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Pharmacoepidemiological Trend and Drug Utilization Review of Breast Cancer at Three Different Tertiary Care Hospitals

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Abstract
Aim
In this study, we have aimed to evaluate the Pharmacoepidemiological trends and Drug utilization review of Breast cancer in three different hospitals in Hyderabad. This study includes the reports of favorable and unfavorable outcomes of breast cancer, extent of usage and appropriateness of chemotherapeutic drugs with respect to diagnosis and regimen.
Method
It is an observational and a qualitative study in which the medical records of the both female and male patients with breast cancer were retrospectively reviewed who have consulted the medical oncology department of the three hospitals between 2010 and 2014. There were 2893 total admissions at all the three hospitals where the study has been carried out, of which 2770 patients met the inclusion criteria and were recorded, reviewed and analyzed for the treatment outcomes.
Result
The Adriamycin-Cyclophosphamide (describe briefly to this biochemical reagent) with the combination of Tamoxifen regimen is found to be more effective when compared to other chemotherapeutic regimens. The prevalence rate is increasing 3% in 1, 00,000 population every year. The incidence rate of breast cancer is more in the tumor size 2-5 cm than in tumor size of <2cm and > 5cm and the therapeutic regimen used is Adriamycin - Cyclophosphamide with the combination of Tamoxifen. The percentages of patients with treatment outcomes assessed in the study are as follows: cured 51.88%, treatment completed 43.27%, Discontinue 1.68%, Failure 2.95%, Death 0.21%. The usage of chemotherapeutic agents is found to be more than that of hormonal regimens.

Keywords: Breast cancer, Pharmacoepidemiological trend, chemotherapeutic agents,

1. Introduction
Incidence of breast cancer in India is on rise and is the second most cause of death in females in southern India (9). This study was aimed to assess the effect of different regimens and other variables on the outcome and to determine the extent of usage of chemotherapeutic drugs for breast cancer as well as to study the Pharmacoepidemiological trends in Breast Cancer in the Medical Oncology unit of three different hospitals in Hyderabad which are providing specialized health care services to all strata of people covering the state of Andhra Pradesh, and nearby states like Tamil Nadu, Karnataka, Madhya Pradesh, Maharashtra and Kerala (3). The data was collected using a questionnaire which had a provision to collect information like the demographic details of the patient, chemotherapeutic drugs and the hormone therapy prescribed, the dose, duration, route of administration and also comprised of provisional diagnosis, laboratory tests, 2-D echo, mammography and present complaints and history of patients. In this study, the demographic data of the patients with breast cancer was collected from the year 2010-2014 so as to find out the Pharmacoepidemiological trends in breast cancer. There were 2893 total admissions at all the three hospitals, out of which 2770 patients met the inclusion criteria and were included in the study. The data was analyzed for the Pharmacoepidemiological trends and appropriateness of utilization of chemotherapeutics and hormonal therapy using standard references like hand book of American System of Hospital Pharmacy (ASHP).

Materials and Methods
It is an observational and a qualitative study in which the medical records of the both female and male patients with breast cancer were retrospectively reviewed who have consulted the medical oncology department of three hospitals between 2010 and 2014. We have carried out a preliminary literature survey in order to support our study and this has been continued

throughout the study period to update the knowledge about the current topic. WHO web service; PUBMED and MEDSCAPE were used in search of journals. All the inpatients with breast cancer between the age group 20 and 85 were included and patients who have renal failure and liver failure, alcohol consumers as well as nicotine users (cigarette smokers) were excluded from the study. The patients prescribed with chemotherapeutic drugs were identified and a total of 2770 patients who met the inclusion criteria were selected for the study based upon the data collected from the patient's case sheets using a patient data collection form. Ethical committee clearance from Ethical committee, of all the three hospitals has been taken. The questionnaire had the provision to collect all the details of the patient, including demographic details, type of cancer, choice of chemotherapeutic drug, type of treatment (prophylactic/therapeutic), mode of treatment (empirical/evidence based), name of chemotherapeutic drug prescribed, its dose, route of admission, duration etc. The patient data collection is shown in Annexure – 1. As a clinical pharmacist, we regularly visited the inpatient wards and collected all the details and recorded in the questionnaire. The data was then analyzed to evaluate the epidemiological trends of Breast Cancer, utilization patterns of chemotherapeutic drugs at all the three hospitals using the standard references. Results were recorded and analyzed using a database system. Microsoft Excel was used to produce related figures. Drug use was evaluated for appropriateness based on whether ASCO guidelines were adopted.

Results and Discussion

Table 1: Age wise distribution

S. no	Age Groups	No. of Patients	Percentage
1	20 – 30	230	8.30
2	30 – 40	474	17.12
3	40 – 50	572	20.65
4	50 – 60	582	21.02
5	60 – 70	486	17.54
6	70 – 80	354	12.78
7	80 - 90	72	2.59

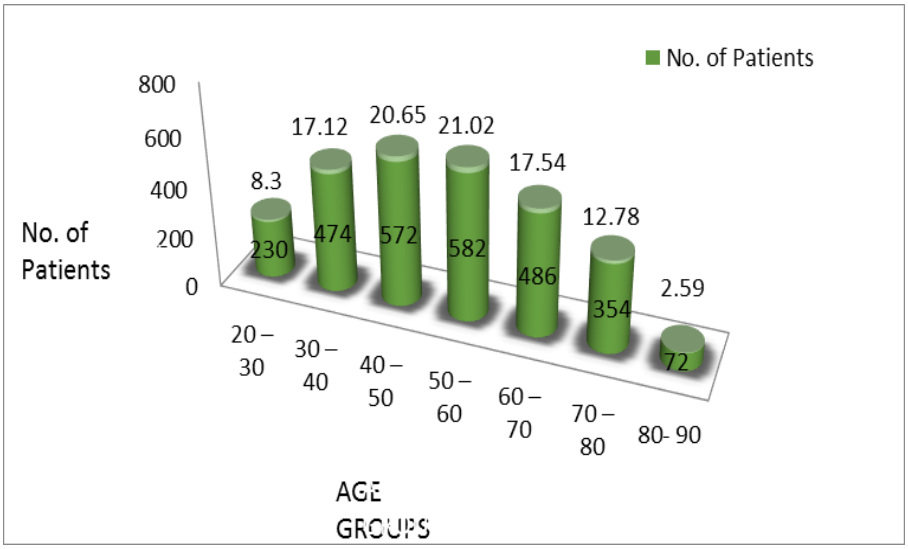


Fig 1: Age wise distribution

Table 2: Sex Wise Distribution

S. no	Sex	No. of patients	Percentage
1	Male	46	1.66
2.	Female	2724	98.34

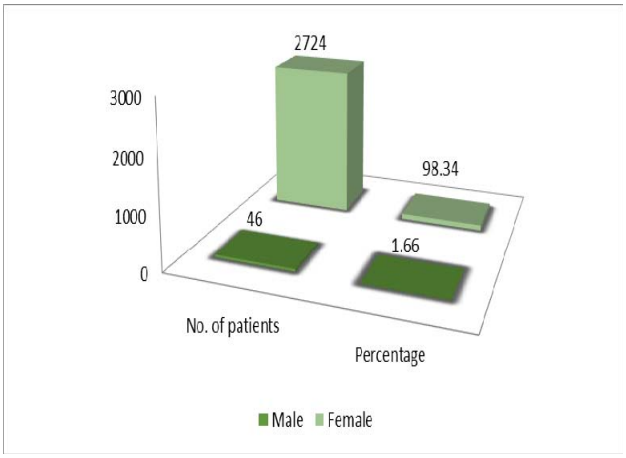


Fig 2: Sex Wise Distribution

Table 3: Demographic Characteristics of Breast Cancer (2010-2014)

Year	No. of Patients	Percentage
2007	396	14.30
2008	473	17.088
2009	793	17.80
2010	770	27.79
2011	638	23.03

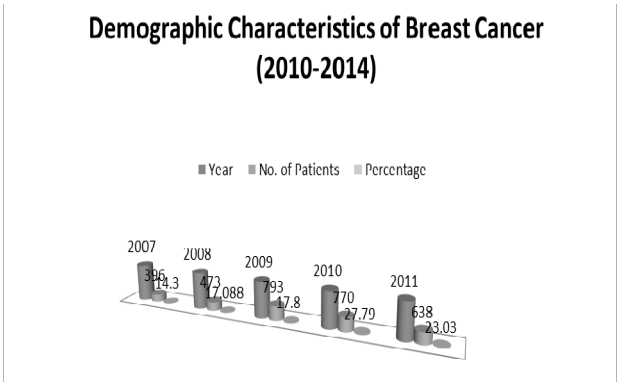


Fig 3: Demographic Characteristics of Breast Cancer (2010-2014)

Table 4: Demographic Characteristic of Breast Cancer (2010-2014)

Year (2010-2014)	Type of Patient		Type of Breast cancer			Total no. of Patients	Percentage
	Male	Female	Invasive Breast Cancer	Non Invasive Breast Cancer	Metastatic Breast Cancer		
Hospital 1/ Sample 1	9	651	201	412	69	660	23.82
Hospital 2/ Sample 2	2	202	62	130	22	204	7.32
Hospital3/ Sample 3	35	1871	547	1152	172	1906	68.87

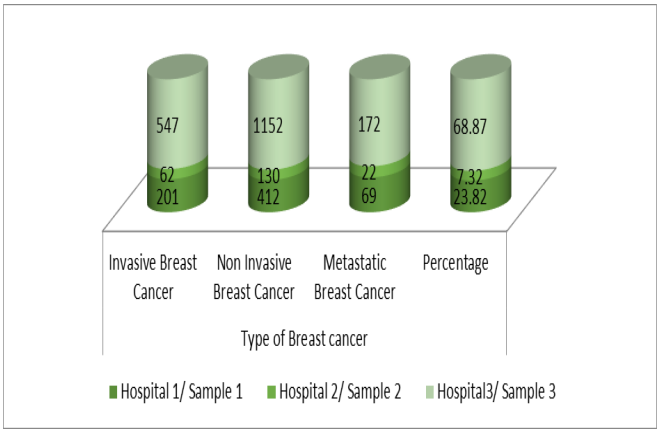


Fig 4: Demographic Characteristic of Breast Cancer (2010-2014)

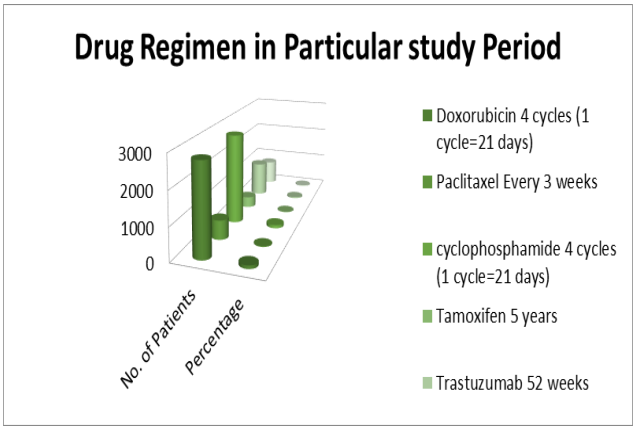


Fig 5: Drug Regimen in Particular study Period

Table 5: Drug Regimen in Particular study Period

S. No.	Chemotherapeutic Drug	ROA	Duration/ Cycles	No. of Patients	Percentage
1	Doxorubicin	I.V	4 cycles (1 cycle=21 days)	2770	100
		Oral	_	_	_
2	Paclitaxel	I.V	Every 3 weeks	588	21.22
		Oral	_	_	_
3	cyclophosphamide	I.V	4 cycles (1 cycle=21 days)	2770	100
		Oral	_	_	_
4.	Tamoxifen	I.V	_	335	12.09
		Oral	5 years	_	_
5.	Trastuzumab	I.V	52 weeks	_	_
		Oral	_	1078	38.91
6.	Docetaxel	I.V	Every 3 weeks	769	27.76
		Oral			

Table 6: Dosage Regimen used in Different conditions of Breast Cancer

S. No.	ER	PR	HER-2	Dosage Regimen	No. of Patients	Percentage
1	-	-	-	AC	923	33.32
2	-	-	+	AC + Trastuzumab	769	27.76
3	+	+	+	AC + Tamoxifen	461	16.64
4	+	+	-	AC + Tamoxifen	311	11.23
5	+	-	-	AC + Tamoxifen	306	11.05

Table 7: Category wise treatment outcomes (2010-2014)

Year	Treatment Outcome		Regimen			
			AC(D)	AC(P)	AC+ Tamoxifen	AC+ Trastuzumab
2010-2014	Favorable	Cured	139	214	757	341
		Treatment Completed	178	351	265	398
2010-2014	Unfavorable	Treatment failure	11	16	42	19
		Discontinue	6	7	12	8
		Death	1	-	2	3

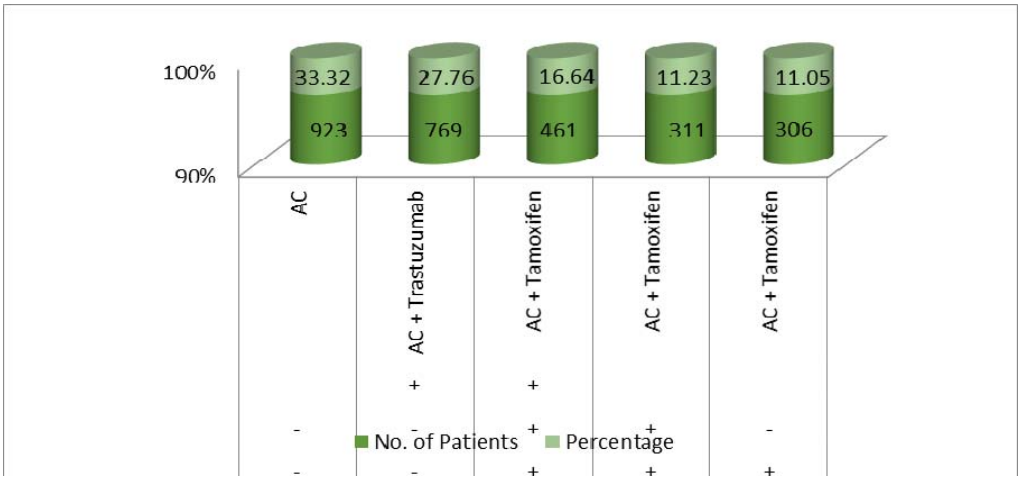
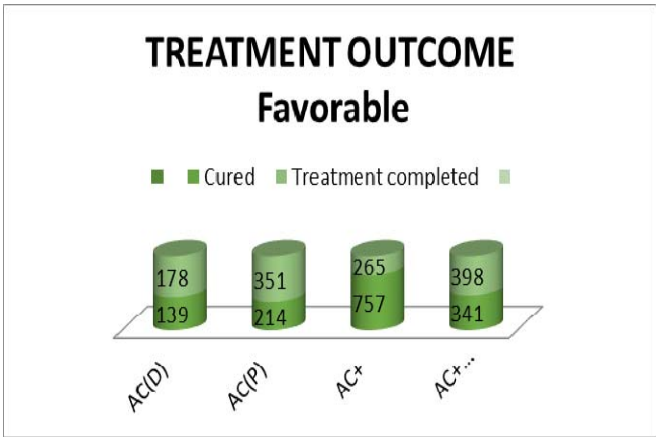


Fig 6: Dosage Regimen used in Different conditions of Breast Cancer



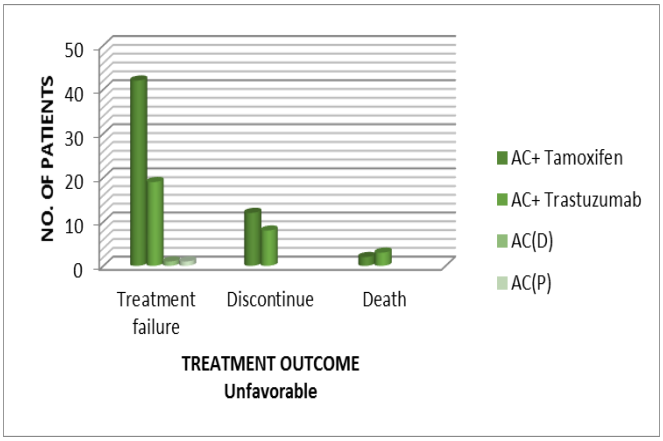


Fig 7: Category wise treatment outcomes (2010-2014)

Fig 7: Category wise treatment outcomes (2010-2014)

Table 8: Treatment outcome of different disease classes of breast cancer (2010-2014)

Year	Treatment Outcome		Types of Breast cancer				
			Invasive breast cancer		Non invasive breast cancer		Metastatic breast cancer
			Ductal	Lobular	Ductal	Lobular	
2010--2014	Favorable	Cured	212	134	745	335	11
		Treatment Completed	340	172	264	392	30
2010-2014	Unfavorable	Treatment Failure	8	14	40	16	4
		Discontinue	4	5	11	6	21
		Death	-	-	1	3	2

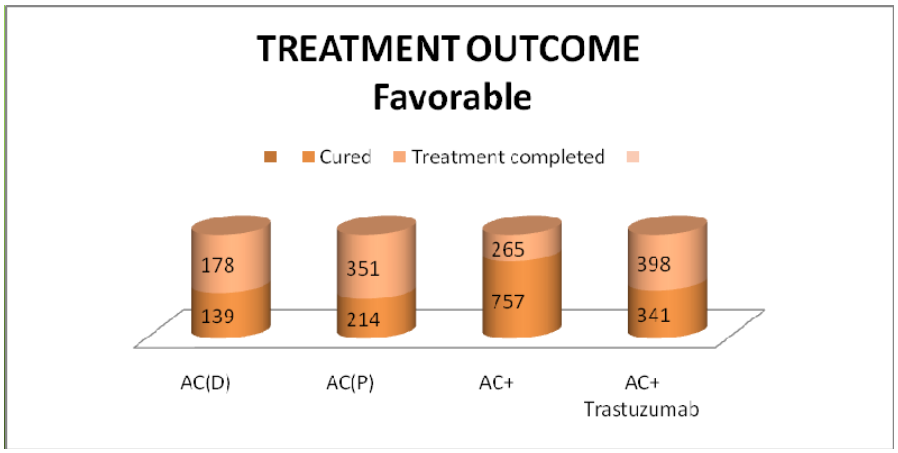


Fig 8: Treatment outcome favorable (2010-2014)

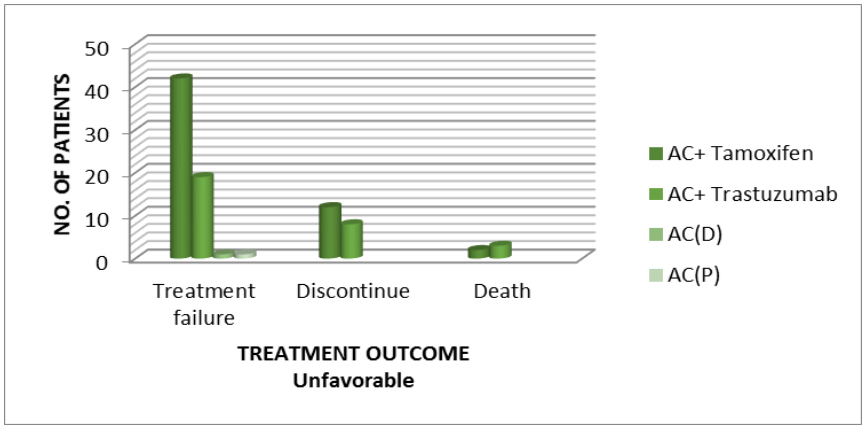


Fig 8: Treatment outcome unfavourable (2010-2014)

Table 9: Details of lymph node status with respect to tumor size and regimen

No. of Patients With Respect To Tumor size and Regimen												
Lymph Node Status	<2cm				2-5cm				>5cm			
	AC(D)	AC(P)	AC+Tam	AC+trast	AC(D)	AC(P)	AC+Tam	AC+trast	AC(D)	AC(P)	AC+Tam	AC+trast
Negative	55	98	176	127	165	290	530	377	54	95	177	127
1-3 Positive	8	14	23	19	21	45	65	55	7	17	28	16
≥4 Positive	5	7	15	8	17	19	52	28	5	4	9	12

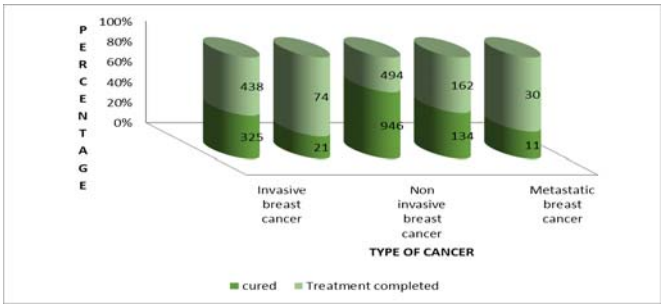


Fig 9: Details of lymph node status with respect to tumor size and regimen

Discussion

The hormone therapy prescribed, the dose, duration, route of This study was aimed to assess the effect of different regimens and other variables on the outcome and to determine the extent of usage of chemotherapeutic drugs for breast cancer as well as to study the epidemiological trend in Breast Cancer in the oncology unit of three different hospitals in Hyderabad. The data was collected using a questionnaire which had a provision to collect information like the demographic details of the patient, chemotherapeutic drugs and administration and also comprised of provisional diagnosis, laboratory tests, 2-D echo, mammography, etc and present complaints and history of patients. The data was analyzed for appropriateness of utilization of chemotherapeutics and hormonal therapy using standard references like hand book of American System of Hospital Pharmacy (ASHP).

The age of the patients who were included into the study ranged from 20 – 90 years and the maximum patients who were admitted to the hospital were of the age group of 50-60 years (Table no.). More females were admitted to the hospital when compared to males (Table no. 3).

In this study, the demographic data of breast cancer was collected from the year 2010-2014 so as find out the epidemiological trends in breast cancer. There were 2893 total admissions at all the three hospitals where the study has been carried out of which 2770 patients met the inclusion criteria and were included in the study. The study revealed that number of patients diagnosed from breast cancer was high in the year 2014. Trend analysis of breast cancer incidence data for the period 2010-2014 showed that the overall rates of breast cancer is increasing with the greater increase among females (Table no.).

From hospital–1, 660 patients met the inclusion criteria out of 684 patients. From hospital-2, 204 patients met the inclusion criteria out of 236 patients and from hospital-3, 1906 patients met the inclusion criteria out of 1972 patients and were included for the study. Number of patients diagnosed as invasive breast cancer from all the three hospitals were 810, those diagnosed as noninvasive breast cancer were 1694 and those with metastatic breast cancer were263 (Table no.).

The study revealed that Doxorubicin and Cyclophosphamide were the most widely prescribed chemotherapeutic drugs for 100% of the patients because of their anthracycline antibiotic activity and anti-tumor action respectively. These drugs were prescribed with the combination of other chemotherapeutics such as Paclitaxel which is a mitotic inhibitor, used for breast carcinoma for 21.22% of the total patients and Docetaxel, an anti-neoplastic agent for 27.76% of the total patients(Table no. 6).

Hormone therapy was recommended for the patients who were showing Estrogen and Progesterone positive. Estrogen was positive in 38.92% of the total patients and progesterone was positive in 27.87% of the total patients for whom Tamoxifen, an Estrogen inhibitor was been prescribed. For those who were expressing HER-2 positive (44.40%) Trastuzumab was been prescribed. And those who fall into the category of triple negative are closely observed as the cancer in those patients is rapidly growing and there might be chances of recurrence. 33.32% of patients were found to be triple negative for whom, Hormone therapy cannot be prescribed and they were prescribed only with Chemotherapeutic drugs and are been

closely observed and monitored as there are chances for recurrence of the breast cancer (Table no. 7 and Fig no. 7).

Among 2770 patients, who were treated with Chemotherapeutics and Hormone therapy during the study period, it revealed that 95.42% of the total patients have come out with favorable treatment outcome with respect to the dosage regimen whereas 4.58% of the patients have shown unfavorable treatment outcome of which 3.18% treatment have failed to show the therapeutic outcome, while 1.91% of the patients have discontinued the prescribed regimen, the rest of the 0.22% is recorded as the death rate (Table no. 8 and Fig no. 8).

Among 2770 patients, the treatment outcome in the patients who were treated with Chemotherapeutics and Hormone therapy during the study period with respect to the type of breast cancer, 32.08% fall under the provisional diagnosis of invasive breast cancer of which 30.97% of them have shown a favorable outcome, in whom 12.49% the cancer is almost cured and in 18.48% of the patients, chemotherapy treatment is completed. And 1.12% have shown unfavorable treatment outcome, of which treatment has failed in 0.79% while 0.32% have discontinued the treatment (Table no. 9 and Fig no. 9).

65.47% fall under the provisional diagnosis of non-invasive breast cancer of which 62.7% of them have shown a favorable outcome, in whom 39% the cancer is almost cured and in 23.7% of the patients, chemotherapy treatment is completed. And 2.77% have shown unfavorable treatment outcome, of which treatment has failed in 2.02% while 0.61% have discontinued the treatment and 0.14% are recorded to be dead (Table no. 9and Fig no 9).(Correct Capital of n)

2.45% fall under the provisional diagnosis of metastatic breast cancer of which 1.48% of them have shown a favorable outcome, in whom 0.39% the cancer is almost cured and in 1.09% of the patients, chemotherapy treatment is completed. And 0.97% have shown unfavorable treatment outcome, of which treatment has failed in 0.14% while 0.76% have discontinued the treatment and 0.07% are recorded to be dead (Table no. 9).

Tumor size and the presence and number of involved lymph nodes are established primary factors in assessing the risk for breast cancer ecurrence and subsequent metastatic disease. Hence analysis has been done on it and the study revealed that 16.46% of the total patients whose tumor size is <2cm, 49.17% of them whose tumor size is 2-5cm and 16.4% whose tumor size is > 5cm have a negative lymph node status with respect to the regimen. 2.31% of the total patients whose tumor size is <2cm, 6.71% of them whose tumor size is 2-5cm and 2.45% whose tumor size is > 5cm have 1-3 positive lymph node status with respect to the regimen. 1.30% of the total patients whose tumor size is <2cm, 4.19% of them whose tumor size is 2-5cm and 1.08% whose tumor size is > 5cm have 1-3 positive lymph node status with respect to the regimen.

Conclusion

In this study, we found the diagnosis of more number of noninvasive breast cancer than the invasive and metastatic cancer.

The usage of chemotherapeutic agents is more than hormonal regimens.

The Adriamycin-Cyclophosphamide with the combination of tamoxifen regimen is more effective when compared to other chemotherapeutic regimens.

The prevalence rate is increasing 3% in 1,00,000 population every year.

The incidence rate of breast cancer is more in the tumour size 2-5 cm than in tumour size of <2cm and >5cm and the therapeutic regimen used is Adriamycin - Cyclophosphamide with the combination of Tamoxifen.

There were 2893 total admissions at all the three hospitals where the study has been carried out, of which 2770 patients met the inclusion criteria and were analysed for the treatment outcomes. The percentages of patients with treatment outcomes assessed in the study are as follows: cured 51.88%, treatment completed 43.27%, Discontinue 1.68%, Failure 2.95%, Death 0.21%, This study finding suggests that males/females had higher risk of unfavourable treatment outcomes than the females/males.

Future Scope

- The future research is needed to study in large cohort population.
- It is recommended to collect the sample data more than 5 Hospitals in different regions for ameliorate Pharmacoepidemiology studies. In addition, future research is needed to use other methods to analyse the study.

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