

## Prevalence of Molecular Breast Cancer Subtypes in Ethiopia: A Review

Bizualem Shenkutie<sup>1\*</sup>, Slemawit Solomon<sup>2</sup>, Asmamawu Menilh<sup>3</sup>

<sup>1</sup>Department of Microbial, Cellular and Molecular Biology, College of Natural and Computational Sciences, Mekdela Amba University, South Wollo, Ethiopia; <sup>2</sup>Department of Microbial, Cellular and Molecular Biology, College of Natural and Computational Science, Raya University, Maichew, Ethiopia; <sup>3</sup>Department of Biology, College of Natural and Computational Science Mekdela Amba University, South Wollo, Ethiopia

### ABSTRACT

Breast cancer is a heterogeneous diseases and it is difficult to provide the right treatment. Molecular markers are good indicators for prognosis and predictive factor. Therefore, the current review was designed to assess the prevalence of Molecular subtypes of Breast cancer in Ethiopia. The review concentrated on current literature on Prevalence, Breast Cancer, Women, Molecular Subtypes, Hormone Receptors and Ethiopia with scientifically proven efficacy was carried out using electronic databases such as Science Direct, Google Scholar and PubMed. Among a total of 4000 studies, six studies were included in this review. The current review showed that the prevalence of ER+, PR+ and Luminal A Breast cancer is high in Ethiopia. For this reason Ethiopian breast cancer patients will be take hormonal therapy. However, further study should be done on the prevalence of molecular subtypes of breast cancer via PCR and other laboratory method for clearly identification of the molecular markers.

**Keywords:** Breast Cancer; Breast Cancer Subtypes; Ethiopia; Hormone Receptor; Prevalence; Women

### ABBREVIATIONS:

ER: Estrogen Receptor; HER2: Human Epidermal Receptor; PR: Progesterone Receptor; WHO: World Health Organization

### INTRODUCTION

Breast cancer is the top cancer in women both in the developed and the developing country. The incidence of breast cancer is increasing in the developing country due to increase life expectancy, increase urbanization and adoption of western lifestyles. Although some risk reduction might be achieved with prevention, these strategies cannot eliminate the majority of breast cancers that develop in low- and middle-income countries where breast cancer is diagnosed in very late stages [1].

According to WHO report, in Ethiopia approximately 60,000 new cases of cancer are diagnosed each year, where carcinoma of cervix and breast cancer are the top two malignancy types having a lion share for the high maternal deaths in the country; accounted for 13.4% (Cervical cancer) and 30.2% (Breast cancer) [1].

Breast cancer is a heterogeneous disease with different morphological and molecular subtypes [2]. The morphological classification is still the foundation of histopathological diagnosis, but in the era of modern personalized medicine, a number of molecular classification systems have been introduced. In this context, Estrogen Receptor (ER) and Progesterone Receptor (PR) analysis in breast carcinomas were the first established biomarker assays with both prognostic and predictive power and they have been in use since the 1970s [3].

Human Epidermal Growth Factor 2 (HER2) was discovered in the 1990s and HER2-targeted therapy was subsequently introduced; the introduction of targeted antibodies that interfere with HER2 signaling followed and their use has led to improved survival among breast cancer patients whose tumors overexpress HER2 [4,5].

The assessments of the prevalence of those molecular markers are very vital for indicating of the treatment previously there are some study done on the proportion of the hormonal receptor and molecular subtypes of breast cancer in Ethiopia, but there is not review on the assessment of the prevalence of molecular

**Correspondence to:** Shenkutie B, Department of Microbial, Cellular and Molecular Biology, College of Natural and Computational Sciences, Mekdela Amba University, South Wollo, Ethiopia, E-mail: bizushen@gmail.com

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subtypes of breast cancer in Ethiopia. So the present study aimed to assess the prevalence of molecular subtypes of breast cancer in Ethiopia. This will help for indicating of the right treatment for the patients without extravagance.

#### PROGNOSTIC AND PREDICTIVE FACTORS IN BREAST CANCER

According to Hayes et al., definition, a prognostic factor is capable of providing information on clinical outcome at the time of diagnosis, independent of therapy [6]. Such markers are usually indicators of growth, invasion, and metastatic potential. In contrast to prognostic factors, Italiano describe that, a predictive factor is a clinical or biological characteristic that is responsible for information on the likely benefit from treatment (either in terms of tumor shrinkage or survival) [7].

Loi et al., explain that, such predictive-factors can be used to identify subpopulations of patients who are most likely to benefit from a given therapy [8]. Indicators of both prognostic and predictive factors are important for the decision of patient outcome and treatment guidance especially for invasive stage of breast cancer disease. Example of both prognostic and predictive factors of breast cancer markers are, hormone receptor breast cancer (HR) and HER2. Yim et al., explain that, estrogen receptor (ER), progesterone receptor (PR) and HER2 have been clinically and statistically proven to be of prognostic value in breast cancer and have been useful in clinical management [9].

Likewise, Duffy et al., believed that, these markers are best for prognostic and predictive value because of them possess ideal of breast cancer biomarker. In general, prognostic markers help to determine whether a patient requires treatment, and a predictive factor is useful in deciding which treatment will be the best [10].

#### Hormone receptor (ER & PR)

Hormone receptors are special proteins that are found within and on the surface of breast cell, these are used to receive message from substance in the blood stream and telling the cells what to do. These hormone receptors are Estrogen Receptor (ER) and Progesterone Receptor (PR).

Estrogens are a group of hormones that plays a key role in women for standard sexual and reproductive growth, but too men. Likewise, Viale et al., held that, certain estrogen-induced proteins, such as PR, are also important for specific metabolic processes in the cell [11].

However, the normal hormone receptor can be changed to cancer because of enhance uncontrolled growth of the hormone receptor and or lower amount of hormone receptors. Depends on the presence or absence of receptor; breast cancer can be ER +/ER- and PR+/PR-, approximately 80% of breast cancers are Estrogen receptor-positive breast cancer (ER+) and they can accept endocrine therapy [12]. The assessment of ER status of breast carcinoma has become the routine practice to predict the likely outcome of Tamoxifen therapy. Likewise, the assessment of PR status along with ER gives a stronger predictive power [13].

According to the report, ER+ and /PR+ breast cancers generally have a better prognosis and are often responsive to anti-estrogen therapy that is tamoxifen. ER-disease is more aggressive and not treated with tamoxifen (Part et al.). Normally this showed that, identification of hormone receptor status is extremely vital in order to guide the right treatment.

#### Human epidermal growth factor (HER2)

Cooke defined that, HER2 which is also called HER2/neu, HER-2 and c-erbB-2, is a gene that sends control signals to cells, telling them to grow, divide and make repairs and also have important function for the control of normal growth regulation [14].

Yardley et al., supposed that a healthy breast cell has 2 copies of the HER2 gene; some kinds of breast cancer were getting started when a breast cell has more than 2 copies of that gene and those copies started over-producing the HER2 protein [15]. HER2 acts as a networking receptor that mediates signaling to cancer cells, causing them to proliferate.

According to Breast cancer org, breast cancers with HER2 gene amplification or HER2 protein over expression are called HER2-positive, compared to HER2-negative breast cancers, it tends to grow faster, more likely to be spread and come back later, and are more aggressive than HER2 negative breast cancers [16].

#### Molecular subtypes of breast cancer

Breast cancer is classified in to four molecular subtypes based on immunohistochemistry analysis. These are: Luminal A (ER+/PR+/HER2-), Luminal B(ER+/PR+/HER+), HER2 subtype (ER-/PR-/HER+) and triple negative (ER-/PR-/HER2-).

Luminal A is the most common molecular subtype and represents 50%-60% of all breast tumors. These tumors commonly have low histological grade, low grade of nuclear pleomorphism and include special histological types (*i.e.*, tubular, invasive cribriform, mucinous and lobular) with good prognosis.

*Luminal-B* tumors contain 15%-20% of all breast cancers [2,17]. However, Luminal B tumors have a characteristic of higher grade than luminal a tumors [18]. The molecular subtype HER2 type is not the same as HER2-positive. Although most HER2 type tumors are HER2-positive (and named for this reason), about 30 percent are HER2-negative HER2 type.

HER2 type tumors tend to be: ER-negative, PR-negative, Lymph node-positive and Poorer tumor grade. About five to 15 percent of breast cancers are HER2 type. Women with HER2 type tumors may be diagnosed at a younger age than those with luminal A and luminal B tumors. HER2 type breast cancers that are HER2-positive can be treated with anti-HER2 drugs such as trastuzumab (Herceptin). Before these drugs were available, HER2 type tumors had a fairly poor prognosis.

When the tumor represented as ER-/PR-/HER2- or lack of expression of all three receptors, it is known as called triple negative breast cancer (Prasad et al., 2016). Triple negative breast cancer patients have higher tumor stage, more aggressive

biological characteristics and poorer prognosis than other breast cancer patients [19,20].

#### THE PREVALENCE OF HORMONE RECEPTOR BREAST CANCER IN ETHIOPIA

Studies showed that most of African women breast cancer patients have aggressive ER- and PR-. Results from East Africa showed 76% of the patients in Kenya and more than two thirds of the patients in Tanzania and Uganda were ER-negative.

The majority of studies from West Africa showed more than half of the patients were ER-negative: in Nigeria and Senegal, 76% in Ghana, 76%, 75% and 53% and in Mali, 61%. One study from Nigeria, one from Uganda, one from Ghana and one large study from South Africa showed lower proportions of ER-negative tumors (35%, 40%, 24% and 37%, respectively).

According to Bravaccini et al., study when compared between Tanzanian and Italian breast cancer patients there were higher prevalent of ER- breast cancer in Tanzanian patients ER-negative (52% vs. 20%) [21]. while a study done in Kenya showed that there was highly prevalence of ER and +PR+219(72.8%) and 195(64.8%) [22].

Finding the prevalence of ER+ and PR+ were 50(65.5%), 29/50(58%), respectively. Similarly another study done by finding showed that from a total of 352 BC patients the ER+ was prevalent accounting for (65%). And also another study done by the prevalence of ER+ was 74(65%) while the prevalence of PR+ was 49(43%). The variation of the result might due to sample size, environmental variation, and sample collection method (Table 1).

**Table 1:** The Hormone Receptors results among different population.

Author, Year	Country	Total Number of Patients	Tissue collection method	% of ER+	%of PR+
Bravaccini et al., 2019	Italy			52%	-
Sayed et al.,2014	Kenya	301		219(72.8%)	195(64.8%)
Kantelhardt et al.,2014	Ethiopia	352	FNAC	74(65%)	
Shenkutie et al.,2017	Ethiopia	87	Biopsy	50(65.5%)	29/50(58%)
Hadgu et al.,	Ethiopia	114	Biopsy	74(65%)	49(43%)

#### THE PREVALENCE OF MOLECULAR BREAST CANCER SUBTYPES IN ETHIOPIA

Study done by Galukande conducted at Uganda cancer institute and Mulago hospital showed that from a total of 226 patient samples the prevalence of Luminal A 38% (83/226) was high followed by Triple Negative Breast Cancer (TNBC) 34% (77/226), HER2 positive 22% (49/226), and Luminal B 5%

(13/226) (Galukande et al., 2014). Studies from Angola indicated that Triple Negative (31.4%) was highest followed by Luminal A (25.7%). According to Sayed et al., study the proportion of Luminal B was high 175 (61.2%), triple negative 58 (20.2%) [22-25]. Regarding finding HER2+(24%) was prevalent next to Luminal A (54%) [26,27] (Table 2).

**Table 2:** The Molecular breast cancer subtype results among different population.

Author, Year	Country	Total Number of Patients	Tissue collection method	%of TNBC	%of Luminal A	% of Luminal B	HER2 Positive
Galukande et al., 2014	Uganda	226	Core Biopsy	34%	38%	5%	22%
Sayed et al.,2014	Kenya	301	-	58(20.2%)	31(10.8%)	175(61.2%)	53(17.6%)
Shenkutie et al., 2017	Ethiopia	50	Biopsy	9/50(18%)	27/50(54%)	15/50(22%)	24%
Adgue et al.,2018	Ethiopia	114	Biopsy	26(23%)	45(40%)	30(26%)	26(23%)
Miguel et al., 2017	Angola	104	-	31.4%	25.7%	7.9%	15.7%

## CONCLUSION

In Ethiopia the prevalence of Hormonal receptor Positive and Luminal A is highly prevalence so the patient can take hormonal receptor treatment.

## RECOMMENDATION

Further researcher should be done the prevalence of molecular subtypes of breast cancer with in a large number of both men and women breast cancer patients.

Should be done the molecular subtypes of breast cancer by PCR technique.

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