were included as control. The study was conducted over a period of 3 years i.e. 2020 to2023. The levels of cancer biomarkers were analysed with the ELISA method. The data was analysed.
Results: In the present study 100 diagnosed patients of breast cancer and 100 healthy controls were compare in reference to cancer biomarkers likeCA 15.3, CA 27.29, CA 125 and CEA.The mean levels of CA15.3 in cases and controls were 24.25 ± 7.83 and 18.23 ± 6.94 U/mL respectively. The mean levels of CA27.29 in cases and controls were 22.98 ± 14.18 and 22.10 ± 8.40 U/mL respectively. The mean levels of CA125 in cases and controls were 25.93 ± 11.60 and 17.94 ± 7.44 U/mL respectively.The mean levels of CEA in cases and controls were 7.36 ± 2.31 and 5.51 ± 1.85 U/mL respectively.
Conclusion: The present study concluded thatCA 15.3, CA 27.29, CA125 and CEA are the most useful serum tumour markers in patients with breast cancer. Serial determination of these markers may be beneficial in monitoring the response to therapy and for early detection of recurrence or metastasis
Keywords: Cancer markers, Breast cancer, CA 15.3, CA 27.29, CA 125, CEA**.**

Introduction

Being characterized by six major hallmarks, carcinogenesis might occur in every cell, tissue, and organ, leading to the pathological alternations that result in a vast number of cancers. The major mechanisms that enable its progression include evasion of apoptosis, limitless capacity to divide, enhanced angiogenesis, resistance to anti-growth signals and induction of own growth signals, as well as the capacity to metastasize.[1]Carcinogenesis is a multifactorial process that is primarily stimulated by both—genetic predispositions and environmental causes. Breast cancer is currently one of the most prevalently diagnosed cancers and the 5th cause of cancer-related deaths.[2] Breast cancer was the most commonly diagnosed female cancer in the world in 2020 with an incidence of over 2.26 million, accounting for 11.7% of total cancer cases worldwide; it was responsible for over 680,000 deaths.[3]Current projections indicate that by 2030 the worldwide number of new cases diagnosed reach 2.7 million annually, while the number of deaths 0.87 million.[4] In low- and medium-income countries, Breast cancer is the most frequent malignancy in women worldwide and is curable in 70–80% of patients with early-stage, non-metastatic disease. Advanced breast cancer with distant organ metastases is considered incurable with currently available therapies.[5] The determination of tumour markers is a useful tool for the clinical management of cancer patients, assisting in diagnostic procedures, staging, evaluation of therapeutic response, detection of recurrence and distant metastasis and prognosis, helping in the development of new treatment modalities.[6]The development of breast cancer involves a progression through series of intermediate processes, starting with ductal hyperproliferation, followed by subsequent evolution to carcinoma in situ, invasive carcinoma, and finally into metastatic disease. Given the variability in clinical progression of disease, the identification of markers that could predict tumour behaviour is particularly important in breast cancer.[7]The CA 27-29, CA 15-3, CA27.29, carcinoembryonic antigen, tissue polypeptide specific antigen, p53, cathepsin D, cyclin E, nestin and HER-2 are tumour markers that are often expressed in people with breast cancer.[8] There is paucity of data

comparing the level of CA15.3, CA 27.29, CA125 in breast cancer patients. Hence, in the present study we compared the level of all these four serum markers and their role in breast cancer patients.

Material and methods

The presentopen observational, comparative study was conducted inDepartment of Biochemistry in collaboration with the Department of Surgery, Guru Nanak Dev Hospital, Government Medical College, Amritsar. The study group included100 diagnosed cases of breast cancer. In the present study 100 cases separated in to two groups-75 new cases those who were recently diagnosed cases of breast cancer by FNAC or Biopsy along with clinical history and 25 old cases, who were under treatment(Chemotherapy or Radiotherapy), attending OPD and admitted in Department of Surgery, Govt. Medical College, Amritsar. 100 normal healthy volunteers from general population were also be included as controls. Patients who were included in this study were diagnosed with breast cancer on basis of clinical history or definitely confirmed by FNAC or Biopsy.

Before starting the study, the ethical clearance was obtained from the institutional ethics committee. Patients were only included after they provided with the informed written consent. Blood samples were collected from both the groups in a dry disposable syringe under aseptic conditions by vein puncture in anti-cubital vein in a sterile dry, acid washed plain vials. The blood samples were centrifuged at 3000rpm for 10 minutes for separation of serum and plasma respectively for estimation of tumour markers.

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. Results on continuous measurements were presented on Mean ± SD (Min-Max) & categorical as Frequency (Percentage). Inferential statistics like Chi-square test/Fischer Exact test, Independent t test was applied. The significance of level adopted was 5%.

Results

In the present study we first compare the 100 diagnosed patients of breast cancer and 100 healthy controls in reference to cancer biomarkers likeCA 15.3, CA 27.29, CA 125 and CEA.The mean levels of CA15.3 in cases and controls were 24.25 ± 7.83 and 18.23 ± 6.94 U/mL respectively. Upon statistical analysis, the mean levels were found to be highly significant in the cases as compared to controls ($p<0.0001$).The mean levels of CA27.29 in cases and controls were 22.98 ± 14.18 and 22.10 ± 8.40 U/mL respectively. Upon statistical analysis, the difference in mean levels was not found to be significant ($p>0.05$).The mean levels of CA125 in cases and controls were 25.93 ± 11.60 and 17.94 ± 7.44 U/mL respectively. Upon statistical analysis, the mean levels were found to be highly significant in the cases as compared to controls ($p<0.0001$)..The mean levels of CEA in cases and controls were 7.36 ± 2.31 and 5.51 ± 1.85 U/mL respectively.

We also compare thecancer biomarkers likeCA 15.3, CA 27.29, CA 125 and CEA with in the 75 new cases according to stagingThe mean levels of CA15.3 in new cases with stage1, stage 2, stage 3 and stage 4 breast cancer were 23.66 ± 5.66, 27.66 ± 6.12, 23.54 ± 8.12 and 31.31 ± 5.36 U/mL respectively. The mean levels of CA125 in new cases with stage1, stage 2, stage 3 and stage 4 breast cancer were 24.78 ± 5.47, 26.55 ± 16.68, 24.85 ± 4.91 and 33.55 ± 21.80 U/mL respectively. The mean levels of CA27.29 in new cases with stage1, stage 2, stage 3 and stage 4 breast cancer were 9.72 ± 5.80, 26.84 ± 15.47, 34.22 ± 12.51 and 40.78 ± 1.82 U/mL respectively. The mean levels of CEA in new cases with stage1, stage 2, stage 3 and stage 4 breast cancer were 7.40 ± 2.08, 7.88 ± 1.38, 8.76 ± 2.11 and 8.57 ± 3.08 U/mL respectively.We also compare thecancer biomarkers likeCA 15.3, CA 27.29, CA 125 and CEA with in the 25 old cases according to staging.The mean levels of CA15.3 in old cases with stage1, stage 2, stage 3 and stage 4 breast cancer were 19.77 ± 11.21, 20.22 ± 11.53, 18.32 ± 5.92 and 18.22 ± 8.81 U/mL respectively. The mean levels of CA125 in old cases with stage1, stage 2, stage 3 and stage 4 breast cancer were 25.90 ± 2.81, 25.52 ± 4.99, 25.13 ± 7.05 and 18.66 ± 5.99 U/mL respectively. The mean levels of CA27.29 in old cases with stage1, stage 2, stage 3 and stage 4 breast cancer were 26.72 ± 5.11, 24.00 ± 8.82, 21.49 ± 7.15 and 24.36 ± 13.61 U/mL respectively. The mean levels of CEA in old cases with stage1, stage 2, stage 3 and stage 4 breast cancer were 6.61 ± 3.53, 5.17 ± 2.18, 5.18 ± 1.21 and 6.30 ± 1.45 U/mL respectively.

Table No. 1: Comparison Of Mean Levels Of Markers Between Cases And Controls

	CASES (N=100)	CONTROL GROUP (N=100)	P VALUE	INFERENCE
CA15.3	24.25 ± 7.83	18.23 ± 6.94	<0.0001	SIGNIFICANT
CA125	25.93 ± 11.60	17.94 ± 7.44	<0.0001	SIGNIFICANT
CA27.29	22.98 ± 14.18	22.10 ± 8.40	0.590	NOT SIGNIFICANT
CEA	7.36 ± 2.31	5.51 ± 1.85	<0.0001	SIGNIFICANT

Table No. 2: Mean Levels Of Markers In New Cases Based On Staging

MARKER	STAGE 1 (N=31)	STAGE 2 (N=24)	STAGE 3 (N=10)	STAGE 4 (N=10)	TOTAL (N=75)
CA15.3	23.66 ± 5.66	27.66 ± 6.12	23.54 ± 8.12	31.31 ± 5.36	25.95 ± 6.63
CA125	24.78 ± 5.47	26.55 ± 16.68	24.85 ± 4.91	33.55 ± 21.80	26.53 ± 12.95
CA27.29	9.72 ± 5.80	26.84 ± 15.47	34.22 ± 12.51	40.78 ± 1.82	22.60 ± 15.68
CEA	7.40 ± 2.08	7.88 ± 1.38	8.76 ± 2.11	8.57 ± 3.08	7.89 ± 2.08

Table No. 3: Mean Levels Of Markers In Old Cases Based On Staging

MARKER	STAGE 1 (N=7)	STAGE 2 (N=6)	STAGE 3 (N=7)	STAGE 4 (N=5)	TOTAL (N=25)
CA15.3	19.77 ± 11.21	20.22 ± 11.53	18.32 ± 5.92	18.22 ± 8.81	19.16 ± 9.03
CA125	25.90 ± 2.81	25.52 ± 4.99	25.13 ± 7.05	18.66 ± 5.99	24.14 ± 5.79
CA27.29	26.72 ± 5.11	24.00 ± 8.82	21.49 ± 7.15	24.36 ± 13.61	24.12 ± 8.39
CEA	6.61 ± 3.53	5.17 ± 2.18	5.18 ± 1.21	6.30 ± 1.45	5.80 ± 2.30

Discussion

Breast cancer is the most commonly diagnosed female cancer in the world in 2020 with an incidence of over 2.26 million, accounting for 11.7% of total cancer cases worldwide and responsible for over 680,000 deaths. While increasingly treatable when discovered in early stages, breast cancer is still a major cause of death worldwide. In the present study 100 diagnosed cases of Breast Cancer, which included 75 new cases and 25 old cases so as to compare the role of four serological markers CA15.3, CA125, CA27.29 and CEA in these patients. The control group included 100 normal healthy volunteers. The new cases included 41.3% patients with stage 1 breast cancer, 32% with stage 2 and 13.3% each with stage 3 and stage 4. The old cases included 28% patients each with stage 1 and stage 3 breast cancer, 24% with stage 2 and 20% with stage 4.

Our study observed that the mean levels of CA15.3 in cases and controls were 24.25 ± 7.83 and 18.23 ± 6.94 U/mL respectively. Upon statistical analysis, the mean levels were found to be significantly higher in the cases as compared to controls ($p<0.05$). An increase in mean levels of CA15.3 was noted with increasing stage in this study. The mean levels of CA15.3 in new cases with stage1, stage 2, stage 3 and stage 4 breast cancer were 23.66 ± 5.66, 27.66 ± 6.12, 23.54 ± 8.12 and 31.31 ± 5.36 U/mL respectively. The mean levels of CA15.3 in old cases with stage1, stage 2, stage 3 and stage 4 breast cancer were 19.77 ± 11.21, 20.22 ± 11.53, 18.32 ± 5.92 and 18.22 ± 8.81 U/mL respectively. The comparison in mean levels of CA15.3 in old cases at any stage was not found to be statistically significant ($p>0.05$).Our study was in accordance with the study conducted by Fakhari A, Gharepapagh E, Dabiri S, Gilani N[9]. One more study was conducted by Lee JS et al[10] also in align with our study In the present study, the mean levels of CA125 in cases and controls were 25.93 ± 11.60 and 17.94 ± 7.44 U/mL respectively. Upon statistical analysis, the mean levels were found to be significantly higher in the cases as compared to controls ($p<0.05$).We also found that the mean levels of CA125 in new cases with stage1, stage 2, stage 3 and stage 4 breast cancer were 24.78 ± 5.47, 26.55 ± 16.68, 24.85 ± 4.91 and 33.55 ± 21.80 U/mL respectively. The mean levels of CA125 in old cases with stage1, stage 2, stage 3 and stage 4 breast cancer were 25.90 ± 2.81, 25.52 ± 4.99, 25.13 ± 7.05 and 18.66 ± 5.99 U/mL respectively. The comparison in mean levels of CA125 in new and old cases at any stage was not found to be statistically significant ($p>0.05$). High preoperative CA125 levels may reflect tumour burden and are associated with aggressive molecular subtype, suggesting that it can be used to predict poor outcome and prognosis of breast cancer patients, shown by a study conducted by Fang C, Cao Y, Liu X, Zeng XT, Li Y[11]Increased CA125 was associated with metastasis in or near the pleura, and in stage IV breast cancer it was related to poor prognosis shown in study conducted by Norum LF, Erikstein B, Nustad K[12]. These studies also in consistent with our study.

The mean levels of CA27.29 in cases and controls were 22.98 ± 14.18 and 22.10 ± 8.40 U/mL respectively. Upon statistical analysis, the difference in mean levels was not found to be significant ($p>0.05$). The mean levels of CA27.29 in new cases with stage1, stage 2, stage 3 and stage 4 breast cancer were 9.72 ± 5.80, 26.84 ± 15.47, 34.22 ± 12.51 and 40.78 ± 1.82 U/mL respectively.The mean levels of CA27.29 in old cases with stage1, stage 2, stage 3 and stage 4 breast cancer were 26.72 ± 5.11, 24.00 ± 8.82, 21.49 ± 7.15 and 24.36 ± 13.61 U/mL respectively. The comparison in mean levels of CA27.29 in old cases at any stage was not found to be statistically significant ($p>0.05$).Our findings are consistent with Gion M et al[13] who concluded that CA27.29 seems more sensitive than CA15.3 to limited variations of tumour extension and it cannot help clinicians in distinguishing stage I patients from stage II patients. In this study, the mean levels of CEA in cases and controls were 7.36 ± 2.31 and 5.51 ± 1.85 U/mL respectively. Upon statistical analysis, the mean levels were found to be significantly higher in the cases as compared to controls ($p<0.05$).The mean levels of CEA in new cases with stage1, stage 2, stage 3 and stage 4 breast cancer were 7.40 ± 2.08, 7.88 ± 1.38, 8.76 ± 2.11 and 8.57 ± 3.08 U/mL respectively. The mean levels of CEA in old cases with stage1, stage 2, stage 3 and stage 4 breast cancer

were 6.61 ± 3.53, 5.17 ± 2.18, 5.18 ± 1.21 and 6.30 ± 1.45 U/mL respectively. The comparison in mean levels of CEA in new and old cases at any stage was not found to be statistically significant ($p>0.05$).Elevated levels of CEA are related to the tumour burden and higher levels may indicate an increased likelihood of systemic metastases.[14]

Conclusion

Our study concluded that CA15.3 and CA 125 both increased in stage 4 of carcinoma breast indicating probable metastasis, but CA15.3 and CA125 are not sensitive or specific in new and old cases of carcinoma breast. CA 27.29 increases gradually as the stage increase from stage 2 to stage 3 and stage 3 to stage 4. CA2 27.29 can help with staging of new cases but not in old cases. CA 27.29 is more sensitive as compared to other markers. Our study are in accordance with some of the studies conducted by De Paterna LR et al.[15]Park BW et al[16]

Our study also concluded that serial determination of these markers may be beneficial in monitoring the response to therapy and for early detection of metastasis.

References

1. Hanahan D, Weinberg RA. The hallmarks of cancer. Cell. 2000;100(1):57-70.
2. Łukasiewicz S, Czeczelewski M, Forma A, Baj J, Sitarz R, Stanisławek A. Breast Cancer-Epidemiology, Risk Factors, Classification, Prognostic Markers, and Current Treatment Strategies-An Updated Review. Cancers (Basel). 2021;13(17):4287.
3. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-249.
4. Ferlay J, Laversanne M, Ervik M, Lam F, Colombet M, Mery L, et al. Global Cancer Observatory: Cancer Tomorrow. International Agency for Research on Cancer: Lyon, France, 2020; Available online: https://gco.iarc.fr/tomorrow.
5. Harbeck N, Penault-Llorca F, Cortes J, Gnant M, Houssami N, Poortmans P, Ruddy K, Tsang J, Cardoso F. Breast cancer. Nat Rev Dis Primers. 2019;5(1):66.
6. Pacheco FA, PASCHOAL ME, Carvalho MD. Marcadorestumorais no câncer de pulmão: um caminho para a terapiabiológica. Jornal de Pneumologia. 2002;28:143-9.
7. Polyak K. Breast cancer: origins and evolution. The Journal of clinical investigation. 2007;117(11):3155-63.
8. Kabel AM. Tumor markers of breast cancer: New prospectives. Journal of Oncological Sciences. 2017;3(1):5-11.
9. Fakhari A, Gharepapagh E, Dabiri S, Gilani N. Correlation of cancer antigen 15-3 (CA15-3) serum level and bony metastases in breast cancer patients. Med J Islam Repub Iran. 2019;33:142.
10. Lee JS, Park S, Park JM, Cho JH, Kim SI, Park BW. Elevated levels of preoperative CA 15-3 and CEA serum levels have independently poor prognostic significance in breast cancer.Ann Oncol. 2013;24(5):1225-31.
11. Fang C, Cao Y, Liu X, Zeng XT, Li Y. Serum CA125 is a predictive marker for breast cancer outcomes and correlates with molecular subtypes. Oncotarget. 2017;8(38):63963-70.
12. Norum LF, Erikstein B, Nustad K. Elevated CA125 in breast cancer--A sign of advanced disease. Tumour Biol. 2001;22(4):223-8.
13. Gion M, Mione R, Leon AE, Lüftner D, Molina R, Possinger K, et al. CA27.29: a valuable marker for breast cancer management. A confirmatory multicentric study on 603 cases. Eur J Cancer. 2001;37(3):355-63.
14. Li J, Liu L, Feng Z, Wang X, Huang Y, Dai H, et al. Tumor markers CA15-3, CA125, CEA and breast cancer survival by molecular subtype: a cohort study. Breast Cancer. 2020;27(4):621-30
15. De Paterna LR, Arnaiz F, Estenoz J, Ortuno B, Lanzos E. Study of serum tumor markers CEA, CA 15.3 and CA 27.29 as diagnostic parameters in patients with breast carcinoma. The International journal of biological markers. 1995;10(1):24-9.
16. Park BW, Oh JW, Kim JH, Park SH, Kim KS, Kim JH, et al. Preoperative CA 15-3 and CEA serum levels as predictor for breast cancer outcomes. Ann Oncol. 2008;19(4):675-81.