IJRAR.ORG E-ISSN: 2348-1269, P-ISSN: 2349-5138

INTERNATIONAL JOURNAL OF RESEARCH AND ANALYTICAL REVIEWS (IJRAR) | IJRAR.ORG

An International Open Access, Peer-reviewed, Refereed Journal

GATA-3 EXPRESSION IN BREAST CANCER AND ITS CORRELATION WITH PROGNOSTIC PARAMETERS (ER, PR, KI-67 AND HER2)

Dr. Shikha Prakash[1], Dr. Mansi Yadav[2], Dr. Garima Dundy[3], Dr. Surabhi Gupta[4], Dr. Surendra Pathak[5]

[1]Associate Professor [2]Junior Resident [3]Professor [4]Professor [5]Professor

Department of Pathology, S.N. Medical College, Agra, India

ABSTRACT

Background: GATA binding protein 3 (GATA-3) is a zinc-finger transcription factor essential for luminal differentiation in the mammary gland. This study reviews and synthesizes evidence regarding its expression in breast carcinoma and its correlation with ER, PR, Ki-67, and HER2. Here we review the related studies to recognize the significance of GATA-3 as a potential bio marker in breast cancer. This review is based on a wide search of journals over a period of 20 years.

KEYWORDS

Breast carcinoma, GATA-3, IHC markers ,Prognosis

I. INTRODUCTION

Breast cancer is the most common malignancy in women worldwide and remains a major cause of cancer-related deaths [1]. Its classification and management depend on clinicopathological and molecular parameters, with ongoing updates in treatment strategies [2].In younger women, breast cancer often shows more aggressive biology and poorer outcomes, underlining the need for better biomarkers [3]. One such marker is GATA binding protein 3 (GATA3), a transcription factor critical for mammary epithelial differentiation and luminal identity [4].GATA3 is a zinc-finger transcription factor with context-dependent roles in breast cancer, where shifts in its regulatory functions can influence both tumour progression and clinical presentation [5]. Clinical studies of advanced breast cancer have shown that GATA3 expression carries prognostic value and may be linked to patterns of organ-specific relapse [6].Beyond its established role in luminal differentiation, accumulating evidence suggests GATA3 may act in dual capacities, functioning as a tumour suppressor in some contexts while exerting oncogenic effects in others [7]. Somatic mutations in GATA3, as observed in The Cancer Genome Atlas (TCGA) cohort, correlate with distinct clinicopathological features and transcriptional profiles [8]. Broad genomic analyses further highlight the heterogeneity of the GATA3 mutational landscape in breast cancer, underscoring its potential impact on tumour biology and therapeutic response [9].GATA3 expression is strongly associated with estrogen receptor (ER) positivity, suggesting its role in defining luminal phenotypes [10]. Functional studies demonstrate that loss of GATA3 disrupts tumour differentiation and enhances dissemination [11].Clinically, GATA3 immunohistochemistry is highly valuable for confirming breast origin in metastatic and cytology specimens [12]. In triple-negative breast cancers,

however, expression is often reduced [13], and similar loss is noted in metaplastic subtypes [14].Correlations have been established between low GATA3 expression and adverse features such as high grade and proliferation indices [15]. Expression patterns also differ across histological and immunohistochemically defined molecular subtypes [16].Population-based studies in India confirm frequent GATA3 positivity in luminal tumours but reduced expression in aggressive subtypes [17], findings echoed in broader regional series [18]. In advanced disease, low GATA3 is associated with organ-specific relapse, particularly lung metastasis [19]. Meta-analyses support its role as a favourable prognostic marker overall [20]. Ki-67 is a nuclear proliferation marker widely applied in breast cancer to assess tumour growth dynamics and stratify prognosis [21]. Broader reviews of breast cancer epidemiology and risk factors also emphasize Ki-67 as a valuable marker for assessing tumour biology, guiding prognosis, and informing treatment decisions.[22] In hormone receptor–negative tumours, combined assessment of GATA3 and FOXA1 may improve prognostic accuracy [23]. Furthermore, germline variants in GATA3 have been linked to treatment response and survival outcomes [24].

II.RETRIEVAL STRATEGY

Literature review was conducted using PubMed database , Sage journal and Elsevier, English language. Full-text articles published between 2005 and 2025 were included in this non-systematic review. The literature search keywords was conducted as follows (1) Breast cancer, (2) GATA-3 (3) IHC. Total 17 studies are analyzed .The study titled "GATA-3 maintains the differentiation of the luminal cell fate in the mammary gland" (Mehr K et al [2006]) [25] was conducted on mice and not on human breast cancer patients. Therefore, its findings may not directly apply to human clinical scenarios.

III.DISCUSSION:

GATA-3 (GATA binding protein 3) is a zinc finger transcription factor that plays a critical role in the differentiation and maintenance of luminal epithelial cells in the mammary gland. GATA-3 is crucial for supporting cell division, growth, and proliferation in a variety of tissues[26]. A deficiency of GATA3, a proto-oncogene group nuclear transcription factor, is linked to HER2/neu over-expression, progesterone and estrogen receptor negativity, and a poor prognosis.[27]

3.1-3 POSITIVITY IN INVASIVE BREAST CANCER

In majority of studies , GATA-3 positivity range from [47%-90%] while Voduc et al [28] shows only 37% positivity.

Across studies, GATA-3 expression has been consistently linked with favorable tumor characteristics in breast cancer. Teja et al. (2025)[29] and Anusha et al. (2024)[30] both observed that GATA-3 positivity was highest in well-differentiated, low-grade tumors, with expression decreasing as tumor grade advanced, suggesting its role in maintaining cellular differentiation. Similar findings were reported by Tabriz et al. (2023) [31] and Suri (2021) [32] , who showed stronger GATA-3 expression in luminal subtypes and weaker expression in HER2-enriched and triple-negative tumors. These results highlight GATA-3 as a luminal-specific marker that helps identify less aggressive disease.

Author (Year)	GATA-3 Expression
Teja R. (2025)	90% positive
K. Anusha (2024)	68% positive
Singh A. (2021)	87.5% positive
Suri T. (2021)	46.7% positive
Cangara H. (2021)	>50% positive
Querzoli P. (2021)	68% positive
Manal I. (2019)	54.1% positive
Ismail A.M. (2017)	88% ER/PR+, 56% ER/PR-
Voduc D. (2008)	32% positive

Table 3.1This table summarizes gata-3 positivity in breast cancer from previous studies

3.2RELATIONSHIP OF GATA-3 WITH KI-67 ,ER,PR ,HER-2 AND AR

The association between GATA-3 and other biomarkers further supports its clinical relevance. Multiple studies, including those by Ismail et al. (2017) [33] , Yildirim et al. (2020) [35] , and Cangara et al. (2021) [36] , demonstrated an inverse relationship with Ki-67 (a known proliferation marker), reinforcing that higher GATA-3 levels are linked with slower tumor proliferation. Positive correlations with ER and PR were reported across nearly all cohorts, including Singh (2021)[36] and Querzoli et al. (2021) [27] , strengthening its role as a marker of hormone-driven cancers.

Interestingly, Singh (2021) [36] found that GATA-3 expression was associated with better partial responses to neoadjuvant chemotherapy, hinting at a predictive role beyond hormone therapy response. 71% (23/32) of GATA-3 positive patients showed partial response to NACT and 12% (4/32) showed complete response while Tominaga et al (2012)[14] observed pathological complete response in 11% of GATA-3 positive tumors versus 39% of GATA-3 negative tumors.

Study (Authors, Year)	ER	PR	HER2	Ki-67	AR	Study Design
Teja R. et al. (2025) N=40	Not reported	Not reported	Not reported	Not reported		Cross sectional observational study
K. Anusha et al. (2024) N=50	73.5% ER+ tumors GATA3+	Associated but less consistent	Less consistent	Not reported		A mixed (prospective + retrospective) observational study
Tabriz H. et al. (2023) N=166	Strong correlation; higher in ER+	Strong correlation	No significant relationship	Lower in GATA3+ tumors		A cross – sectional observational study
Singh A. (2021) N=40	Most frequent in Luminal A (ER+)	Present in Luminal A	Seen in high positivity 42%(3/7) HER2-+ve	Not reported		A prospective observational study
Suri T. (2021) N=30	63% of luminal tumors	Significant positive link	14% HER 2 +ve	Not reported		Cross-sectional observational study
Cangara H. (2021) N=89	>50% ER +VE	>50% PR +VE	—	Lower Ki-67 in GATA3+ tumors		A retrospective study
Querzoli P. et al. (2021) N=608	ER+ strongly linked (68%)	PR+ strongly linked	HER2 negativity correlated	Better survival with low Ki-67		A retrospective cohort study
Yildirim E. et al. (2020) N=90	High ER in GATA3+ tumors	High PR in GATA3+ tumors	Higher HER2 in GATA3– tumors	Inverse: GATA3+ linked to low Ki-67		A retrospective study

Manal I. et al. (2019) N=61	Strong positive correlation	Strong positive correlation	—	Lower Ki-67 in GATA3+ tumors	Co-expression with AR predicted best relapse-free survival; retained significance in multivariate analysis	A retrospective study
Faraejwh A. et al. (2018) N=241	Higher in ER+ tumors	Higher in PR+ tumors	—	Better prognosis with low Ki-67		Observational study
Boto A. (2017) N=259	Positive association	Positive association	—	—Lower Ki-67 in GATA3+ tumors	Strong correlation with AR; luminal differentiation marker	A retrospective study
Ismail A.M. et al. (2017) N=40	88% in PR+	88% in PR+	—	Inverse correlation		Cross sectional observational study
Yoon N. et al. (2010) N=242	Higher ER +ve linked	Higher PR +ve linked	—	Not reported		A retrospective study
Jacquemier J. et al. (2009) N=832	Protective in ER+ tumors	—	—	Inverse relationship		A retrospective study
Ciocca V. et al. (2008) N=166	Better ER+ve outcomes	Better PR+ve outcomes	—	Not reported		A retrospective study
Voduc D. et al. (2008) N=3119	Nearly exclusive to ER+ cases	Positive correlation	HER2 negative linked	Not reported		A retrospective study
Mehra R. et al. (2005) N=139	Positive correlation	Positive correlation	HER2 overexpression linked to low GATA3	Not reported		

Table 3.2This table summarizes reported percentages and association of GATA-3 expression with ER , PR , HER-2 , KI-67 markers across multiple breast cancer studies and type of study .(N= number of cases in each study)

When considering prognosis, findings are somewhat mixed. Mehra et al. (2005) [25] , Faraejwh et al. (2018)[39] and Querzoli et al. (2021) [27] reported that GATA-3 retained independent prognostic value, with higher expression correlating with longer survival rates. 3,5,10 year disease specific survival rate were 74% ,68% and 64% [39], even after adjusting for clinicopathological factors , hazard ratio was reduced by 40% [27]. In contrast, Voduc et al. (2008)[28] and Ciocca et al. (2008) [40] concluded that although GATA-3 positivity was associated with favorable survival in univariate analysis, it lost significance in multivariable models, suggesting it largely reflects its association with ER positivity rather than providing independent prognostic

information. Jacquemier et al. (2009) [41]and Boto et al(2017) [42] added further gradation by showing that GATA-3, when combined with other markers such as Ki-67, p53, or AR, can improve prognostic stratification.

Author (Year)	Prognostic Marker
Tabriz H. (2023)	Not independent
Querzoli P. (2021)	Independent
Yildirim E. (2020)	Not independent
Manal I. (2019)	Independent
Ismail A.M. (2017)	Not independent
Jacquemier J. (2009)	Independent
Ciocca V. (2008)	Not independent
Voduc D. (2008)	Not independent
Mehra R. (2005)	Independent

Table 3.3This table Summarizes studies evaluating GATA-3 prognostic value in breast cancer

Additionally , GATA-3 expression was linked to longer disease free survival [34] and relapse free survival [43].

IV. CONCLUSION

Based on observation from multiple published studies , there is a evidence that GATA-3 favours good prognosis in breast cancer and has a positive correlation with ER , PR and inverse relationship with HER-2 and Ki-67. Despite its promise, several limitations are evident across studies. Many, including Suri (2021)[32] , Manal et al. (2019) [43] , and Teja et al. (2025)[29] , were based on relatively small cohorts, while others used retrospective designs with limited follow-up. Variability in scoring methods and cutoff values for positivity also complicates direct comparison. Moreover, while the biological role of GATA-3 as a regulator of ER pathways has been suggested (Faraejwh et al. 2018)[39] , its influence on tumor progression and treatment response is still not fully clarified.

Overall, these findings suggest that GATA-3 is a robust marker of luminal differentiation and favorable tumor biology. While its independent prognostic value remains debated, its consistent association with ER/PR positivity, lower grade, and better outcomes makes it a valuable addition to biomarker panels . With stronger evidence from future prospective studies, GATA-3 may become valuable not only for tumor classification but also for improving prognostic assessment and informing treatment strategies in invasive breast cancer. Many of the ER+ve tumours are not responsive to the hormonal therapy . so there is a need to look for alternative strategies for treatment based on finding of novel biomarker in breast cancer.

V. ACKNOWLEDGEMENT

Financial and Clinical support from Multi-disciplinary Research Unit, Sarojini Naidu Medical College Agra is highly acknowledged. DHR-ICMR is also duly acknowledged.

REFERENCES

[1].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.

[2]. Wahba HA, El-Hadaad HA. Breast Cancer. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.

[3]. Narayanan GS, Nair S, Devi NR, et al. Breast Cancer in Young Women: Analysis of Incidence, Clinicopathological Profile and Biological Behaviour in a Tertiary Care Institute from South India. Asian Pac J Cancer Biol. 2020;5(4):143–50.

[4]. Chou J, Provot S, Werb Z. GATA3 in development and cancer differentiation: Cells GATA have it! J Cell Physiol. 2010;222(2):243–50.

[5]. Kouros-Mehr H, Kim JW, Bechis SK, Werb Z. Shift in GATA3 functions, and GATA3 mutations, control progression and clinical presentation in breast cancer. Breast Cancer Res. 2008;10(4):R80.

[6]. McCleskey BC, Penedo TL, Zhang K, Hameed O, Siegal GP, Wei S. GATA3 expression in advanced breast cancer: prognostic value and organ-specific relapse. Am J Clin Pathol. 2015;144(5):756–63.

[7]. Dydensborg AB, Rose AA, Wilson BJ, Zijlstra A, Emerman JT, Siegel PM. GATA3 in Breast Cancer: Tumor Suppressor or Oncogene? Stem Cell Reports. 2009;2(4):279–87.

[8]. Miao Y, Wang J, Li Q, Quan W, Wang Y. GATA3 somatic mutations are associated with clinicopathological features and expression profile in TCGA breast cancer patients. Sci Rep. 2017;7:42002.

[9]. Banerji S, Cibulskis K, Rangel-Escareno C, Brown KK, Carter SL, Frederick AM, et al. Genomic characterization of the GATA3 mutational landscape in breast cancer. J Clin Oncol. 2012;30(15_suppl):10506.

[10]. Hoch RV, Thompson DA, Baker RJ, Weigel RJ. GATA-3 is expressed in association with estrogen receptor in breast cancer. Int J Cancer. 1999;84(2):122–8.

[11]. Kouros-Mehr H, Slorach EM, Sternlicht MD, Werb Z. GATA-3 links tumor differentiation and dissemination in a mammary tumor model. Cancer Cell. 2008;13(2):141–52.

[12]. Braxton DR, Cohen C, Siddiqui MT. Utility of GATA3 immunohistochemistry for diagnosis of metastatic breast carcinoma in cytology specimens. Diagn Cytopathol. 2015;43(4):271–7.

[13]. Byrne DJ, et al. GATA3 expression in triple-negative breast cancers. Histopathology. 2017;71(3):423–31.

[14]. Cimino-Mathews A, Subhawong AP, Elwood H, Montgomery EA, Argani P. GATA3 expression in breast carcinoma: utility in triple-negative and metaplastic carcinomas. Hum Pathol. 2013;44(7):1341–9.

[15]. Cakir A, et al. GATA3 expression and its relationship with clinicopathological parameters in invasive breast carcinomas. Pathol Res Pract. 2017;213(8):909–16.

[16]. Shaoxian T, et al. Characterisation of GATA3 expression in invasive breast cancer: differences in histological subtypes and immunohistochemically defined molecular subtypes. Histopathology. 2017;71(6):901–10.

[17]. Banik L, Pal M, Mayur N. Study of GATA-3 Expression in Breast Carcinoma in a Tertiary Care Hospital in Eastern India. Arch Breast Cancer. 2022;9(2):115–21.

[18]. Narayanan GS, Nair S, Devi NR, et al. Breast Cancer in Young Women: Analysis of Incidence, Clinicopathological Profile and Biological Behaviour in a Tertiary Care Institute from South India. Asian Pac J Cancer Biol. 2020;5(4):143–50.

[19]. McCleskey BC, Penedo TL, Zhang K, Hameed O, Siegal GP, Wei S. GATA3 expression in advanced breast cancer: prognostic value and organ-specific relapse. Am J Clin Pathol. 2015;144(5):756–63.

[20]. Guo Y, Guo H, Zhou Q. Prognostic and clinicopathological value of GATA binding protein 3 in breast cancer: a systematic review and meta-analysis. Oncotarget. 2017;8(26):44117–25.

[21]. Allred DC, Clark GM, Tandon AK, Molina R, Tormey DC, Osborne CK, et al. Coexistence of HER2 over-expression and p53 protein accumulation is a strong prognostic molecular marker in breast cancer. Breast Cancer Res. 1992;2(1):13–20.

[22]. Azamjah N, Soltan-Zadeh Y, Zayeri F. Breast cancer and associated factors: a review. J Med Life. 2019;12(2):69–82.

[23]. Albergaria A, Paredes J, Sousa B, et al. Expression of FOXA1 and GATA-3 in breast cancer: the prognostic significance in hormone receptor-negative tumours. BMC Cancer. 2009;9:279.

[24]. Reiner AS, John EM, Brooks JD, et al. Germline genetic variants in GATA3 and breast cancer treatment outcomes in SWOG S8897 trial and the Pathways Study. Clin Cancer Res. 2019;25(13):3955–63.

[25]. Mehra R, Varambally S, Ding L, Shen R, Sabel MS, Ghosh D, Chinnaiyan AM, Kleer CG. Identification of GATA3 as a breast cancer prognostic marker by global gene expression meta-analysis. Cancer Res. 2005 Dec 15;65(24):11259-11264. doi:10.1158/0008-5472.CAN-05-2495

[26]. Lanigan F, O'Connor D, Martin F, Gallagher WM. Molecular links between mammary gland development and breast cancer. Cell Mol Life Sci. 2007 Dec;64(24):3159-84. doi: 10.1007/s00018-007-7386-2. PMID: 17955178; PMCID: PMC11136244.

[27]. Querzoli P, Pedriali M, Rinaldi R, Secchiero P, Rossi PG, Kuhn E. GATA3 as an Adjunct Prognostic Factor in Breast Cancer Patients with Less Aggressive Disease: A Study with a Review of the Literature. Diagnostics. 2021 Mar 28;11(4):604.

[28]. Voduc D, Cheang M, Nielsen T. GATA-3 Expression in Breast Cancer Has a Strong Association with Estrogen Receptor but Lacks Independent Prognostic Value. Cancer Epidemiology Biomarkers & Prevention. 2008 Feb 4;17(2):365–73.

[29]. CN RT, HK SK, Kumar KAK, Rajendran P, G N. GATA3 Expression in Invasive Breast Carcinoma. Eur J Cardiovasc Med. 2025 Feb;15(2):240-246.

[30]. Anusha K, Swapna N, Shantha G, Durga KV. Study of GATA3 expression in breast carcinomas. Int J Pharm Clin Res. 2024;16(4):364-368.

[31]. Tabriz HM, Farmani E, Nazar E, Javadi AE. GATA Binding Protein 3 (GATA-3) expression evaluation as prognostic factor in breast cancer and its relationship with other immunemarkers. Indian J Pathol Microbiol. 2023 Apr-Jun;66(2):286-290. doi: 10.4103/ijpm.ijpm_453_21. PMID: 37077069.

[32]. Suri T, Ahluwalia C. Immunohistochemical Analysis of Expression of GATA3 in Carcinoma Breast and its Correlation with Prognostic Parameters. Ann of Pathol and Lab Med [Internet]. 2021 Feb. 28 [cited 2025 Sep. 25];8(2):A26-32.

[33]. Ismail AM, Khalifa SE, Saied EM, El-Tamamy MM. Immunehistochemisal study of GATA-3 expression versus estrogen and progesterone receptor in invasive mammary carcinomas. Kast Al Ainy Med J 2018;24:40-6

[34]. Yildirim E, Bektas S, Gundogar O, Findik D, Alcicek S, ErdoganKo, et al. The Relationship of GATA3 and Ki-67 With Histopathological Prognostic Parameters, Locoregional Recurrence and Disease-free Survival in Invasive Ductal Carcinoma of the Breast. Anticancer Research. 2020 Sep 28;40(10):5649–57.

[35]. Husni Cangara M, Miskad UA, Masadah R, Nelwan BJ, Wahid S. Gata-3 and KI-67 expression in correlation with molecular subtypes of breast cancer. Breast Dis. 2021;40(S1):S27-S31. doi: 10.3233/BD-219004. PMID: 34057115.

[36]. Singh A, Karnik A, Anand A. Prevalence of GATA-3 in invasive breast cancer and its significance in predicting response to neoadjuvant chemotherapy: a tertiary center experience. Int Surg J [Internet]. 2021 May 28 [cited 2025 Sep. 25];8(6):1833-8.

[37]. Tominaga N, Naoi Y, Shimazu K, Nakayama T, Maruyama N, Shimomura A, Kim SJ, Tamaki Y, Noguchi S. Clinicopathological analysis of GATA3-positive breast cancers with special reference to response to neoadjuvant chemotherapy. Ann Oncol. 2012 Dec;23(12):3051-3057. doi: 10.1093/annonc/mds120. Epub 2012 Jul 5. PMID: 22767585.

[38]. Fararjeh AS, Tu SH, Chen LC, Liu YR, Lin YK, Chang HL, Chang HW, Wu CH, Hwang-Verslues WW, Ho YS. The impact of the effectiveness of GATA3 as a prognostic factor in breast cancer. Hum Pathol. 2018 Oct;80:219-230. doi: 10.1016/j.humpath.2018.06.004. Epub 2018 Jun 11. PMID: 29902578.

[39]. Ciocca V, Daskalakis C, Ciocca RM, Ruiz-Orrico A, Palazzo JP. The significance of GATA3 expression in breast cancer: a 10-year follow-up study. Hum Pathol. 2009 Apr;40(4):489-95. doi: 10.1016/j.humpath.2008.09.010. Epub 2008 Dec 11. PMID: 19084267.

[40]. Jacquemier J, Charafe-Jauffret E, Monville F, Esterni B, Extra JM, Houvenaeghel G, Xerri L, Bertucci F, Birnbaum D. Association of GATA3, P53, Ki67 status and vascular peritumoral invasion are strongly prognostic in luminal breast cancer. Breast Cancer Res. 2009;11(2):R23. doi: 10.1186/bcr2249. Epub 2009 Apr 30. PMID: 19405945; PMCID: PMC2688952.

[41]. Boto A, Harigopal M. Strong androgen receptor expression can aid in distinguishing GATA3+ metastases. Hum Pathol. 2018 May;75:63-70.

[42]. ManalIAbd-Elghany, El F, Toni NisreenDM, MagiSBoshra. GATA-binding protein 3 and androgen receptor expressions in invasive breast cancer: the relationship with molecular phenotypes, disease progression, and survival outcomes. Egyptian Journal of Pathology. 2019 Jan 1;39(1):212–2.