

Distribution Of Age Groups Among The Different Stages Of Breast Cancer Patients

Kumaraswamy Barla^{1*}, Hasesha.Kolli², M. James Vardhan³, Malakalapalli Lavanya⁴, M. Krishna⁵, Dr K. Eswar Kumar⁶

¹Research Scholar, Department of Pharmaceutical Sciences, Andhra University, Visakhapatnam, India., Email: ¹kumaraswamy.barla@gmail.com

^{2,3,4}Pharm. D Student, Sir. C. R. Reddy College of Pharmaceutical Sciences, Eluru, Andhra Pradesh, India., Email:

²kollihasesha@gmail.com, ³jamesmotru@gmail.com, ⁴lavanyamalakalapalli@gmail.com

⁵ Assistant Professor, Sir. C. R. Reddy College of Pharmaceutical Sciences, Eluru, Eluru, Andhra Pradesh, India., Email: ⁵krishna.mannem@gmail.com

⁶ Associate Professor, Department of Pharmaceutical Sciences, Andhra University, Visakhapatnam, India.

Email: ⁶ekilari@gmail.com

*Corresponding Author: - Kumaraswamy Barla

^{*}Research Scholar, Department of Pharmaceutical Sciences, Andhra University, Visakhapatnam, India., Email: kumaraswamy.barla@gmail.com

DOI: 10.47750/pnr.2022.13.S05.326

Abstract

Almost 2 million fresh breast cancer cases were diagnosed worldwide in 2020. Female patients aged >50 years account for 80% of breast cancer cases, and 1 in 8 women report an incidence of breast cancer. In our study of age and staging, a total of 294 patients had included. We observed various histological types of breast cancers like ductal carcinoma (81.63%), lobular carcinoma (6.8%), and papillary and mucinous carcinoma with 2%. Out of 294 patients, 8 were at stage I, and 100 were at stage IIA. Almost 86 of the patients were at stage IIB, 44 patients accounted for stage IIIA, and 28 were at stage IIB and IIIC. We observed that nearly 254 patients are aged >40 years. About 34% of patients presented to the hospital at stage IIA, and 29.25% came to the hospital at stage IIB. Among 294 patients, 23.8% were at the age of 40-46, 16.3% were at the age of 54-60, and 15% were at the age of 61-67. Appropriate screening and awareness regarding breast cancer could help the patient for early diagnosis of the disease and increase the patient's survival rate.

Index Terms— Age, Breast cancer, Staging, Types of Breast Cancer.

INTRODUCTION

Breast cancer is the most commonly diagnosed and fifth leading cause of cancer-related mortality [1]. Almost 1 in 8 women report an incidence of breast cancer. A higher incidence of breast cancer occurred in high-income regions compared to lower-income areas. Breast cancer mortality is high in the majority of low and middle-income regions. It might be due to delayed diagnosis presentation or minimal treatment access. The ethnicity of the population can also affect the incidence of breast cancer. Many investigations have shown that breast cancer occurs earlier in Asian women aged 40-50 compared to western parts.

Along with ethnicity, a positive family history of breast cancer can increase the risk of incidence of breast cancer. Almost 10% of breast cancers have a positive family history and are inherited [4]. Age is one of the most critical elements in determining one's likelihood of developing breast cancer [7].

Classification of breast cancer:

Breast cancer is classified based on its histological appearance, epithelial origination and morphologically, whether the tumour is limited to epithelial components or has invaded other tissues [6].

Carcinomas: These tumours originate from epithelial components that consist of cells that line lobules and terminal ducts in the breast. These tumours include:

- **Insitu carcinoma:** These cancerous cells are pre-invasive and do not invade the breast tissue.
- **Invasive carcinoma:** These cancer cells have the potential to grow into breast connective tissue and can invade other parts of the body. It is the most common histological type and occurs in 50-60% of patients. It includes two types
 - ◇ Invasive ductal carcinoma: Carcinoma occurs in the lining of milk ducts and can invade the walls of ducts. It is the most common histological type in 50-60% of patients [3].
 - ◇ Invasive lobular carcinoma: A type of cancer occurs in 5-15% of patients at the duct lobules [2].

1. **Sarcomas:** These are rare and arise from the connective tissue components of the breast [2].

Based on histology [5],

◇ **Invasive ductal carcinoma, no specific type:** It is the most common type and accounts for about 40-75% of invasive carcinomas of the breast. The tumour cells present necrosis, calcifications, protruding nucleoli, and pleomorphic and have numerous mitoses.

- ◇ **Medullary carcinoma** accounted for 5% of invasive carcinomas diagnosed in patients aged 30-40. It presents sizeable pleomorphic tumour cells with a syncytial growth pattern and lymphoplasmacytic infiltration.
- ◇ **Metaplastic carcinoma:** It is observed mainly in post-menopausal women. The tumour cells are heterogenous and contain squamous, spindle, chondroid, bone, and myoepithelial cells and have lymph node involvement.
- ◇ **Apocrine carcinoma** is a high histological grade carcinoma with large tumour cells with granular eosinophilic cytoplasm, prominent nucleoli, and multinucleated nuclei.
- ◇ **Mucinous carcinoma:** These tumours contain mucin with clusters of tumour cells grown in different patterns with nuclear atypia.
- ◇ **Cribriform carcinoma:** It affects patients at the age of 50 years old. The tumour appears in cribriform with low-grade atypia and is associated with Ductal Carcinoma In situ without stromal invasion.
- ◇ **Tubular carcinoma:** These carcinomas are premalignant and have prominent angles and oval or elongated tubules with an unorganised disposition. A layer of epithelium covers the open lumen without necrosis and mitosis presentation.
- ◇ **Invasive lobular carcinoma** is identified by small tumour cells uniformly distributed in a concentric pattern throughout the stroma.
- ◇ **Neuroendocrine carcinoma:** The tumour cells are alveolar, trabecular or rosette in an infiltrative growth pattern. These carcinomas have an eosinophilic granular cytoplasm.

Based on molecular subtypes: The molecular subtypes are characterised based on gene expression of estrogen receptors (ER), progesterone receptors (PR), human epidermal growth factors-2 (HER2) and cell proliferation regulator (Ki-67).

◇ **Luminal A:** Based on the Immunohistochemical profile, it is an ER+ with $\geq 1\%$, PR with $\geq 20\%$, HER-2 $\leq 10\%$ and Ki-67 with $\leq 14\%$ expression.

◇ **Luminal-B:** This subtype has two types-

Luminal B HER2-: ER with $\geq 1\%$, PR- or $< 20\%$, HER2- of $\leq 10\%$ and Ki-67 with $\geq 20\%$ expression.

Luminal B HER2+: ER+ with $\geq 1\%$, HER2+ with $> 10\%$ and any PR and Ki-67 levels.

◇ **HER2+** has the highest expression of HER2 $> 10\%$ and Ki-67 of $> 20\%$, with negativity for ER of $< 1\%$ and PR with $< 20\%$ of face.

◇ **Triple-negative:** It lacks expression of ER with $< 1\%$ and PR with $< 20\%$, and HER2 oncoprotein with $\leq 10\%$ expression with high proliferative activity.

Role of Staging in Breast Cancer:

The significance of staging inpatient treatment cannot be overstated. The essential function of staging stands to identify patients into clusters with similar prognoses and treatments. Without this paradigm, relevant clinical trials would be challenging to conduct. The second objective of staging is to facilitate comparisons among vast populations, either inside geopolitical borders or between diverse nations. Due to the global nature of the current anatomical (TNM) staging technique, the significance of this comparative opportunity increases. Thirdly, staging provides a framework for conversations, particularly among clinicians caring for a specific patient. Staging is the "language of cancer"[14].

The TNM classification had initially developed to permit the designation of classes showing the level of local, regional, and global illness extension at the point of primary treatment, providing an accurate and permanent description [12]. The TNM Classification explains the anatomical progression of cancer. It is based on the notion that therapeutic alternatives and survival possibilities were connected to the size of the tumour at the preceding site (T), the existence or lack of the tumour in the regional lymph nodes (N), and the presence or scarcity of metastasis further regional lymph nodes (M). Tumours are categorised before therapy (i.e., clinical or cTNM) and after excision (i.e., pathological or pTNM) [13].

Tumour (T) indicates the tumour's size and degree of local invasion of nearby structures. The lymph nodes draining the breast tissues must be carefully evaluated for staging and treatment. The diagnosis of metastasis (M) remains the least difficult. It is classed as (M1) if there is any evidence of extraneous disease. The presence of metastatic lesions boosts the total stage to terminal IV, even though it is the most specific component. Only one-fifth of patients diagnosed with cancer at stage IV are expected to survive five years [11].

Breast cancer management depends on the availability of accurate clinicopathological predictive and prognostic indications to guide patient treatment selection. The standard practice uses lymph node (LN) condition, tumour size, and histological grade as the three most significant prognostic markers in early-stage breast cancer, where systemic therapy must be evaluated for each patient[10].

The TNM system's goals are to

- 1) Assist the clinician in treatment planning,
- 2) provide some indications of prognosis,
- 3) Aid in assessing outcomes, and
- 4) Promote information interchange [13].

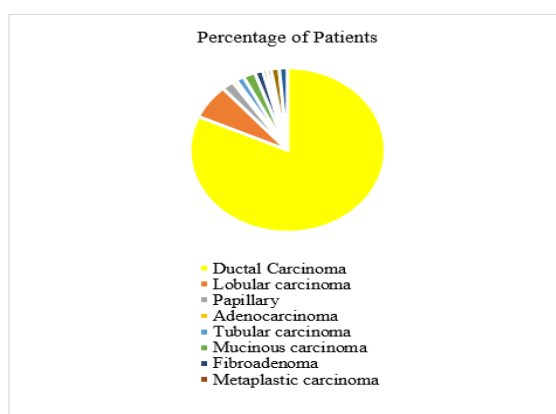
METHODOLOGY

The translational cancer research study was carried out at Good Samaritan Cancer and General Hospital, Eluru. Two hundred ninety-four female patients from 2018–2022 with confirmatory breast cancer staging reports were included, while patients with incomplete reports were excluded from the study. Sturge's formula was used to determine the class intervals. All patients were separated into eight groups based on age and cancer staging.

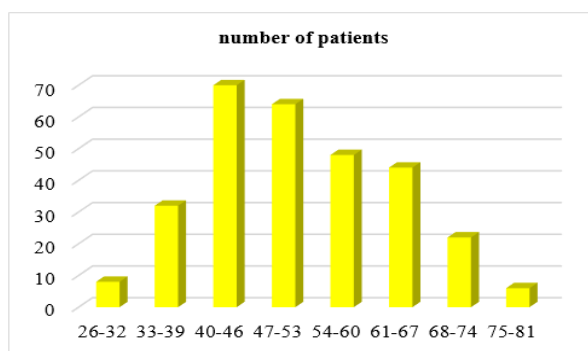
RESULTS

Following our inclusion criteria, 294 patients were included in the study. We detected numerous histological subtypes of breast cancer (fig.1), including ductal carcinoma (81.63%), lobular carcinoma (6.1%), papillary carcinoma (2.0%), and mucinous carcinoma (2.0%). The remaining cancer rates were approximately 0.6%, 1.36 %, and 2%. About 81.6% of patients had Ductal carcinoma, while 6.8% were with Lobular carcinoma.

The Histological type of breast cancer	Number of patients	Percentage
Ductal Carcinoma	240	81.63%
Lobular carcinoma	20	6.80%
Papillary carcinoma	6	2%
Adenocarcinoma	2	0.68%
Tubular carcinoma	4	1.36%
Mucinous carcinoma	6	2%
Fibroadenoma	4	1.36%
Metaplastic carcinoma	2	0.68%
Spindle carcinoma	2	0.68%
Comedo carcinoma	4	1.36%
Medullary carcinoma	4	1.36%

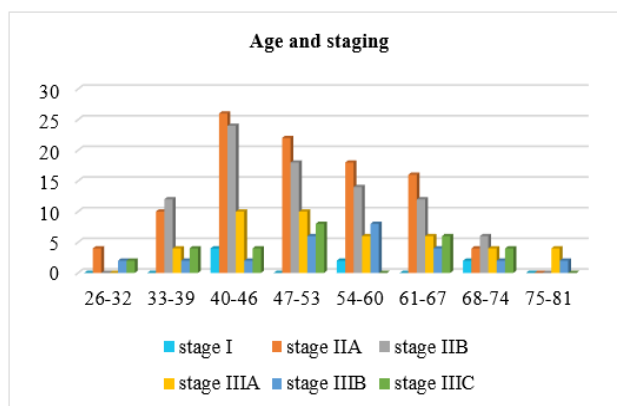


Age groups	Number of patients	Percentage
26-32	8	2.7
33-39	32	10.9
40-46	70	23.8
47-53	64	21.8
54-60	48	16.3
61-67	44	15
68-74	22	7.5
75-81	6	2



Above fig.2 represents number of patients in different age groups. Out of 294 patients, eight were 26-32 age group, and 32 were 33-39 age group. The highest number of patients was from the 40-46 age group, about 70. The age group 47-53 accounts for about 64 patients, the 54-60 age group were about 48 patients, the 61-67 age group accounted for about 44 patients, whereas the 68-74 age group had 22 patients. The least number of patients observed in 75-81 patients, which is about only six patients.

Age groups	STAGE					
	stage I	stage IIA	stage IIB	stage IIIA	stage IIIB	stage IIIC
26-32	0	4	0	0	2	2
33-39	0	10	12	4	2	4
40-46	4	26	24	10	2	4
47-53	0	22	18	10	6	8
54-60	2	18	14	6	8	0
61-67	0	16	12	6	4	6
68-74	2	4	6	4	2	4
75-81	0	0	0	4	2	0



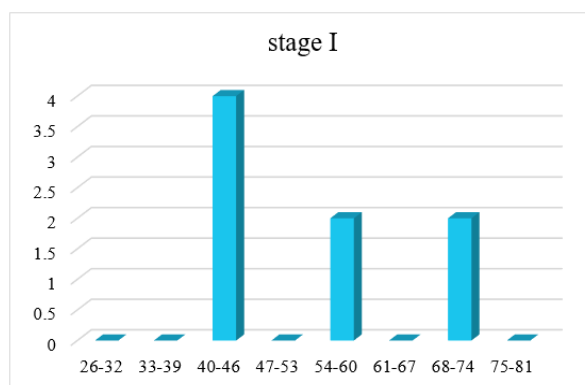
Above Fig.3 represents stages of breast cancer in different age groups. The age group, 26-32, comprises four patients diagnosed with stage IIA, 2patients diagnosed with stage IIIB and stage IIIC.

The age group, 33-39, contains ten patients diagnosed with stage IIA, 12 with stage IIB, four with stage IIIA, two with stage IIIB, and four with stage IIIC.

The age group 40-46 accounts for the highest number of breast cancer cases in stages I, IIA, IIB, and IIIA. The age group, 47-53, contains 22 patients diagnosed with stage IIA; 18 were with stage IIB, ten were with stage IIIA, six were with stage IIIB, and eight were with stage IIIC. The age group, 54-60, contains two patients diagnosed with stage I, 18 patients with stage IIA, 14 patients with stage IIB, six patients were stage IIIA and eight patients with stage IIIB. The age group, 61-67, comprises 16 patients diagnosed with stage IIA, 12 patients with stage IIB, six patients with stage IIIA, four patients with stage IIIB, and six patients with stage IIIC.

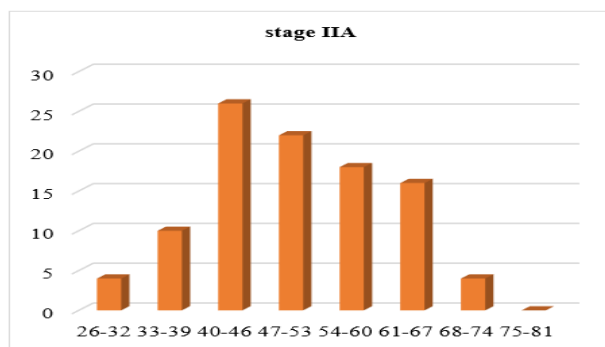
The age group, 68-74, comprises two patients with stage I, 4 with stage IIA, six with stage IIB, four with stage IIIA, two with stage IIIB, and four with stage IIIC. The age group contains four patients with stage IIIA and two with stage IIIB.

Age groups	stage I
26-32	0
33-39	0
40-46	4
47-53	0
54-60	2
61-67	0
68-74	2
75-81	0



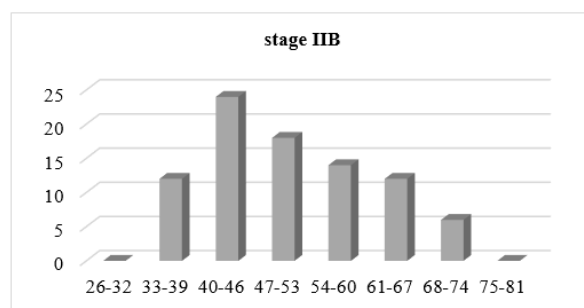
From Fig.4, Out Of 294 Patients, Patients Who Were At Stage I Account For About 8 Cases. The Age Groups For The Background Were 26-32,33-39,40-46,47-53,54-60,61-67,68-74 And 75-81.

Age groups	stage IIA
26-32	4
33-39	10
40-46	26
47-53	22
54-60	18
61-67	16
68-74	4
75-81	0



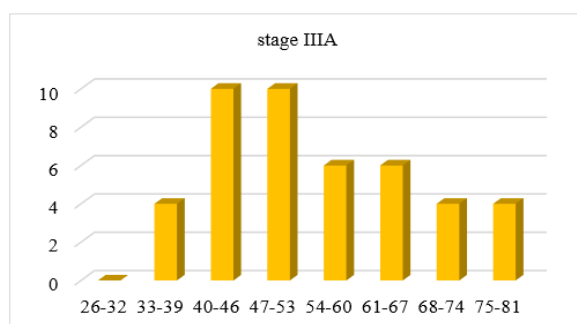
From Fig.5, Out Of 294 Patients,100 Patients Were At Stage IIA. The Maximum Number Of Patients With Breast Cancer Is Aged 40 To 46. 47-53-Year-Olds Account For 22 Instances At Stage IIA.

Age groups	stage IIB
26-32	0
33-39	12
40-46	24
47-53	18
54-60	14
61-67	12
68-74	6
75-81	0



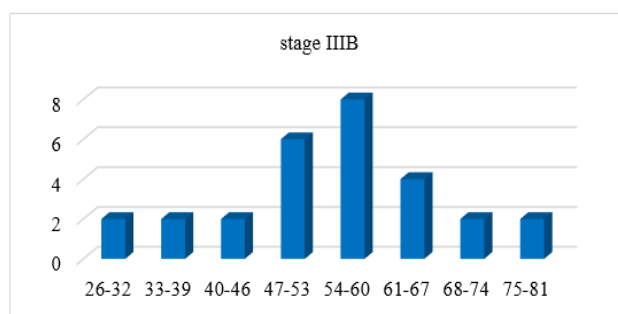
From Fig.6, Out Of 294 Patients, 86 Patients Were At Stage IIB. The Age Group, 40-56, Reports The Maximum Number Of Breast Cancer Cases, 24. The Age Group 47-53 Contains 18 Patients With Stage IIB.

Age groups	stage IIIA
26-32	0
33-39	4
40-46	10
47-53	10
54-60	6
61-67	6
68-74	4
75-81	4



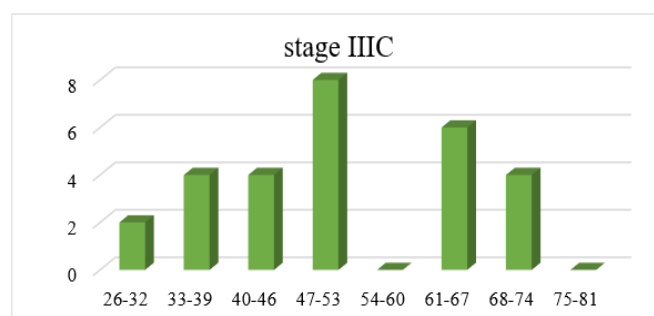
From Fig.7, Of 294, 44 Were At Stage IIIA Of Breast Cancer. The Age Group 40-46,47-53 Reports An Equal Number Of Cases. Similarly, The Age Groups 54-60 And 61-64 Report An Equal Number Of Patients.

Age groups	stage IIIB
26-32	2
33-39	2
40-46	2
47-53	6
54-60	8
61-67	4
68-74	2
75-81	2



From Fig.8, Out Of 294 Patients, 28 Patients Were At Stage IIIB. The 26-32,33-39,40-46,68-74 And 75-81 Reports An Equal Number Of Cases Compared To Other Age Groups. The Maximum Number Of Patients Was From The 54-60 Age Group.

Age groups	stage IIIC
26-32	2
33-39	4
40-46	4
47-53	8
54-60	0
61-67	6
68-74	4
75-81	0



From Fig.9, Out Of 294 Patients, 28 Patients Were At Stage IIIC. The Age Groups 47-53 Report The Maximum Number Of Stage IIIC Breast Cancer Cases.

DISCUSSION

Almost 12% of women worldwide are getting affected by breast cancer. The breast cancer risk for women is about 1/8 in their lifetime. As the age increases, the risk of incidence of breast cancer also increases in women. The incidence of breast cancer is approximately 10.04% and was commonly observed in women aged 40-50 years women [9]. The age group >65 accounts for almost 60% of mortality due to breast cancer. The estimated risk in the 50-59 age group is about 1/43[8]. Therefore; age is one of the significant risk factors for developing breast cancer. The incidence rate of breast cancer is maximum in menopause as the estrogen receptor overexpression increases with increasing age that is up to 50 years of age. Menarche at an early age can be associated with breast cancer due to exposure to estrogen activity for a long time.

Our study observed that almost 254 patients are aged >40 years, with 86.3%. About 34% of patients were presented to the hospital at stage IIA, and 29.25% were given to the hospital at stage IIB. Among 294 patients, 23.8% were at the age of 40-46, 16.3% were at the age of 54-60, 15% were at the age of 61-67. Our study observed that 81.6% of patients were diagnosed with ductal carcinoma. Most patients were diagnosed with stage IIA of breast cancer, with 100 cases out of 294. We also found the least number below 40 years of age.

CONCLUSION

Patients who are older than 45 years old had a greatly greater risk of developing advanced stages of breast cancer, as demonstrated by both previous studies and our own analysis. Even if there are no indications or symptoms of the disease at the moment, it is extremely vital to start going for periodic breast cancer screening as soon as menopause age is reached. As a result of this, there is a possibility that the patient's survival rate and overall quality of life will both increase.

Conflict of Interest: None declared

Ethical approval: This study was approved by Institutional Ethics Committee.

REFERENCES

1. Sergiusz Lukaszewicz, MarcinCzeczulewski, AndrzejStanislawek- Breast Cancer-Epidemiology, Risk factors, Classification, Prognostic Markers and Current Treatment Strategies-An Updated Review. *Cancers (Basel)*. 2021 Sep; 13(17): 4287.Published online 2021 Aug 25.DOI:10.3390/cancers13174287.
2. Types of Breast Cancer-Breast Pathology | Johns Hopkins Pathology (jhu.edu)
3. Adrienne G. Waks, MD; Eric P. Winer, MD- Breast Cancer Treatment A Review. *JAMA*. 2019;321(3):288-300. doi:10.1001/jama.2018.19323
4. Nadia Harbeck, Frédérique Penault-Llorca, Javier Cortes, Michael Gnant, Nehmat Houssami, Philip Poortmans, Kathryn Ruddy, Janice Tsang and Fatima Cardoso-Breast Cancer. *Nat Rev Dis Primers*. 2019 Sep 23;5(1):66. doi: 10.1038/s41572-019-01111-2.
5. Renan Gomes do Nascimento, KaléuMorminoOtoni-Histological and molecular classification of breast cancer: what do we know? *Mastology* 2020;30:e20200024.DOI:10.29289/25945394202020200024
6. Jaffar Makki-Diversity of Breast Carcinoma: Histological Subtypes and Clinical Relevance. *Clin Med Insights Pathol*. 2015 Dec 21;8:23-31 DOI:10.4137/XPath.S31563
7. Akruwala S. D, Sharma V-A retrospective study of female breast cancer: Stage and age correlation.April-June 2018/ Vol 4/ Issue 2.
8. Andrew McGuire, James A.L. Brown, MichaelJ. Kerin-Effects of Age on the detection and Management of Breast Cancer. *Cancers (Basel)*. 2015 Jun; 7(2): 908–929.DOI:10.3390/cancers7020815
9. MuhammadAkram, MehwishIqbal, Muhammad Daniyal and AsmatUllah Khan-Awareness and current knowledge of breast cancer. *Biol Res*. 2017 Oct 2;50(1):33DOI 10.1186/s40659-017-0140-9.
10. Emad A Rakha , Jorge S Reis-Filho , Frederick Baehner , David J Dabbs , Thomas Decker , Vincenzo Eusebi, Stephen B Fox, Shu Ichihara, Jocelyne Jacquemier , Sunil R Lakhani, José Palacios, Andrea L Richardson, Stuart J Schnitt, Fernando C Schmitt, Puay-Hoon Tan, Gary M Tse, Sunil Badve and Ian O Ellis-Breast cancer prognostic classification in the molecular era: the role of histological grade.Rakha et al. *Breast Cancer Research* 2010, 12:207 <http://breast-cancer-research.com/content/12/4/207>.
11. Sara BishiAlgarni, Maha Mohammad Alsugair, Mohammed KifahAlkhars, Mohammed Jamil Addas, MoayadAbdulhameed Hakeem, AlAnoud Abdullah AlSalman, Yasmen Riyadh AlFaresi, Abdullah MtrikAlqahtani, Abdulaziz Fahad Almalki, Hanadi Naeem Abu Jabr, Naif Ali Alamri- Evaluation role of imaging studies in the staging of breast cancer.*Archives of Pharmacy Practice* | Volume 11 | Issue 4 | October – December 2020.
12. Y. H. Park, S. J. Lee,E. Y. Cho,Y.La. Choi, J. E. Lee, S. J. Nam, J.-H. Yang, J. H. ShinE. Y. Ko, B.-K. Han, J. S. Ahn, Y.-H. Im-Clinical relevance of TNM staging system according tobreast cancer subtypes. *Annals of Oncology* 22: 1554–1560, 2011.doi:10.1093/annonc/mdq617. Published online 17 January 2011.
13. Leslie H.Sobin,MD-TNM: Evolution and Relation to Other Prognostic Factors.*Seminars in Surgical Oncology* 2003; 21:3–7.
14. Frederick L. Greene, MD; Leslie H. Sobin, MD-The Staging of Cancer: A Retrospective and Prospective Appraisal.*CA Cancer J Clin* 2008;58:180–190.DOI: 10.3322/CA.2008.0001.