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An Observational Study to Ferret Out the Treatment Regimens in Various Stages of Triple Negative Breast Cancer Accompanied with Susceptibility of Women

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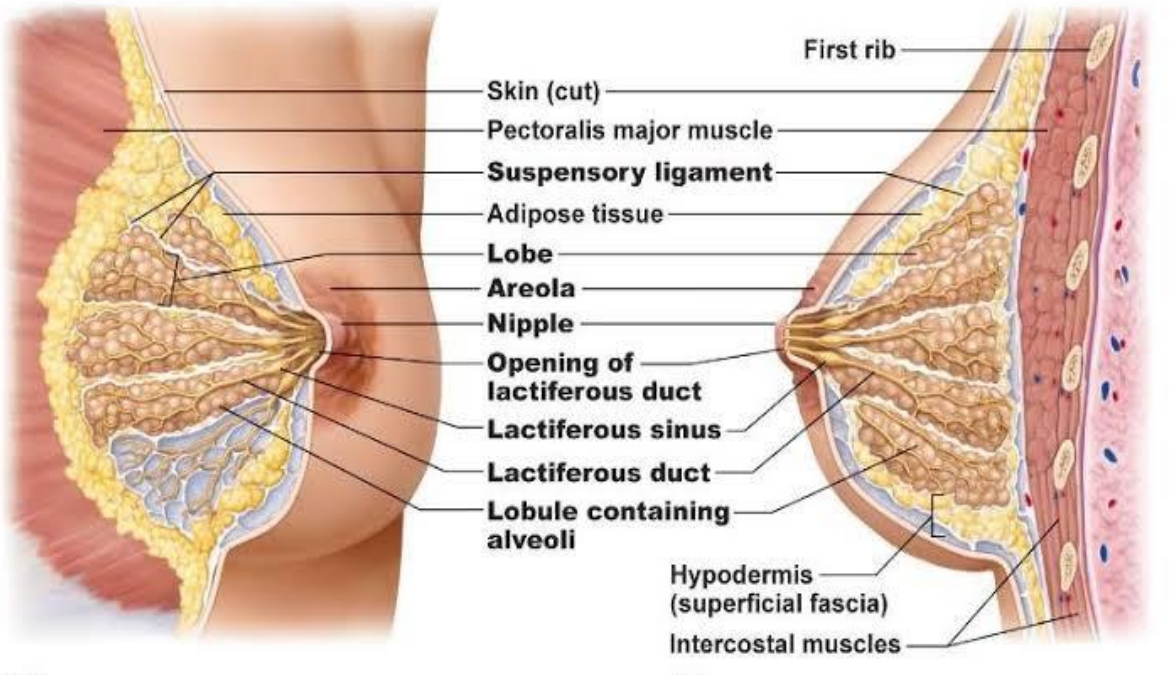
ABSTRACT

Oncology is a branch of science that deals with Neoplasms, these are a mass of tissue formed as a result of abnormal, excessive, uncoordinated, and purposeless proliferation of cells. Neoplasms are either benign (localized, slow growing without causing damage to other tissues) or malignant (metastasize and highly proliferative and spreads throughout the body and even cause death to the host). The eventually common name for malignant tumor is Cancer. Among the cancers, Breast cancer is the leading type among all cancers. When the cells of breast undergo apoptosis, they began to grow uncontrollably i.e., cancer to the breast. Triple Negative Breast cancer (TNBC) is characterized by absence of estrogen (ER), progesterone (PR) and doesn't overexpress the Human Epidermal growth factor Receptor 2 (HER2) protein negative. Causes of TNBC are due to early menarche, late menopause, BRCA1 gene mutation, race, ethnicity, obesity, prolonged use of oral contraceptives, dense breast tissue and due to intended or unintended radiation exposure. This study (n=110) reports most commonly prescribed class of chemotherapy drugs, particular chemotherapy drug and most preferred combinational chemotherapy agents used in various stages of triple negative breast cancer including demonstration of women prone to triple negative breast cancer based on their age, menses history, family history, co-morbidities and chi-square analysis of the included parameters.

INTRODUCTION:

Triple Negative Breast Cancer (TNBC) is a poor prognostic, basal type and known to have a confined treatment options. Patients diagnosed with TNBC are found to be negate with estrogen (ER), progesterone (PR) receptors and doesn't overexpress the Human Epidermal growth factor Receptor 2(HER2) protein [3]. Factors effecting are early menarche, late menopause, BRCA1 gene mutation, race-ethnicity, obesity, prolonged use of oral contraceptives, dense breast tissue and due to intended or unintended radiation exposure [1]. Prognostic factors include tumor size, tumor grade or histological grade, axillary lymph node status, lymphatic channel invasion, mitotic figure count, hormone receptor status, human epidermal growth factor receptor, p53 and BRCA genes, cathepsin D, Ki67 protein.

ER - Negative, PR - Negative, HER2 - Negative = TNBC.



Globally all TNBC cases accounts approximately 10-20% [1]. The incidence of TNBC has been increasing worldwide from several decades, the greatest raise in TNBC is found in Asian countries (especially in India). It is estimated that 2,07,090 cases of breast cancer are diagnosed, in 39,840 women die of breast cancer, where 54,010 cases of non-invasive [4]. Nearly 1million cases of breast cancer are diagnosed annually worldwide within that 1,70,000 cases are of Triple negative phenotype. The prevalence of TNBC is highest in pre-menopausal African American women 39%. Researchers found that the incidence of TNBC disease among African American women (47%) is more or twice than of white women (22%) population of people diagnosed with TNBC.

ADJUVANT/ NEO-ADJUVANT CHEMOTHERAPY REGIMEN OF TRIPLE NEGATIVE BREAST CANCER:

TREATMENT FOR STAGE I, II, IIIa TNBC:

PREFFERED REGIMEN	
DRUG REGIMEN	**DOSING**
Doxorubicin + Cyclophosphamide (AC) with Paclitaxel (T):	**Day1:** Doxorubicin 60mg/m2 IV over 60 min. **Day1:** Cyclophosphamide 600mg/m2 IV over 30 min. **Followed by:** Paclitaxel 175mg/m2 IV over 3 hours Repeat every 3 weeks.
Docetaxel + Cyclophosphamide (TC):	**Day1-5:** Docetaxel 75mg/m2 IV over 1 hour. **Day1-** Cyclophosphamide 400- 1800 mg/m2. Repeat cycles Weekly 2-5 days every 2-4 weeks.
BENEFICIAL REGIMEN IN SOME CIRCUMSTANCES:	
Cyclophosphamide+ Methotrexate + Fluorouracil (CMF):	**Day 1, 15-** cyclophosphamide 100mg/m2 PO, OD. **Day 1,8-** Methotrexate 40mg/m2 IV rush. **Day 1,8-** Fluorouracil 600mg/m2 IV rush. Repeat every 3 weeks.
Epirubicin + Cyclophosphamide (EC):	**Day 1-** Epirubicin 100mg/m2 IV over 1 hour. **Day 1-** Cyclophosphamide 60mg/m2 IV over 30 min. Repeat for every 2 weeks 4 cycles.

TREATMENT FOR STAGE III TNBC:

PREFFERED REGIMEN:	
Doxorubicin + Cyclophosphamide (AC) with Paclitaxel (T):	**Day1:** Doxorubicin 60mg/m2 IV over 60 min every 21 days. **Day1:** Cyclophosphamide 600mg/m2 IV over 30 min every 21 days. **Followed by:** Paclitaxel 175mg/m2 IV over 3 hours Repeat every 3 weeks.
Docetaxel + Cyclophosphamide (TC):	**Day1-5:** Docetaxel 75mg/m2 IV over 1 hour. **Day1-** Cyclophosphamide 400- 1800 mg/m2. Repeat cycles Weekly 2-5 days every 2-4 weeks.
Cyclophosphamide + Methotrexate + Fluorouracil (CMF):	**Day 1, 14-** cyclophosphamide 100mg/m2, OD **Day 1,8-** Methotrexate 40mg/m2 IV rush. **Day 1,8-** Fluorouracil 600mg/m2 IV rush. Repeat every 3 weeks.
BENEFICIAL IN SOME CIRCUMSTANCES:	
Epirubicin + Cyclophosphamide (EC):	**Day 1- Epirubicin** 100mg/m2 IV over 1 hour. **Day 1- Cyclophosphamide** 60mg/m2 IV over 30 min. Repeat cycle every 2 weeks 4 cycles with **PEGFILGRASTIM (G-CSF)** after 3-10 days of each cycle of EC infusion in febrile neutropenia after reducing dose of Epirubicin to 60mg/m2.
Docetaxel + Doxorubicin + cyclophosphamide (TAC):	**Day 1- Docetaxel** 75mg/m2. **Day 1-** Doxorubicin 500mg/m2. **Day 1-** Cyclophosphamide 500mg/m2. Repeat cycle for 3 weeks
BENEFICIAL IN PRE-OPERATIVE SETTING:	
Paclitaxel + Carboplatin:	**Day 1- Paclitaxel** 175-200 mg/m2 IV over 3 hours. **Followed by:** Carboplatin 250 mg/m2 IV over 30 min. Repeat the cycle for 3 weeks.

TREATMENT FOR STAGE IV:

PREFFERED REGIMEN:	
Gemcitabine:	**Day 1, 8, 15 -** 800-1200 mg/m2 IV over 30 min. Repeat cycle for 3 weeks
Liposomal Doxorubicin:	**Day 1-** 40-50 mg/m2 IV. Repeat cycle for every 4 weeks.
Vinorelbine:	**Day 1-** 20-30 mg/m2 IV infusion slowly for 3-5 min or rapid IV infusion. Repeat for every 1 week.
Olaparib (For BRCA 1,2 mutation in TNBC):	300 mg PO BID. Continue for 1 year until reoccurrence or unacceptable toxicity.
Talazoparib (For BRCA 1,2 mutation in TNBC):	1 mg oral capsule, 0.25 mg capsule available for dose reduction. Continue until disease progression or unacceptable toxicity.
Cisplatin (For BRCA 1,2 mutation in TNBC):	**Day 1-** 75 mg/m2 IV over 60 min. Repeat cycle for every 3 weeks.
Carboplatin (For BRCA 1,2 mutation in (TNBC):	**Day 1-** AUC 6 IV over 30 min. Repeat cycle for every 3 weeks.
Capecitabine:	**Day 1-** 1,000-1,250 mg/m2. Repeat cycle for every 3 weeks.
Larotrectinib (For NTRK fusion):	**Day1-4-** 100 mg BD, PO as a capsule or liquid for 28 days i.e., 28 cycles for 7 weeks.
Entrectinib (For NTRK fusion):	600 mg OD, PO as a capsule.
Pembrolizumab (For MSI-H):	**Day 1-** 200 mg IV every 3 weeks or 400 mg every 6 weeks. Continue until disease progression or un acceptable toxicity or up to 24 months if no disease progression.
Ixabepilone:	**Day 1-** 40 mg/m2 IV infusion over 3 hours, not exceeding dose of 88 mg. Repeat cycle for every 3 weeks. **NOTE:** Give H1 or H2 blocker 1 hour prior before infusion, to prevent the patient from hypersensitivity reactions of the drug.

BENEFICIAL REGIMEN IN SOME CIRCUMSTANCES:	
Docetaxel + Capecitabine:	**Day 1-** Docetaxel 75 mg/m2 IV over 60 min. **Day 1, 15-** Capecitabine 950- 1,250 mg/m2 PO, BID Repeat the cycle for every 3 weeks.
Doxorubicin + Cyclophosphamide (AC):	**Day1-** Doxorubicin 60mg/m2 IV over 60 min. **Day 1-** Cyclophosphamide 600mg/m2 IV over 30 min. Repeat cycle every 3 weeks.
Epirubicin + Cyclophosphamide (EC):	**Day 1,8-** Epirubicin 100mg/m2 IV over 1 hour. **Day 1,8-** Cyclophosphamide 60mg/m2 IV over 30 min. Repeat for every 2 weeks 2 cycles.
Cyclophosphamide+ Methotrexate + Fluorouracil (CMF):	**Day 1, 15-** cyclophosphamide 100mg/m2 PO, OD. **Day 1, 8-** Methotrexate 40mg/m2 IV rush. **Day 1, 8-** Fluorouracil 600mg/m2 IV rush. Repeat every 3 weeks.
Paclitaxel+ Bevacizumab:	**Day 1, 8, 15-** Paclitaxel 90mg/m2 IV over 60 min. **Day 1, 15 –** Bevacizumab 10mg/kg IV Repeat cycle every 3 weeks.
Gemcitabine + Carboplatin:	**Day 1, 8-** Gemcitabine 1,000 mg/m2 IV over 30 min. **Day 1, 8-** AUC 2 IV over 30 min. Repeat cycle every 2 weeks.
Gemcitabine + Paclitaxel (GT):	**Day 1, 8-** Paclitaxel 175 mg/m2 IV over 3 hours. **Followed by:** Gemcitabine 1,250 mg/m2 IV over 30 min Repeat cycle for every 3 weeks.

AIM:

The Aim of the study is to focus on treatment regimens in various stages of Triple Negative Breast Cancer and to demonstrate the susceptibility of women.

OBJECTIVES:

Primary objectives:

- To analyze the treatment patterns and advice to Triple Negative Breast Cancer patients in various stages.
- To elucidate the histological feature in Triple Negative Breast Cancer diagnosed patients.
- To explore the type of women prone to Triple Negative Breast Cancer based on menarche, menopausal, menstrual history, usage of oral contraceptives and breastfeeding status.

Secondary Objectives:

- To make a statistical analysis on treatment patterns and exposure of women to Triple Negative Breast Cancer.

METHODOLOGY:

STUDY DESIGN:

- This is a Retrospective observational study to be conducted on Triple Negative Breast Cancer diagnosed patients.
- Patients who have been treated under the Oncologists will be enlisted in the study.
- This study will only be observing the medications prescribed to the patients and no medication will be administered by the investigators as a part of the study.
- The required data to be collected includes the patient's age, demographic details, complete menstrual history and breast-feeding status, age at first childbirth, usage of hormonal contraceptives, diagnostic and laboratory reports accompanying medications.

STUDY SITE:

A Retrospective study conducted in the department of oncology in a tertiary care cancer center.

STUDY DURATION:

The whole duration of study period is about six months.

STUDY POPULATION/ SAMPLE SIZE:

The total number of patients involved in the study is 110 (n=110).

STUDY CRITERIA:

INCLUSION CRITERIA:

- All the patients for whom Immunohistochemistry for ER, PR, HER2 is done and reported as Triple Negative Breast Cancer.
- Patients undergoing various treatments of Triple Negative Breast Cancer.
- Case sheets with sufficient and appropriate data are required for our study.

EXCLUSION CRITERIA:

- Patient's age group below of 18 years.
- Case sheets with insufficient data.
- Pregnant patients.
- Lactating Patients.

SOURCES OF DATA:

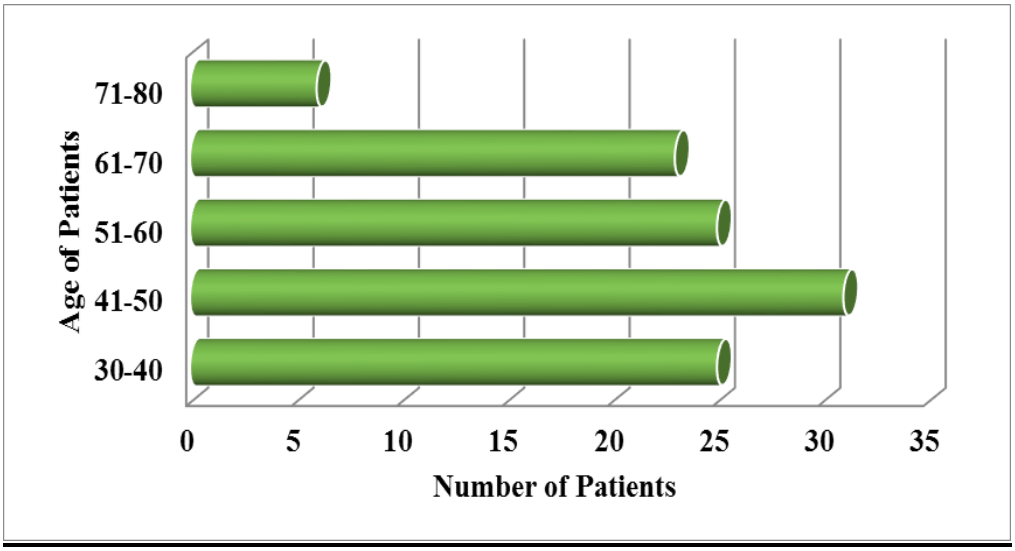
- Patient case files.
- Medication chart review.
- Laboratory and diagnostic reports.

DATA ANALYSIS:

- The Collected data is recorded in MS Excel and analysed in International Business Machines (IBM), software of Statistical Package of Social Sciences (SPSS) Version 26.
- Results are represented in tables and graphs.

RESULTS:

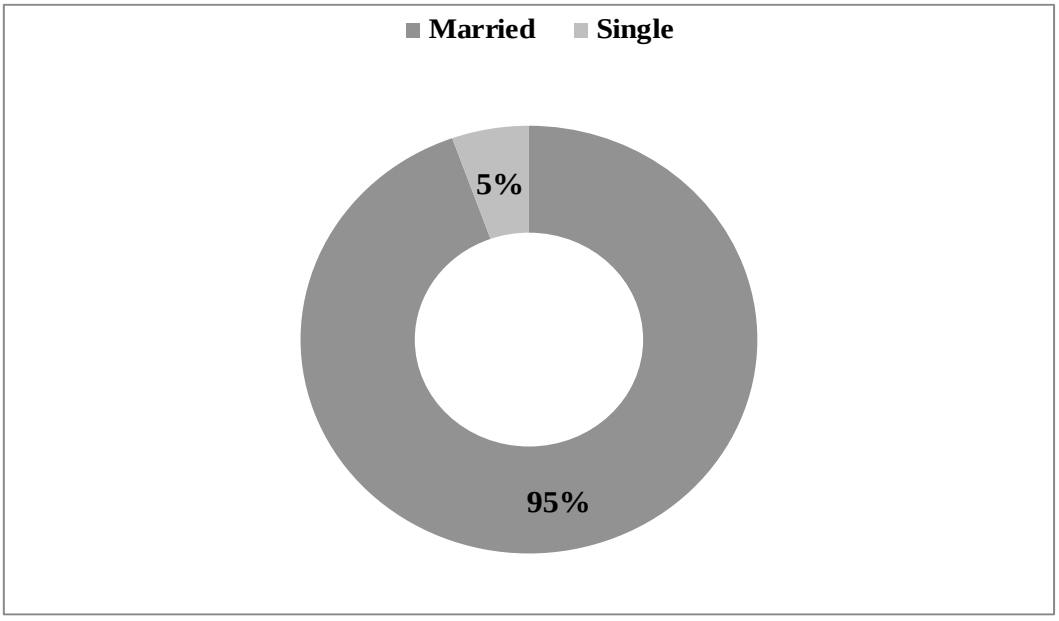
AGE WISE DISTRIBUTION:



S. No	Age in Years	TNBC patients	Percentage
1.	30-40	25	22.72%
2.	41-50	31	28.18%
3.	51-60	25	22.72%
4.	61-70	23	20.90%
5.	71-80	6	5.54%

Age wise distribution of included subjects among TNBC patients shows, greater number of the subjects, n= 31(28.18%) are between the age of 41-50 years followed by n=25 (22.72%) between the age of 30-40 years, similarly n=25 (22.72%) was between the age of 51-60 years. Remaining participants with other age groups n=23 (20.90%) was between the age of 61-70 years and the least participants n=6 (5.54%) was between the age of 71-80 years.

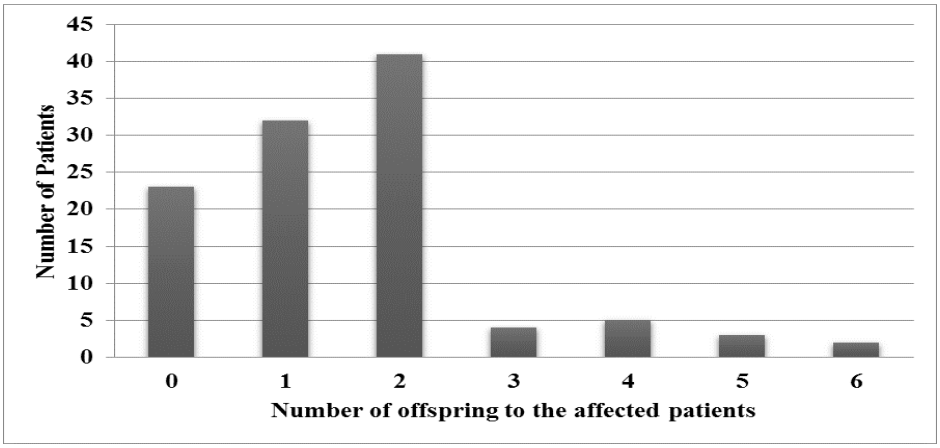
MARITAL STATUS WISE DISTRIBUTION:



S. No	Marital Status	TNBC patients	Percentage
1.	Married	104	94.54%
2.	Single	6	5.45%

Distribution of subjects based on marital status, n= 104 (94.54%) are married and the remaining n=6 (5.45%) was unmarried.

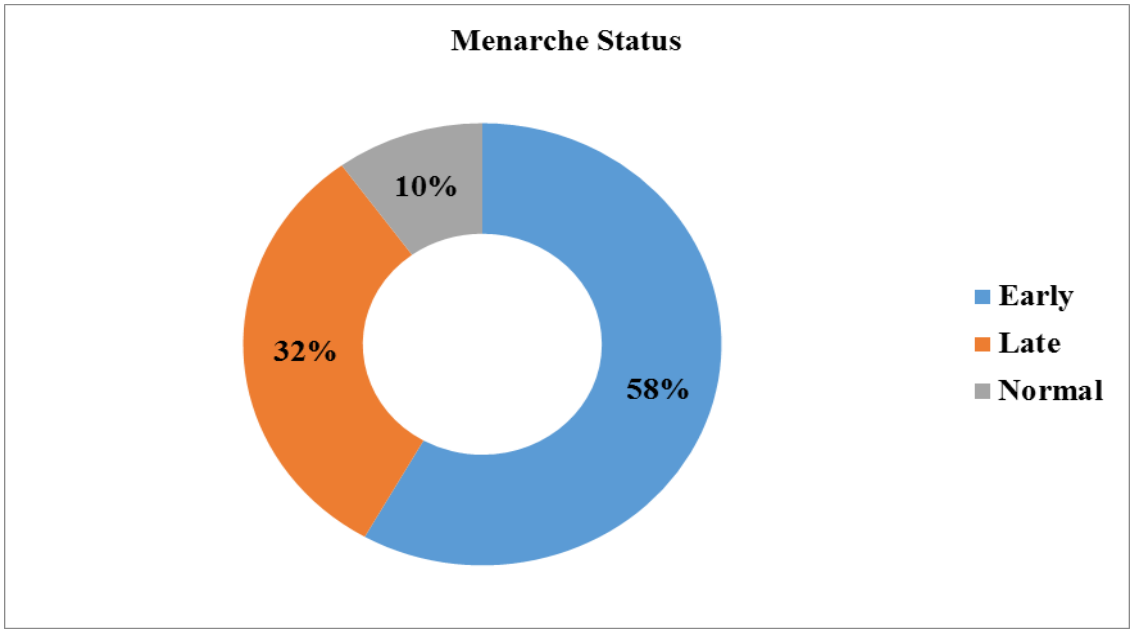
DISTRIBUTION OF NUMBER OF OFF SPRING TO THE AFFECTED PATIENTS:



S. No	Number of Children	TNBC patients	Percentage
1.	0	23	20.90%
2.	1	32	29.09%
3.	2	41	37.27%
4.	3	4	3.63%
5.	4	5	4.54%
6.	5	3	2.72%
7.	6	2	1.81%

Distribution of number off spring to the TNBC affected patients shows, n=41 (37.27%) for 2 children to the patients followed by n=32 (29.09%) for 1 child to the patients, n=23 (20.90%) for 0 children to the patients. Remaining n=5 (4.54%) for 4 children to the patients, n=4 (3.63%) for 3 children to the patients and n=3 (2.72%) for 5 children to the patients and least is n=2(1.81%) for 6 children to the patients.

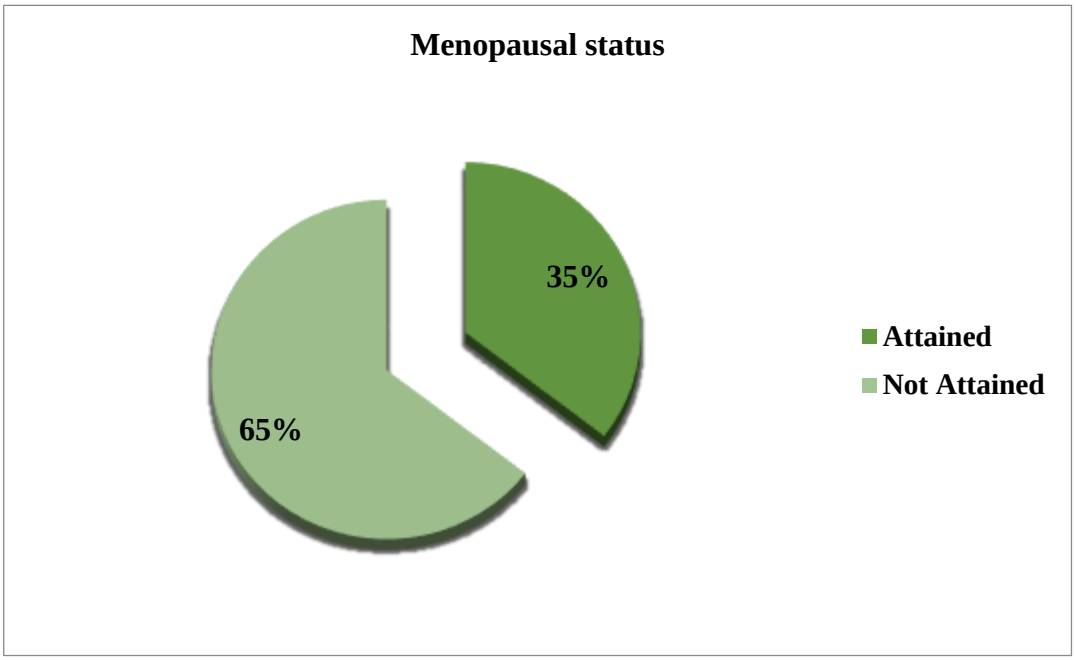
MENARCHE STATUS WISE DISTRIBUTION:



S. No	Menarche Status	TNBC patients	Percentage
1.	Early	64	58.18%
2.	Late	35	31.81%
3.	Normal	11	10%

From the menarche status of distribution most of the subjects with early menarche status n=64 (58.18%), subjects with late menarche are n=35 (31.81%) and subjects with normal menarche are n=11 (10%).

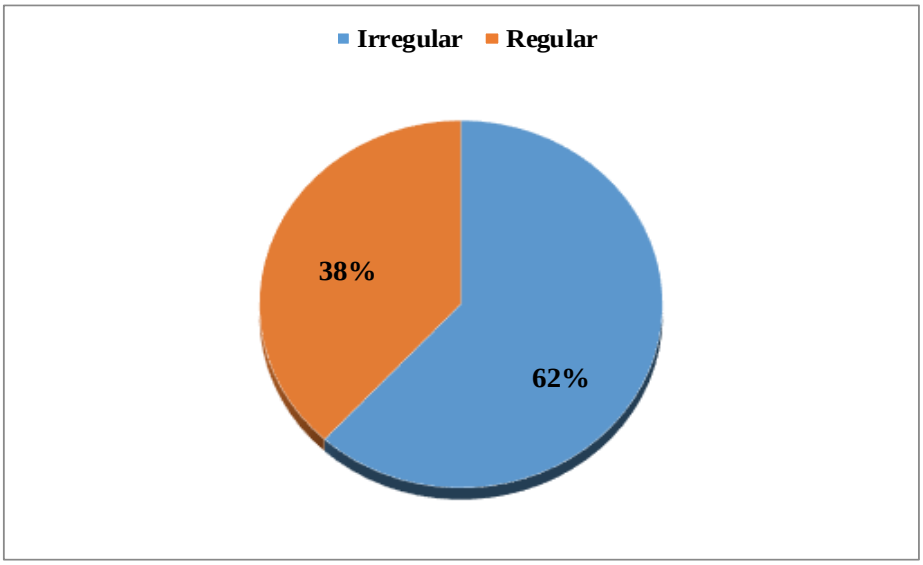
MENOPAUSAL STATUS WISE DISTRIBUTION:



S. No	Menopausal Status	TNBC patients	Percentage
1.	Attained	39	35.45%
2.	Not Attained	71	64.54%

Menopausal status wise distribution shows, subjects n=71 (64.54%) was not attained to menopause and subjects n=39 (35.45%) attained to menopause.

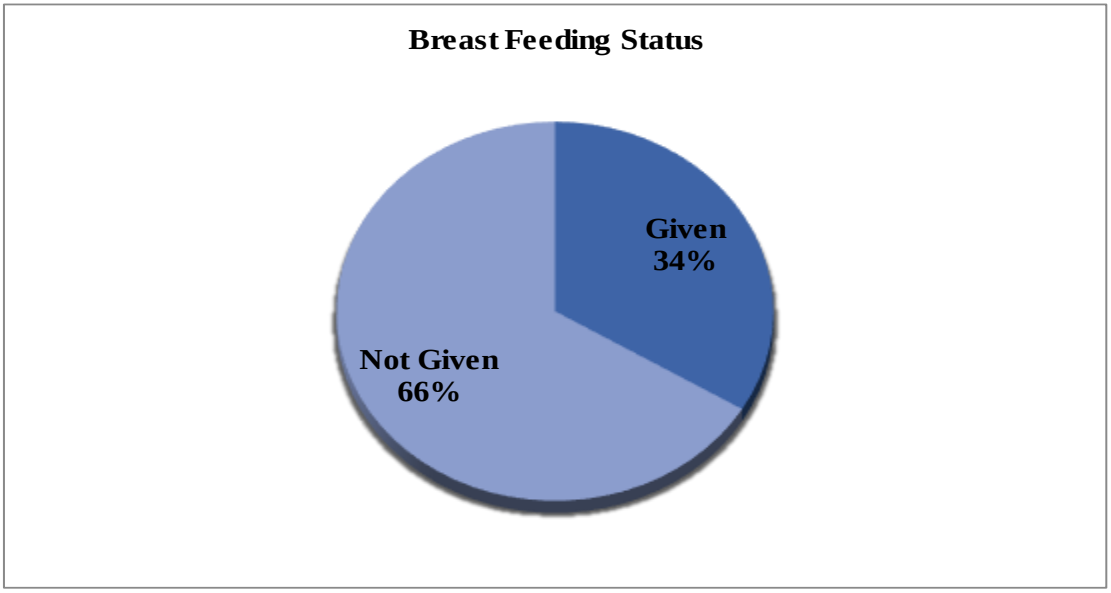
MENSTRUAL HISTORY WISE DISTRIBUTION:



S. No	Menstrual History	TNBC patients	Percentage
1.	Irregular	68	61.81%
2.	Regular	42	38.18%

Categorization of menstrual history shows n=68 (61.81%) subjects with irregular menses and n=42 (38.18%) with regular menstrual history.

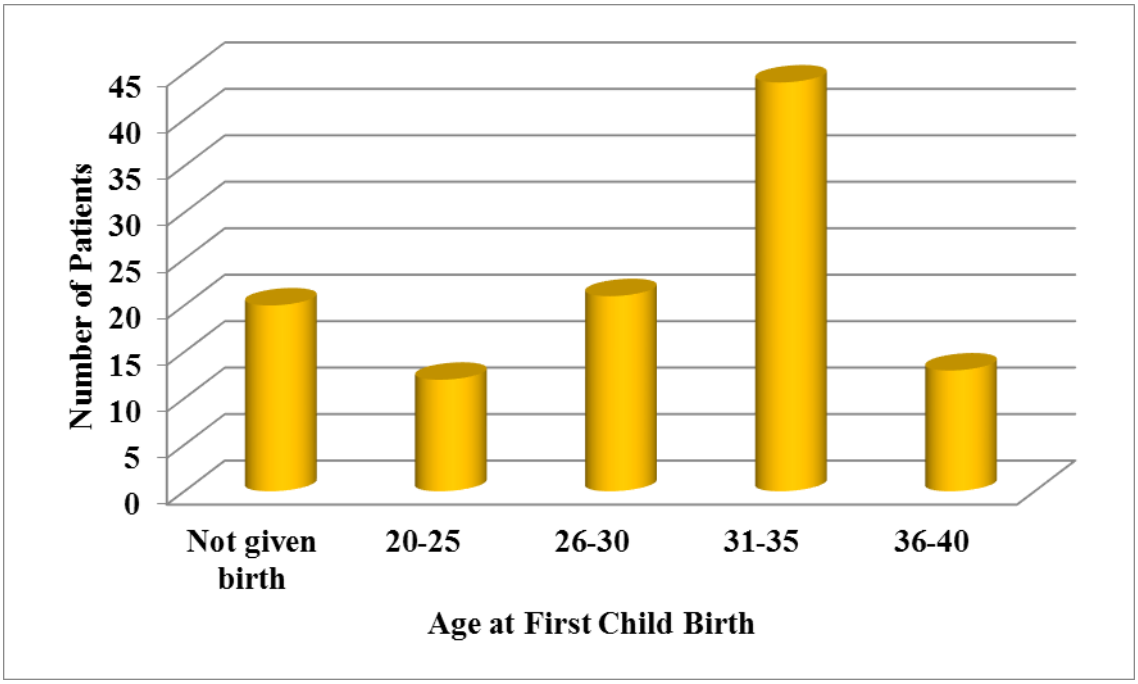
BREAST FEEDING STATUS WISE DISTRIBUTION:



S. No	BREAST FEEDING	TNBC patients	Percentage
1.	Given	37	33.63%
2.	Not Given	73	66.36%

Breast feeding status wise distribution shows, majority of the patients didn't give breastfeeding n=73 (66.36%) and patients who gave breast feeding are n=37 (33.63%).

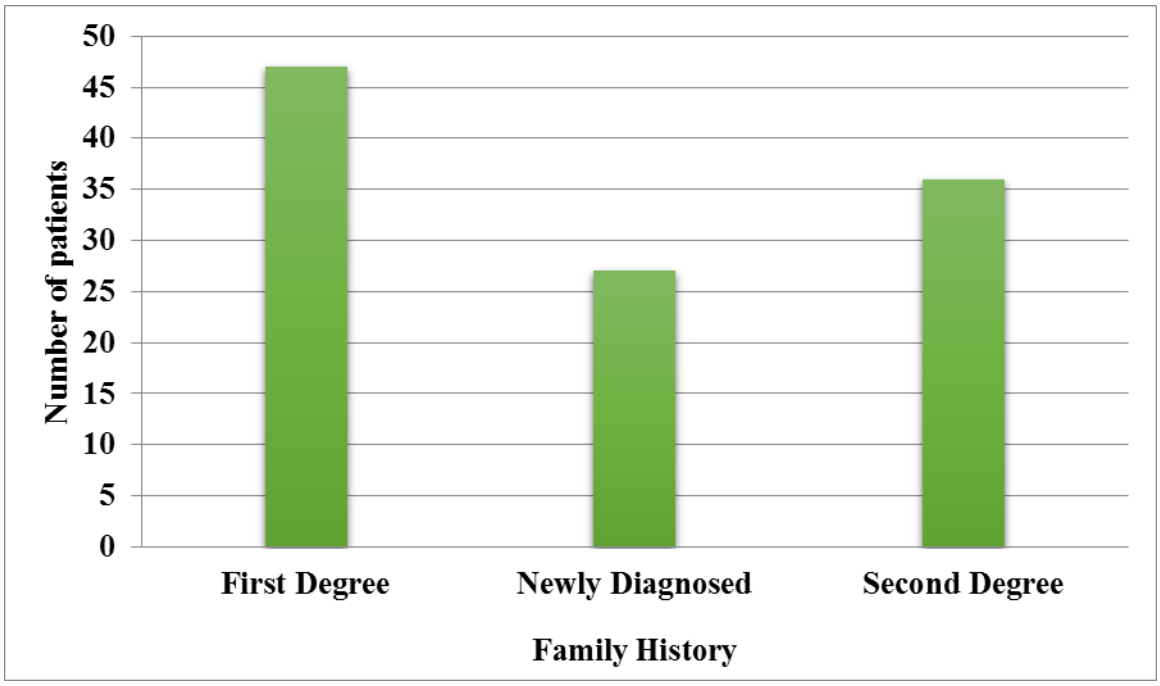
AGE AT FIRST CHILD BIRTH WISE DISTRIBUTION:



S. No	Age at First Child Birth	TNBC patients	Percentage
1.	Not given birth	20	18.18%
2.	20-25	12	10.90%
3.	26-30	21	19.09%
4.	31-35	44	40%
5.	36-40	13	11.81%

Age of patients at first childbirth shows most of the people are at the age 31-35 are n=44 (40%) followed by 26-30 n=21 (19.09%), not given birth are n=20 (18.18%) and n=13 (11.81%) of 36-40 age group. The least is 20-25 age group where n=12 (10.90%).

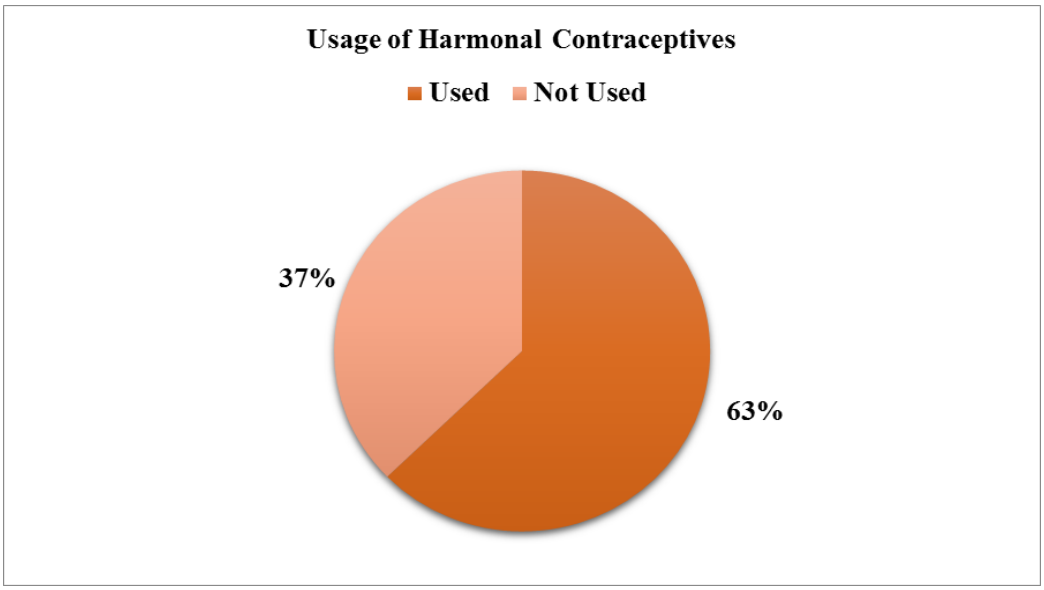
FAMILY HISTORY WISE DISTRIBUTION:



S. No	Family History	TNBC patients	Percentage
1.	First Degree	47	42.72%
2.	Newly Diagnosed	27	24.54%
3.	Second Degree	36	32.72%

Family history wise distribution shows most of the affected patients are from their first degree relatives n=47 (42.72%) and n=36 (32.72%) are affected from second degree relatives followed by newly diagnosed are n=27 (24.54%).

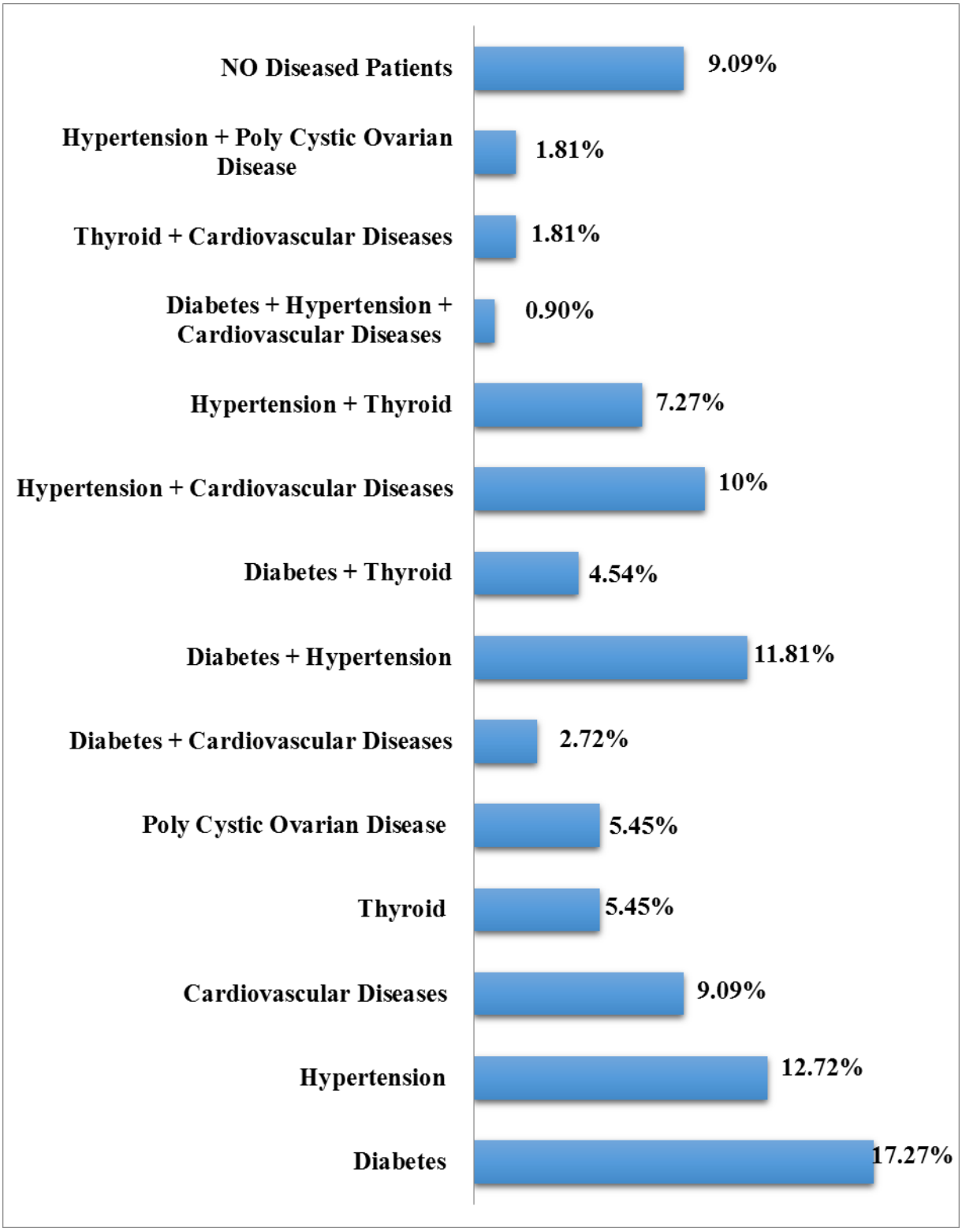
USAGE OF HORMONAL CONTRACEPTIVES WISE DISTRIBUTION:



S. No	Usage of Hormonal Contraceptives	TNBC patients	Percentage
1.	Used	69	62.72%
2.	Not Used	41	37.27%

Usage of hormonal contraceptives distribution shows patients used hormonal contraceptives are n=69 (62.72%) and patients who haven't used contraceptives are n=41 (37.27%).

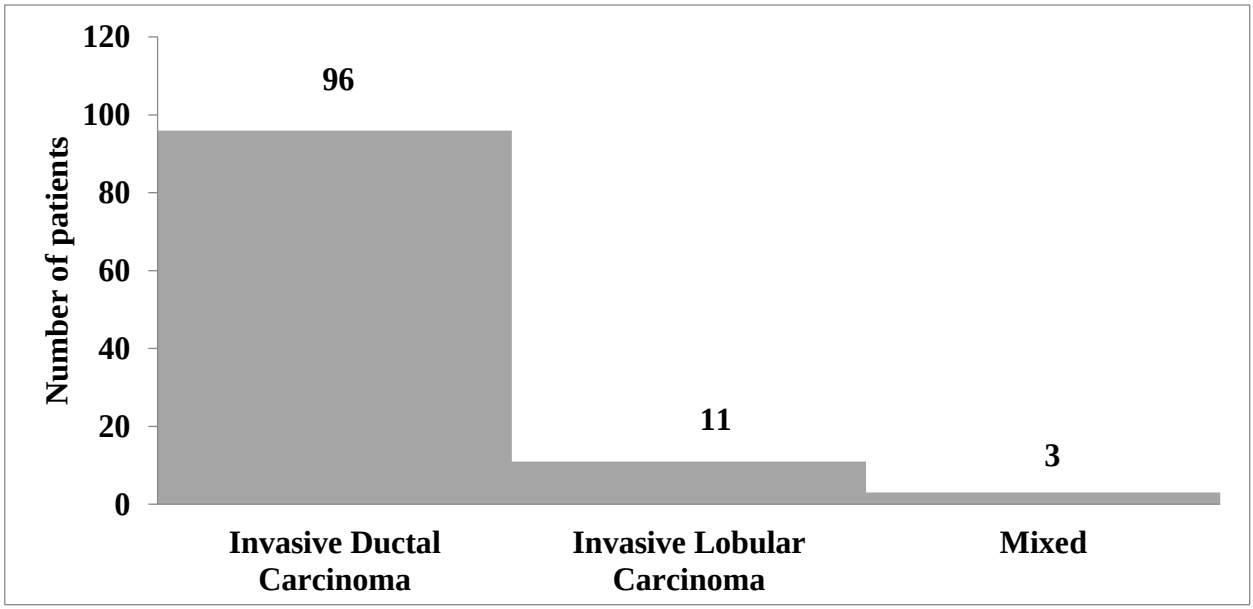
CO-MORBIDITIES WISE DISTRIBUTION:



S. No	Co-morbidities	TNBC Patients	Percentage
1.	Diabetes	19	17.27%
2.	Hypertension	14	12.72%
3.	Cardiovascular Diseases	10	9.09%
4.	Thyroid	6	5.45%
5.	Poly Cystic Ovarian Disease	6	5.45%
6.	Diabetes + cardiovascular diseases	3	2.72%
7.	Diabetes + Hypertension	13	11.81%
8.	Diabetes + Thyroid	5	4.54%
9.	Hypertension + cardiovascular diseases	11	10%
10.	Hypertension + Thyroid	8	7.27%
11.	Diabetes + Hypertension + cardiovascular diseases	1	0.90%
12.	Thyroid + cardiovascular diseases	2	1.81%
13.	Hypertension + Poly Cystic Ovarian Disease	2	1.81%
14.	No Diseased Patients	10	9.09%

Other co-morbidities wise distribution shows, majority of the people are affected with Diabetes n=19 (17.2%) followed by Hypertension n=14 (12.27%), Diabetes + Hypertension n=13 (11.81%), Hypertension + Cardiovascular Diseases n=11 (10%), Cardiovascular Diseases n=10 (9.09%), No Diseased Patients n=10 (9.09%), Hypertension + Thyroid n=8 (7.27%), Thyroid n=6 (5.45%), Poly Cystic Ovarian Disease n=6 (5.45%), Diabetes + Thyroid n=5 (4.54%), Diabetes + Cardiovascular Diseases n=3 (2.72%), Thyroid + Cardiovascular Diseases n=2 (1.81%), Hypertension + Poly Cystic Ovarian Disease n=2 (1.81%), Diabetes + Hypertension + Cardiovascular Diseases n=1 (0.90%).

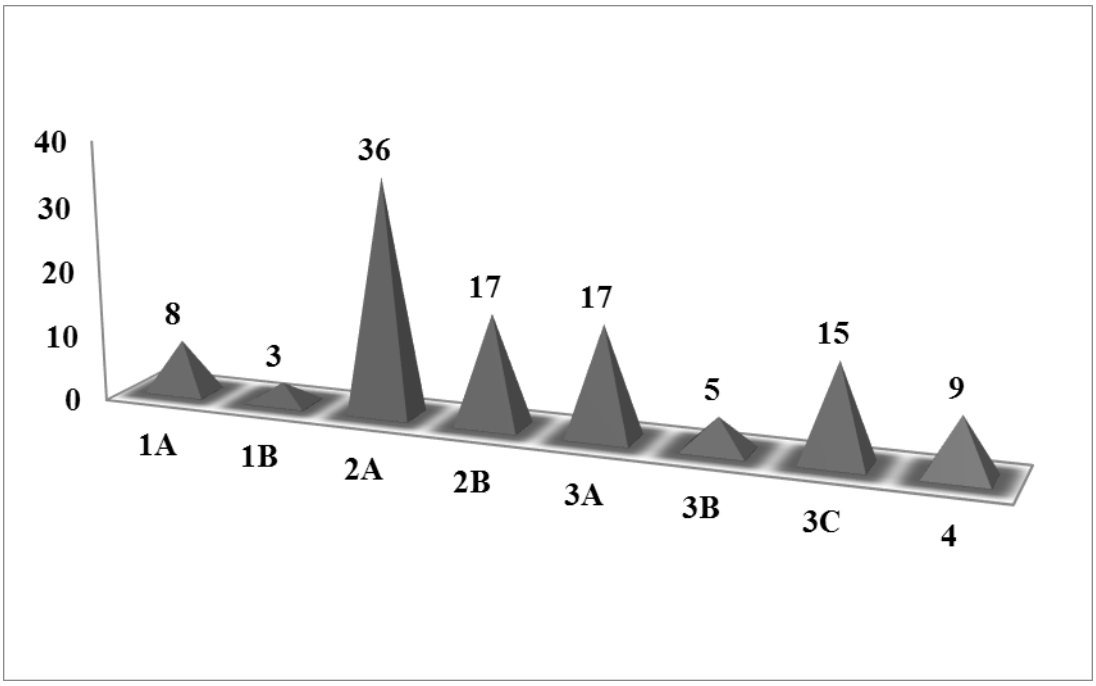
HISTOLOGICAL FEATURE WISE DISTRIBUTION:



S. No	TYPE OF SURGERY	TNBC patients	Percentage
1.	Invasive Ductal Carcinoma	96	87.27%
2.	Invasive Lobular Carcinoma	11	10%
3.	Mixed	3	2.72%

From histological feature wise distribution majority of the patients were diagnosed with Invasive Ductal Carcinoma n=96 (87.27%) followed by Invasive lobular Carcinoma n=11 (10%) and Mixed type n=3 (2.72%).

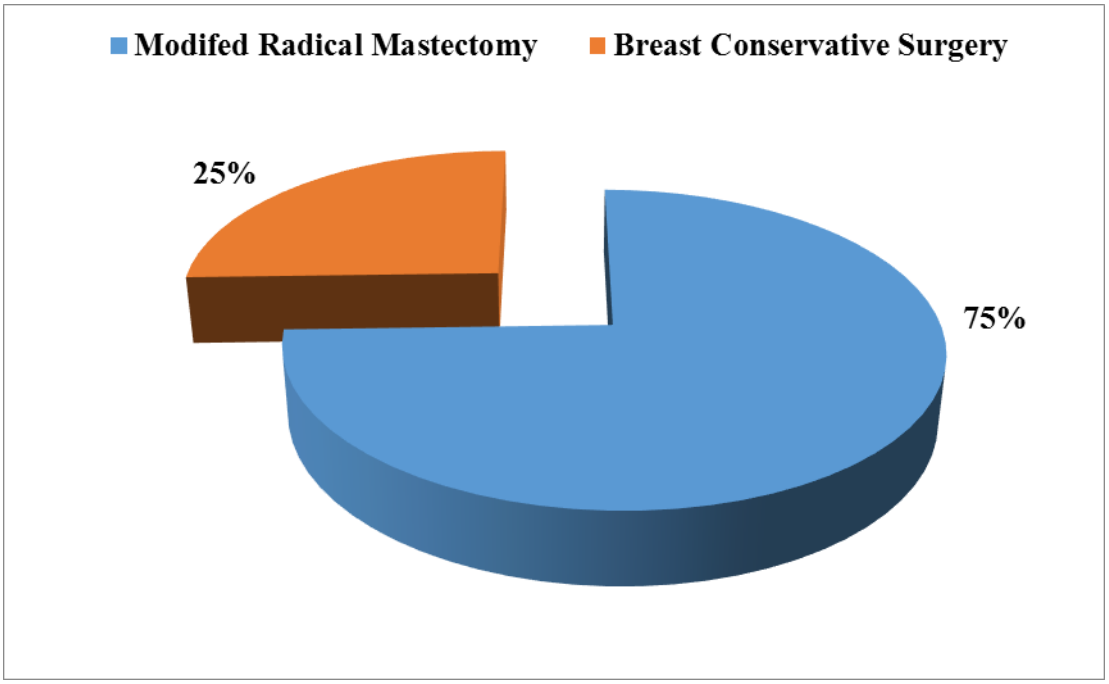
STAGE GROUP WISE DISTRIBUTION:



S. No	Stage Group	TNBC patients	Percentage
1.	1A	8	7.27%
2.	1B	3	2.27%
3.	2A	36	32.72%
4.	2B	17	15.54%
5.	3A	17	15.45%
6.	3B	5	4.54%
7.	3C	15	13.63%
8.	4	9	8.18%

From stage group wise distribution majority of people are in 2A stage n=36 (32.72%) followed by 2B stage n=17 (15.54%) similarly for 3A stage n=17 (15.54%), at 3C stage n=15 (13.63%), at stage 4, n=9 (8.18%), at stage 1A n=8 (7.27%), at 3B stage n=5 (4.54%) and least count of patients are in 1B stage n=3 (2.27%).

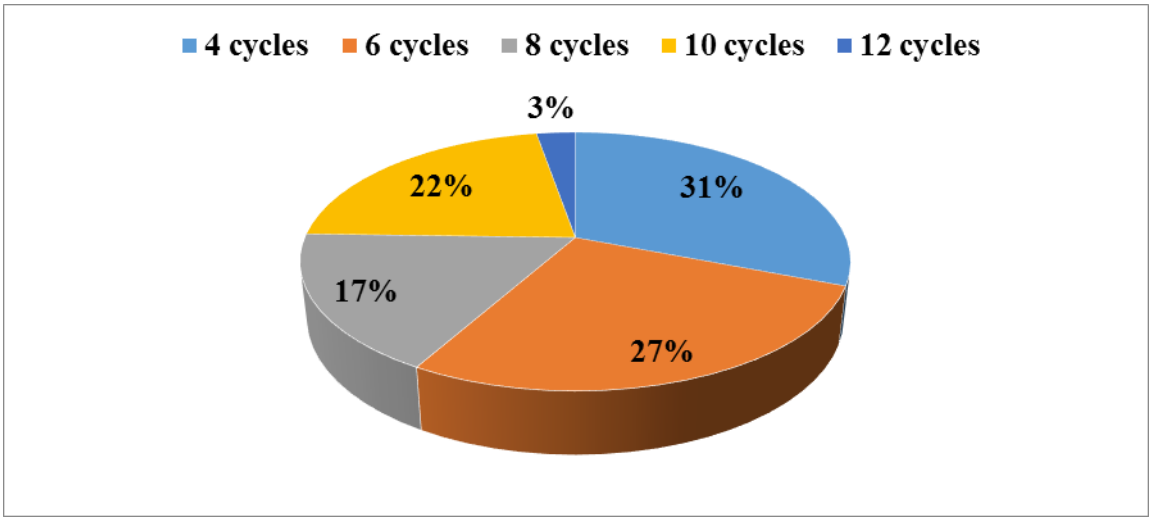
TYPE OF SURGERY PERFORMED WISE DISTRIBUTION:



S. No	Type of Surgery	TNBC Patients	Percentage
1.	Modified Radical Mastectomy	82	74.54%
2.	Breast Conservative Surgery	28	25.45%

Type of Surgery performed to the patient wise distribution shows, many of the people have undergone modified radical mastectomy n=82 (74.54%) and others with breast conservative surgery n=28(25.45%).

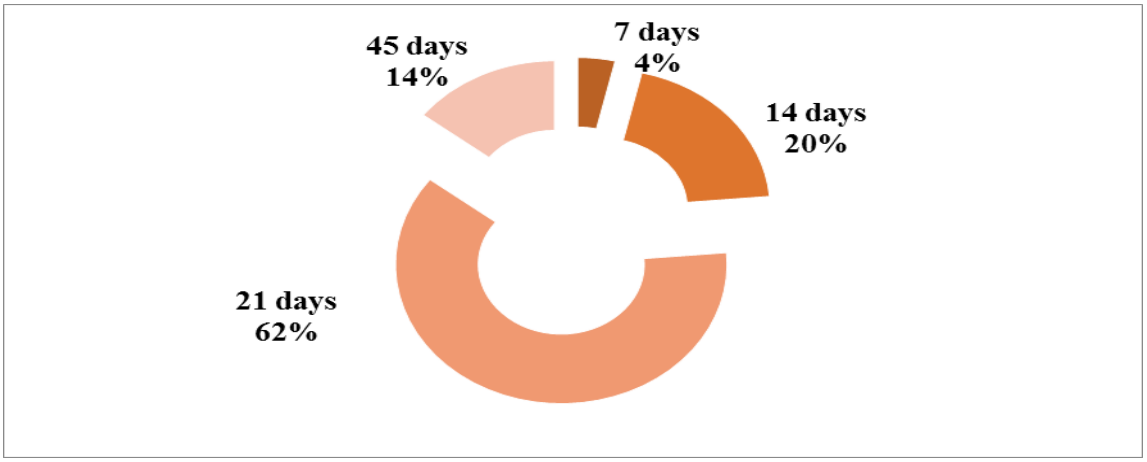
DISTRIBUTION OF NUMBER OF CHEMOTHERAPY CYCLES ADMINISTRED TO THE PATIENTS:



S. No	Number of Chemotherapy Cycles	TNBC patients	Percentage
1.	4 cycles	34	30.90%
2.	6 cycles	30	27.27%
3.	8 cycles	19	17.27%
4.	10 cycles	24	21.81%
5.	12 cycles	3	2.72%

Distribution of number of chemotherapy cycles administered to the patient shows most of the people administered with 4 cycles n=34 (30.90%) followed by n= 30 (27.27%) of 6 cycles, n=24 (21.81%) of 10 cycles, n=19 (17.27%) of 8 cycles and n= 3 (2.72%) for 12 cycles.

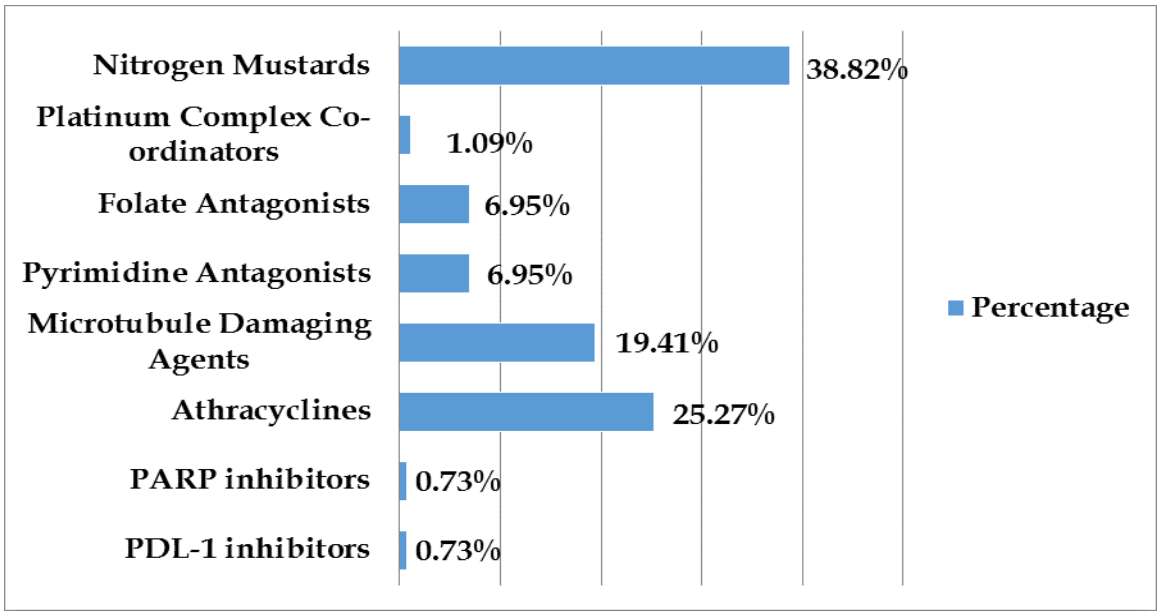
DISTRIBUTION OF NUMBER OF RADIATION THERAPY DAYS USED TO TREAT THE PATIENTS:



S. No	Number of Radiation Days	TNBC patients	Percentage
1.	7 days	4	3.63%
2.	14 days	22	20%
3.	21 days	68	61.81%
4.	45 days	16	14.54%

The distribution of number of radiation therapy days used to treat the patient shows, the majority of people have undergone with 21 days radiation n=68 (61.81%) followed by n=22 (20%) of 14days radiation, n=16 (14.54%) of 45days radiation and n=4 (3.63%) of 7 days radiation.

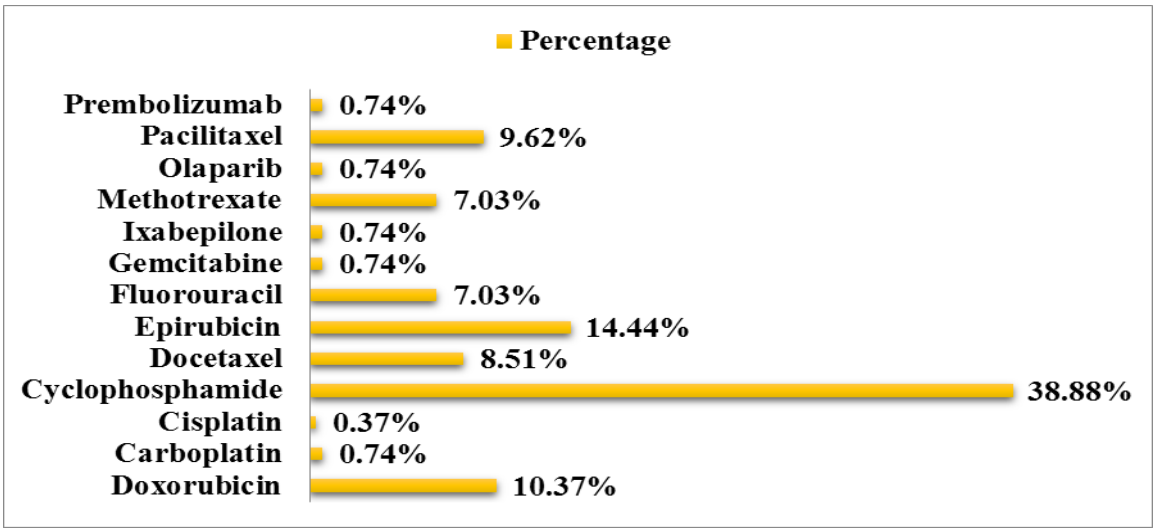
DISTRIBUTION OF CHEMOTHERAPY DRUG CLASS PRESCRIBED:



S. No	Class of Chemotherapy Drugs Prescribed	TNBC Patients	Percentage
1.	PDL-1 inhibitors	2	0.73%
2.	PARP inhibitors	2	0.73%
3.	Anthracyclines	69	25.27%
4.	Microtubule Damaging Agents	53	19.41%
5.	Pyrimidine Antagonists	19	6.95%
6.	Folate Antagonists	19	6.95%
7.	Platinum Complex coordinators	3	1.09%
8.	Nitrogen Mustards	106	38.82%

From the analysed data of class of chemotherapy drugs prescribed shows most prescribed class of drugs are Nitrogen mustards n=106 (38.82%) followed by Anthracyclines n=69 (25.27%), microtubule damaging agents n=53 (19.41%), for pyrimidine antagonists n=19 (6.95%) and similarly folate antagonists n=19 (6.95%), for platinum complex co-ordinators n=3 (1.09%), for PDL-1 inhibitors n=2 (0.73%) and similarly for PARP inhibitors n=2 (0.73%).

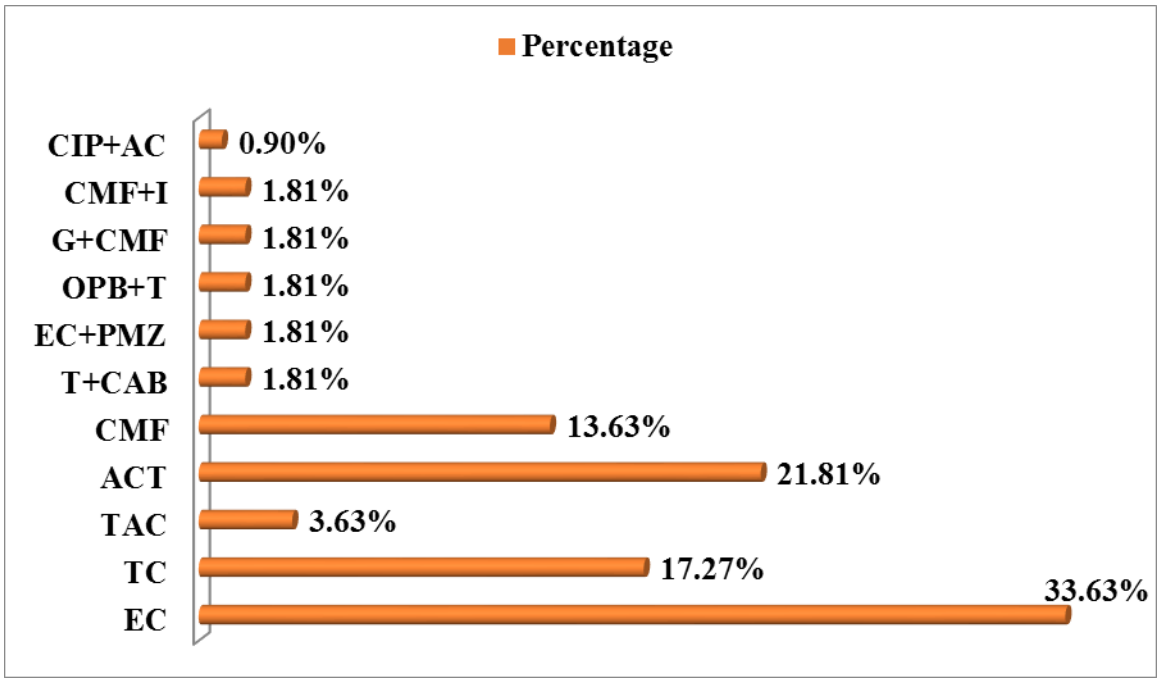
DISTRIBUTION OF CHEMOTHERAPY DRUGS PRESCRIBED:



S. No	Chemotherapy Drugs	TNBC patients	Percentage
1.	Doxorubicin	28	10.37%
2.	Carboplatin	2	0.74%
3.	Cisplatin	1	0.37%
4.	Cyclophosphamide	105	38.88%
5.	Docetaxel	23	8.51%
6.	Epirubicin	39	14.44%
7.	Fluorouracil	19	7.03%
8.	Gemcitabine	2	0.74%
9.	Ixabepilone	2	0.74%
10.	Methotrexate	19	7.03%
11.	Olaparib	2	0.74%
12.	Paclitaxel	26	9.62%
13.	Pembrolizumab	2	0.74%

From the analysed data of chemotherapy drugs prescribed shows, most prescribed chemotherapeutic agent is Cyclophosphamide n=105 (38.88%) followed by Epirubicin n=39 (14.44%), for Doxorubicin n=28 (10.37%), for Paclitaxel n=26 (9.62%), for Docetaxel n=23 (8.51%), for Fluorouracil n=19 (7.03%) similarly for Methotrexate n=19 (7.03%), for Gemcitabine n=2 (0.74%), Carboplatin n=2 (0.74%), Pembrolizumab n=2 (0.74%), Olaparib n=2 (0.74%), Ixabepilone n=2 (0.74%), and for Cisplatin n=1 (0.37%).

DISTRIBUTION COMBINATIONAL CHEMOTHERAPY DRUGS PRESCRIBED:



S. No	Combinational Chemotherapy Drugs	TNBC patients	Percentage
1.	Epirubicin+Cyclophosphamide (EC)	37	33.63%
2.	Docetaxel+Carboplatin (TC)	19	17.27%
3.	Docetaxel+Doxorubicin+Cyclophosphamide (TAC)	4	3.63%
4.	Doxorubicin+Cyclophosphamide+Paclitaxel (ACT)	24	21.81%
5.	Cyclophosphamide+Methotrexate+Fluorouracil (CMF)	15	13.63%
6.	Paclitaxel+Carboplatin (T+CAB)	2	1.81%
7.	Epirubicin+Cyclophosphamide+Prembrolizumab (EC+PMZ)	2	1.81%
8.	Olaparib+Docetaxel (OPB+T)	2	1.81%
9.	Gemcitabine+ Cyclophosphamide+Methotrexate+Fluorouracil (G+CMF)	2	1.81%
10.	Cyclophosphamide+Methotrexate+Fluorouracil+ Ixabepilone (CMF+I)	2	1.81%
11.	Cisplatin+Doxorubicin+Cyclophosphamide (CIP+AC)	1	0.90%

From the analyzed data of combinational chemotherapy drugs prescribed shows, most prescribed combinational chemotherapeutic agent is EC n= 37 (33.63%) followed by for ACT n= 24 (21.81%), for TC n=19 (17.27%), for CMF n=15 (13.63%), for TAC n=4 (3.63%), for T+CAB n=2 (1.81%), similarly for EC+PMZ n=2 (1.81%), OPB+T n=2 (1.81%), G+CMF n=2 (1.81%), CMF+I n=2 (1.81%) and for CIP+AC n=1 (0.90%).

CHI-SQUARE STATISTICAL ANALYSIS FOR TREATMENT AND WOMEN PRONE TO TRIPLE NEGATIVE BREAST CANCER

S. No	Parameter	Cramer's V correlation Value	Strength of Relation ship	Significance (2 tailed)
1.	Age vs. Menopause	0.744	Strong Relation ship	**(0.001) S***
2.	Age vs. Group stage	0.636	Strong Relation ship	**(0.029) S***
3.	Breast feeding vs. Oral Contraceptives	0.741	Strong Relation ship	**(0.000) S***
4.	Group stage vs. Chemotherapy Drugs	0.540	Strong Relation ship	**(0.000) S***
5.	Group stage vs. Radiation Days	0.315	Moderate Relation ship	**(0.049) S***
6.	Chemotherapy Cycles vs. Radiation Days	0.244	Weak Relation Ship	**(0.073) S***
7.	Group stage vs. Oral Contraceptives	0.733	Strong Relation ship	**(0.000) S***
8.	Group stage vs. Breast feeding	0.715	Strong Relation ship	**(0.000) S***
9.	Group stage vs. Marital status	0.722	Strong Relation ship	**(0.000) S***
10.	Other Co-morbidities vs. Oral Contraceptives	0.804	Very Strong Relation ship	**(0.000) S***

At 95% confidence interval '**P' value <0.005** then it is considered to be **significant** and **p value >0.005** is considered to be **not significant**.

CRAMER'S V CORRELATION VALUES:

Correlation value	Verbal designation strength of Relationship
0	No relation ship
0.01-0.1	Very Weak
0.11-0.25	Weak
0.26-0.50	Moderate
0.51-0.75	Strong
0.76-0.99	Very Strong
1	Perfect Association

CONCLUSION:

TNBC is an aggressive and typical type of Breast cancer and response to chemotherapy is still under development. In our study most of the TNBC diagnosed patients are with early menarche status, not attained menopause and with irregular menstrual history. So, we conclude that patients presenting with these characteristics are more susceptible to TNBC.

Patients who had late child birth (above 30 years of their age) and patients who have not given birth to children and more than 50% in our study. Subjects in our study have not given breast feeding to their off springs. So, we conclude that these patients may have more exposure to TNBC.

Women of First and Second-degree relatives of cancers have a chance for TNBC occurrence. So, having a family history is warning signal to healthy individuals, and to prevent further consequences, its better to maintain healthy life style. In our study approximately 63% of patients have used hormonal contraceptives and these patients may have a greater chance of TNBC occurrence. Invasive Ductal Carcinoma is the most presenting Histological feature. Many of the patients diagnosed at stages 2A, 2B and 3A of their disease progression.

Majorly NITROGEN MUSTARDS in 106 patients, ANTHRACYCLINES in 69 patients and MICRO TUBULE DAMAGING AGENTS in 53 patients are the most preferred class of drugs prescribed and further particular chemotherapy drugs like CYCLOPHOSPHAMIDE in 105 patients, EPIRUBICIN in 39 patients, DOXORUBICIN in 28 patients, DOCETAXEL in 23 patients and PACILITAXEL in 26 patients are commonly administered drugs and most

preferred class of chemotherapy drugs are EPIRUBICIN+ CYCLOPHOSPHAMIDE (EC) in 37 patients and Doxorubicin+Cyclophosphamide+Paclitaxel (ACT) in 24 patients are prescribed.

In our study population, most of the people have undergone 4 chemotherapy cycles (30.90%), and 6 cycles (27.27%) and 61.81% of study population are prescribed with 21days of radiation therapy.

The conclusion against prevailing of TNBC (an alarming disease) across the globe is to conduct screening and awareness programs in urban and remote areas around the globe. So, most probably there will be chances of diagnosing the disease in the primary stages and treatment will be more effective, proportional to rise in cure and survival rates of the victims which directly decrease the mortality rate. By encouraging and giving preference to conduct more clinical trials for various newly extracted and designed compounds we can hope for a faster heal against the deadly disease.

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We believe that some supernatural power would be guiding us and that's none other than GOD, who keeps on paving us a better path. **This research is dedicated to our parents for their endless love and surplus motivation.**

EXPECTED BENEFITS OF THE STUDY: The core expectation is to report the most commonly prescribed class of chemotherapy drugs, particular chemotherapy drug and the most preferred combinational chemotherapy agents in various stages of triple negative breast cancer including demonstration of women prone to triple negative breast cancer.

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