

Effects of chemotherapy in cancer patients

Chole Laxmi Jalinadar, Guide and Principal Dr.Hingne L.D.

Aditya Pharmacy College, Beed

INTRODUCTION TO CANCER:

Cancer causes death worldwide with an estimated 14.1 million new cases and 8.2 million cancer related deaths in 2012 compared with 12.7 million. According to WHO cancer cases may increase by more than 70%.¹ Cancer mortality mainly observes in the patients suffering from breast cancer and cervical cancer. Breast cancer has increased by more than 20% since 2008 estimates, while mortality has increased by 14%. Breast cancer is majorly diagnosed cancer among women in 140 countries out of total 184 countries. Cervical cancer is the 4th most commonly diagnosed cancer in women worldwide.

Cancer is curable. But the mortality rate of patients of breast cancer is very high. According to World Health Organization (WHO) breast cancer is commonly found in the cancer and adversely affecting to the millions of women over the world. But after 1990 due to screening, early detection, awareness and improved treatment the mortality rate is decreasing day by day.² The main reasons of breast cancer are age, sex of the patient, breast conditions of the patient, alcohol consumption, obesity, family genetic history etc. It is estimated that 1.67 million of new cancer cases are diagnosed in 2012 and 1.38 million new cancer cases were detected in 2008. In the developing countries and developing areas, the cases of breast cancer are most frequent. In the developed countries, breast cancer ranks 2nd after the lungs cancer even it is most frequent death cause in the less developed regions. In the less developed countries approximately 883000 new cases were estimated in 2012.² It shows the cases of breast cancer are more as compared to 2008. The rate of incidence changes from 19.3 per 100,000 women in western Europe, 27 per 100,000 in middle Africa and eastern Asia to 96 in western Europe and are high in developed regions of the world and low in the most of the developing regions.^{3,4,5}

TYPES OF CANCER:

BREAST CANCER:

Breast cancer is the one of the leading causes of cancer deaths among women. There are number of different types of breast cancer. The most common form of breast cancer is ductal carcinoma. The development of breast cancer is a multi-step process involving many cell types, and its prevention remains challenging in the world. Early diagnosis of breast cancer is one of the best approaches to avoid this disease. In some developed countries, the 5-year relative survival rate of breast cancer patients is above 80% due to early prevention. In the recent decade, great progress understanding of breast cancer as well as in the development of preventative methods. The pathogenesis and tumor drug-resistant mechanisms are revealed by discovering breast cancer stem cells, and many genes are found related to breast cancer. Currently, people have more drug options for the chemo prevention of breast cancer, while biological prevention has been recently developed to improve patients' quality of life.³

Pathogenesis:

Breast tumors usually start from the ductal hyperproliferation, and then develop into benign tumors or even metastatic carcinomas after constantly stimulation by various carcinogenic factors. Tumor microenvironments such as the stromal influences or macrophages play vital roles in breast cancer initiation and progression. The mammary gland of rats could be induced to neoplasm when only the stroma was exposed to carcinogens, not the extracellular matrix or the epithelium.^{13,14} Macrophages can generate a mutagenic inflammatory microenvironment, which can promote angiogenesis and enable cancer cells to escape immune rejection.^{15,16}

LUNG CANCER:

Lung cancer remains the leading cause of cancer mortality in men and women in the and worldwide. About 90% of lung cancer cases are caused by smoking and the use of tobacco. However, other factors such as radon gas, asbestos, air pollution, and chronic infections can contribute to lung cancer. In addition, multiple inherited and acquired mechanisms of susceptibility to lung cancer have been proposed. Lung cancer is divided into two broad histological classes, which grow and spread differently: small-cell lung carcinomas (SCLC) and non-small cell lung carcinomas (NSCLC). Treatment for lung cancer mainly include chemotherapy surgery, radiation therapy, and targeted therapy. Therapeutic-modalities recommendations depend on several factors, including the type and stage of cancer. Despite the improvements in diagnosis and therapy made during the past 25 years, the prognosis for patients with lung cancer is still unsatisfactory. The responses to current standard therapies are poor except for the most localized cancers. However, a better understanding of the biology pertinent to these challenging malignancies, might lead to the development of more efficacious and perhaps more specific drugs.

SARCOMA:

Sarcoma is a rare tumor type that occurs mostly in connective tissue. Despite its uncommon occurrence, sarcoma research has provided the means for ground breaking research that has advanced our understanding of general cancer mechanisms. It is through sarcoma research that the pioneering efforts of cancer immunotherapy were explored, that we understand the inherent genetic nature of cancer mutations, and that we appreciate the sub classification of general cancer types to make more accurate prognoses. This review explores the brief history of sarcoma research and what sarcomas can still teach us about the future of cancer research especially in regard to novel immunotherapy targets, the role of epigenetics in disease progression and chemo resistance.²⁵

In the recent 2017 cancer progress report, produced by the American Association for Cancer Research, there is reason for optimism as progress against cancer is evident. Since the 1990s, the cancer death rate among adults and children in the United States has decreased 25 and 35%, respectively. Despite these positive trends, cancer remains the second leading cause of death in the United States of America. The predictions for the future rise in new cancer cases per year is projected to be 35% more in the United States and 60% more worldwide by the year 2030. More needs to be done to accomplish the goals of the cancer moon shot initiative and win the war against cancer. Many recent discoveries in cancer therapy have come through basic science research efforts that strive to understand the mechanisms that drive cancer. Targeted therapies designed to attack the Achilles heel of specific cancers are demonstrating promising results with fewer side effects than traditional chemotherapies.^{26, 27, 28} To emphasize this point in shifting the approach to more targeted and personalized therapies, in the past 12 months the FDA has approved 16 new anticancer therapeutics, each designed and approved for a cancer with a specific molecular indication. In spite of these advances in therapeutics, there are cancer subtypes that suffer from it. Due to a lack of response to current therapies.

PROSTATE CANCER:

Prostate cancer is one of the most frequent tumours in males. Globally about 235000 new cases were estimated to occur in 1980. The cancer is particularly frequent in America, where rate in blacks are often double those in whites, and in several European countries, being rare in much of Asia. After migration to the US, Chinese and Japanese show increases.³⁰ Incidence may be distorted by inclusion of varying numbers of so-called 'latent' cancers. 'Small' latent cancers seem to be uniformly distributed respective of the incidence of the clinically manifest form. The incidence of prostate cancer seems to be increasing in most populations, particularly in Asia and Eastern Europe. General mortality follows suit. Birth cohort analysis shows that for US non-whites, cohorts born before 1896-1900 showed an increase in mortality for all age groups, but the death rates fell for cohorts born subsequently, a phenomenon also observed in Australia and England and Wales. Clinical cancer of the prostate is one of the most common tumours in males. About 235 000 newly diagnosed cases of clinical prostatic cancer were estimated to have occurred in the world in 1980, this form of malignancy thus being in fifth rank for cancer in males throughout the world and in second or third rank in the industrialized countries.³⁰

Latent cancer of the prostate:

Latent cancer is much more frequent than clinical cancer. There are several problems linked to the epidemiology of cancer of the prostate, in that this disease attacks the oldest ages, when diagnosis is frequently imprecise and when latent cancer is three to eight times more frequent than the clinical form of disease.³¹ Incidental discovery following histological examination of tissue removed during surgical intervention for adenomatous hyperplasia or at autopsy is very frequent. For example, in Malmo in Sweden, where the proportion of all dead necropsied is very high, in 1981 the age-adjusted incidence for the cancers was

OVARIAN CANCER:

Ovarian cancer (OC) is the seventh most commonly diagnosed cancer among women in the world and the tenth most common in China. Epithelial OC is the most prevalent pathologic subtype, with five major histo types that differ in risk factors, origination, pathogenesis, molecular alterations and prognosis. Genetic susceptibility is manifested by rare inherited mutations with high to moderate penetrance. Genome-wide association studies have additionally identified 29 common susceptibility alleles for OC, including 14 subtype-specific alleles. Several reproductive and hormonal factors may lower risk, including parity, oral contraceptive use, and lactation, while others such as older age at menopause and hormone replacement therapy confer increased risks. These associations differ by histo type especially for mucinous OC likely reflecting differences in etiology. Endometrioid and clear cell OC share a similar, unique pattern of associations with increased risks among women with endometriosis and decreased risks associated with tubal ligation. OC risks associated with other gynaecological conditions and procedures, such as hysterectomy to pelvic inflammatory disease, and polycystic ovarian syndrome, are less clear. Other possible risk factors include environmental and lifestyle factors such as asbestos and talc powder exposures, and cigarette smoking. The epidemiology provides clues on etiology primary prevention, early detection, and possibly even therapeutic strategies.³³

INTRAHEPATIC SPLENOSIS:

Splenosis is a common benign condition mostly occurred due to traumatic splenic rupture or splenectomy. In splenosis, splenic tissue has been transplanted automatically to a heterotopic location.³⁵ Intrahepatic splenosis is a rarely observed situation occurred after splenectomy (it is a surgical procedure to remove your spleen). It is a very rarely observed phenomenon and usually diagnosed accidentally.³⁶ This condition may cause a significant diagnostic dilemma³⁷

THYROID CANCER:

Thyroid gland is butterfly shaped gland at the base of the neck.

Thyroid Cancer Early Detection, Diagnosis, and Staging:

Early detection of cancer often allows for more treatment options. Some early cancers may have signs and symptoms that can be noticed, but that is not always the case. Staging of cancer after the diagnosis can provide important information about the serious extent of cancer in the body and it can help in anticipation response to treatment.

Signs and Symptoms of Thyroid Cancer:

Thyroid cancer can cause the following signs or symptoms:⁴¹

- A lump in the neck (sometimes they grow quickly)
- Pain in the front of the neck, sometimes going up to the ears

- Swelling in the neck
- Hoarseness or other voice changes that do not go away
- Trouble breathing
- Trouble swallowing
- A constant cough that is not due to a cold

Tests for Thyroid Cancer⁴¹

- Medical history and physical exam
- Imaging tests:
 - Ultrasound:
 - Radioiodine scan:
 - (radioiodine) therapy.
 - Chest x-ray:
 - Computed tomography (CT) scan
 - Magnetic resonance imaging (MRI) scan:
 - Positron emission tomography (PET) scan:
- Blood test

DIAGNOSIS OF CANCER:

- **Physical exam.**

Doctor can feel areas of your body for lumps that may indicate cancer. During a physical exam, your doctor may look for defects, such as changes in skin color or expansion of an organ that may indicate the existence of cancer.⁴²

- **Laboratory tests.**

Laboratory tests, such as urine and blood tests, may help your doctor identify abnormalities that can be caused by cancer. For instance, in people with leukemia, a common blood test called complete blood count may reveal an rare number or type of white blood cells.⁴²

- **Imaging tests:**

Imaging tests allow your doctor to test your bones and internal organs in a non-invasive way. Imaging tests used in diagnosing cancer may contain a computerized tomography (CT) scan, bone scan, magnetic resonance imaging (MRI), positron emission tomography (PET) scan, ultrasound and X-ray, among others.⁴²

- **Biopsy:**

- 1) During a biopsy, your doctor gathers a sample of cells for testing in the laboratory. There are several methods of collecting a sample. Which biopsy procedure is right for you depends on your type of cancer and its location. In most situations, a biopsy is the only mode to definitively diagnose cancer.⁴²
- 2) In the laboratory, doctors look at cell samples under the microscope. Normal cells look uniform, with similar sizes and orderly organization and Cancer cells look less orderly, with variable sizes and without apparent organization.⁴²
- 3) The first subject addresses the early detection and diagnosis of cancer. In this, Ghebeh and Al-Alwan. discussed the role of Cancer Stem Cells (CSCs) in the generation of immune-suppressive microenvironment that can lead to immune escape of cancer.⁴³

TREATMENT OF CANCER:

- There are a many types of cancer treatment. The types of the cancer treatment will depend on type of cancer you have and how advanced it is
- Some people with cancer will have one treatment but most people have a combination of treatment such as surgery with chemotherapy and radiation therapy.

- **Gene Therapy**

Usually, tumour cells that containing antigen on surface that separate from normal cells. Therefore, probability of that retrovirus attaching to that noncancerous cell is low in presence of cancer cell then cancer antigen is specific then retrovirus modified antibody which bind to that antigen then virus to logged themselves and inject viral DNA into cell. Then team that insert functional tumour suppressor gene into that viral vector which incorporated into virus that injected its DNA. Then suppressor gene taken by cell and include in that DNA allow cell to regain the function of self-regulation and apoptosis.⁴⁵

- **Surgery**

Surgery used for diagnosis, treatment and to prevention of cancer. In that greatest chance for cure, if cancer not spread to other part of body.⁴⁵

- It precise local treatment.⁴⁶
- May remove portion of primary tumour.⁴⁶

- **Radiation Therapy**

- Local treatment in which energy is directed in that specific part target.⁴⁷
- Surgery for to prevent that primary tumour.⁴⁷
- May be given the radioimmunotherapy, combining a radioisotope and monoclonal antibody.⁴⁷

- **Immunotherapy**

In that treatment uses your own body immune system to fight against cancer.⁴⁵

- **Hyperthermia**

In that the idea of using heat to treat that cancer has been around for some time but shown mixed result. Today newer tools allow precise delivery of heat and hyperthermia is being studied for use against many types of cancer.⁴⁵

- **Steam Cell Transplant:**

Bone marrow transplant and other type of steam cell transplant that are use to that treatment of cancer. Transplant is like for most people and discuss some issues come with it.⁴⁵

- **Photodynamic Therapy:**

In that photodynamic therapy uses special drug called then as photosensitizing agent along with that light these kill the cancer cell. These drug work after they activated by certain type of light.⁴⁵

- **Targeted Therapy:**

These is a newer type of cancer treatment that uses a drug or other substance to more precisely identify and attack cancer cell and damage that normal cell also.⁴⁵

RADIOTHERAPY:

Radiotherapy is one of the main components of modern cancer treatment it requires substantial capital investment or trained professionals in several disciplines and high precision equipment and a particular external and internal organisational structure. The most of the indications for radiotherapy are related to cancer treatment, it is not possible to set up a cancer control programme if radiotherapy is not available. Radiotherapy is one of the experienced a fast technological advance in the last two decades, which has improved precision in treatment planning and delivery.⁴⁸

NEED FOR RADIOTHERAPY:

The data Sources Economies were classified according to the definitions of the World Bank for the 2015 fiscal year. The list from the World Bank includes 214 economies, from which 139 are in the category of LMIC.⁴⁹ LMIC are grouped into regions, defined as per division used by the International Atomic Energy Agency (IAEA) Technical Cooperation Department. Europe and Central Asia include LMIC from Europe and the post-Soviet countries in Asia. Asia and the Pacific refers to LMIC from the rest of Asia and Oceania.

Need for radiotherapy in Europe

There are several observations are relevant to assessing the need for radiotherapy in the national contexts arise:

1. Under the reasonable assumptions, it is feasible to assess demand for radiotherapy at the country level using a combination of evidence-based indications, population-based data on incidence stage of diagnosis.

Radiotherapy and Its Side Effects

Radiotherapy is associated with considerable side effects. Patient collectively participating in the Dutch study was evaluated for late side effects of short-course preoperative radiotherapy. In patients without a stoma, mean bowel frequency during the day was significantly higher in irradiated patients as compared to patients after surgery alone. The evaluated variables to determine bowel function were faecal incontinence during the day and at night, anal blood and mucus loss, and higher rates of pad wearing. Irradiated patients were affected significantly more frequently by reported variables. Other factors, such as impact of bowel function on daily activities or overall satisfaction with bowel function, were more frequently reported by irradiated patients, as compared to surgery-alone patients, but this difference did not reach statistical significance. No difference in satisfaction between two groups was noted in patients with a stoma.⁵⁴

CHEMOTHERAPY:

Chemotherapy literally means the use of chemicals in order to inhibit malignant cell or to the infectious agents of a disease such as micro-organism without much affecting the host cells

NEED OF CHEMOTHERAPY:

- **To cure the cancer without other treatment**

Chemotherapy can be used as the primary or sole treatment for cancer.⁵⁶

- **After other treatment, to kill hidden cancer cells**

Chemotherapy can have used after other treatment, such as surgery, to kill any cancer cells that might remain I the body.⁵⁶

- **To prepare you for other treatment**

Chemotherapy can be used to shrink a tumor so that other treatment, such as radiation and the surgery, are possible. Doctors call the neoadjuvant therapy.⁵⁶

- **To ease sign and symptoms**

Chemotherapy may help relived sign and symptoms of cancer by killing some of the cancer cells. Doctors calls this palliative chemotherapy.⁵⁶

Chemotherapy refers to the use of any drug to treat any disease. But to most people, the word chemotherapy (or "chemo") means drugs used for cancer treatment. It's important to know that that not all medicines and drug to treat cancer in same way. It use to be that the only kind of drug that could treat cancer war traditional or standard chemo, but now there are lots of different kinds of drug use to treat cancer.

Chemotherapy:

A) Systemic therapy in that drugs are distributed throughout body by bloodstream.⁶¹

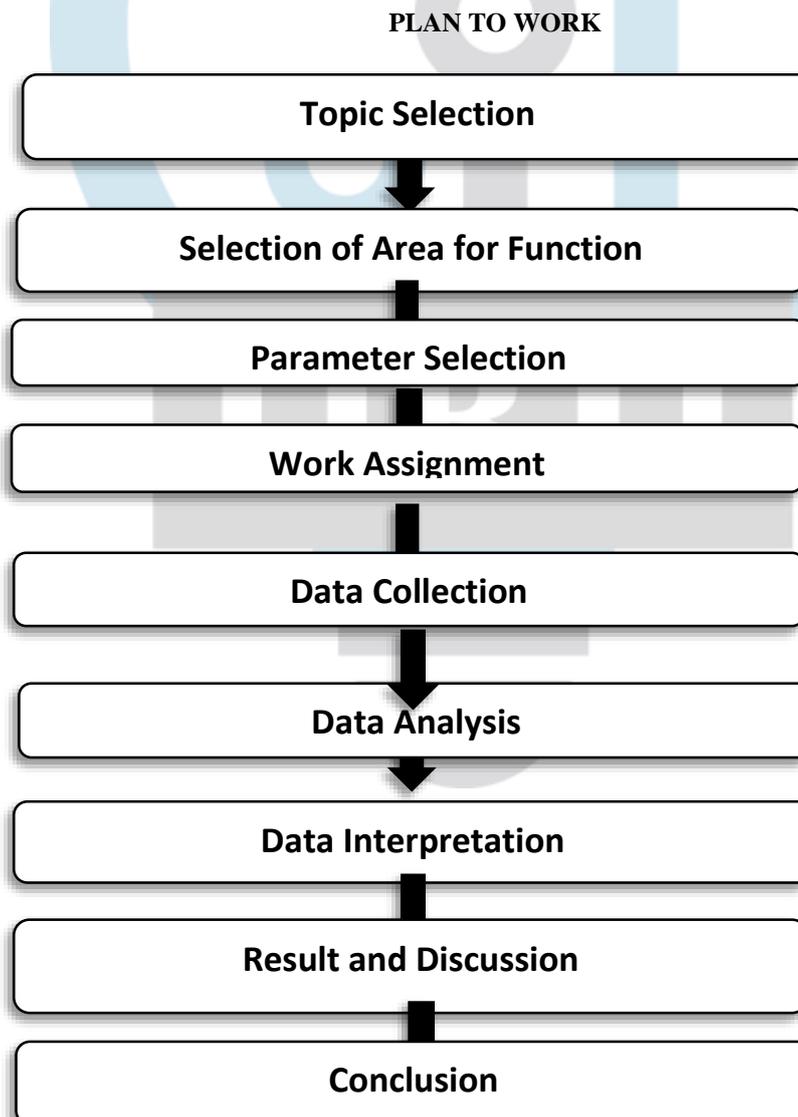
B) Use single agent or combination.

World Cancer Day 2020: International Public Opinion Survey on Cancer

This report aims are to findings of an international survey on public perceptions around cancer led by the Union for International Cancer Control (UICC). It is one of the few multi-country studies to have been conducted on this issue. More than 15,000 adults across 20 countries were surveyed online from 25th October to 25th November 2019, for providing an important insight into public for aware about cancer in a number of different countries, regions and demographic groups. People were asked questions relating to their concern about cancer, its effects on themselves and their families, their perceptions of risk factors and their personal attitudes and behaviour, together with their expectations of their governments.⁶⁹

AIMS AND OBJECTIVE:

1. To collect the data of cancer patients in periphery.
2. To calculate the survey rates of cancer patients and treated by chemotherapy.
3. To describe the efficacy of chemotherapy in controlling the pain of cancerous patients.
4. To calculate the survival rate of patient with cancer treated by chemotherapy.



METHODOLOGY:**Study design and Setting:**

This is a prospective observational study (survey) carried out by the 19 students at the S.N.D. college of pharmacy, Yeola, from the 1st of April 2022 to 20th of June 2022. Study of several patients have been done. From the study the patients who have been taken the chemotherapy and their drug dose was observed.

Data collection:

All information about variables collected from patient as age and gender, types of Tumor, information about Chemotherapy and their follow up conditions,

Participants:

35 Patients, who were suffering from cancer and referred for Chemotherapy, enrolled into the study after informed consent from all patients. Selection of participants by using the questionnaires sheet.

Follow-up:

Patients were assessed between the time period of 30-40 days before received chemotherapy and after receiving chemotherapy. During this period patient were followed by phone for assessment of condition status. Follow-up was based on patient's conditions like stable, curative, no pain, worse and dead.

Statistical methods:

All variables were collected in Excel sheet then analysed by variables, frequency and their percentage. Pie diagram was drawn in excel according to their percentage.

RESULTS:**Table 1: Gender and age frequencies of the study.**

Variable		N	%
Gender	Male	18	51.4%
	Female	17	48.5%
	Total	35	
Age(years)	<30	6	17.1%
	30-40	9	25.7%
	41-50	5	14.2%
	51-60	8	22.8%
	61-70	6	17.1%
	>70	1	2.8%
	Total	35	

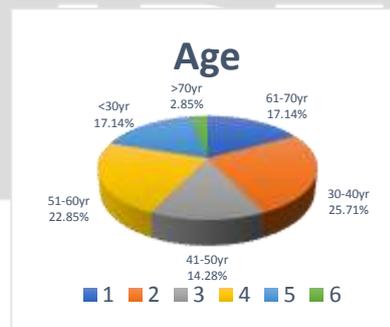
**Diagram 1: Gender of patients****Diagram 2: Age of patients**

Table 2: cancer variable frequencies of study

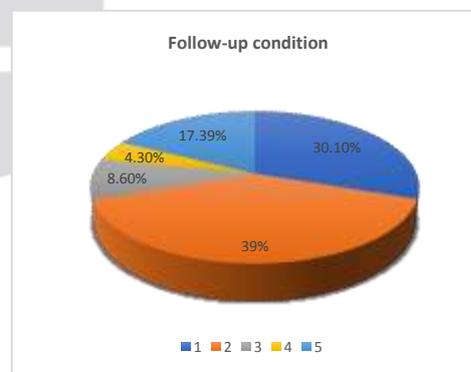
Variable	N	%	
Tumor type	Leukemia	8	22.85
	Breast	7	20
	Oesophagus	2	5.71
	Liver	1	2.85
	Abdomen	2	5.71
	Bone marrow	3	8.57
	Head and neck	4	11.4
	Stomach	1	2.85
	Mouth	2	5.71
	Renal	1	2.85
	Uterine fibroid	1	2.85
	Ovaries	1	2.85
	Penile	1	2.85
	Cervix	1	2.85
	Total	35	

Table 3: Chemotherapy variable of study

Variable	Total patients	Chemotherapy given	Chemotherapy not given	Percentage
Leukemia	8	4	4	50
Breast	7	7	0	100
Oesophagus	2	1	1	50
Liver	1	1	0	100
Abdomen	2	0	2	0
Bone marrow	3	2	1	66.6
Head and neck	4	3	1	75
Stomach	1	1	0	100
Mouth	2	1	1	50
Renal	1	0	1	0
Uterine fibroid	1	0	1	0
Ovaries	1	1	0	100
Penile	1	1	0	100
Cervix	1	1	0	100
Total	35	23	12	65.71

Table 4: Follow-up conditions of the patients after chemotherapy

Conditions	N	%
Stable	7	30.10%
Curative	9	39%
No change	2	8.60%
Worse	1	4.30%
Dead	4	17.39%
Total	23	



DISCUSSION:

- Reports of total 35 patients were observed, analysed and studied. It was found that out of 35 patients 18 were male and 17 female.
- The most frequent age group was of 30-40 years, followed by 51-60 years.
- Among all types of cancer, leukemia came in first rank in our research, as there 8 patients of leukemia were found.
- Out of the 35 patients, 23 have been given chemotherapy.
- All the patients of breast cancer are on chemotherapy.
- Result obtained from follow-up after chemotherapy, it can be observed that out of 23 patients 7 were stable and 9 were curative.

CONCLUSION:

Present study of cancer survey was successfully conducted at the periphery of Yeola.

Following findings obtained from the survey,

- Leukemia came in first rank among all the cancer type
- All the patients of breast cancer are taking chemotherapy, having better result.
- Patients on chemotherapy are getting good results.

FUTURE SCOPE:**Palliative radio therapy:**

Palliative radio therapy offers a quick, inexpensive and effective way of reducing many of the focal symptoms of advance, incurable cancer whether these arise from the primary tumor or from metastatic deposits. It can improve quality of life while being associated with limited treatment burden in terms of hospital attendances and side effects.⁷⁰

- In this survey article we have studied about the effect of chemotherapy and in future we want to study about palliative radiotherapy.

REFERENCE:

1. IARC Press release, 2013. Available from <http://ci5.iarc.fr/> [Accessed on May 02, 2014].
2. Breast Cancer Deadline 2020 (2012). Retrieved May 10, 2014, from www.breastcancerdeadline2020.org/
3. Jemal A, Bray F, Center MM, et al (2011). Global cancer statistics. *CA: A Cancer J Clin*, 61, 69-90.
4. Zhu YY, Zhou L, Jiao SC, Xu LZ (2011). Relationship between soy food intake and breast cancer in China. *Asian Pac J Cancer Prev*, 12, 2837-40.
5. Ferlay J, Soerjomataram I, Ervik M, et al (2014). GLOBOCAN 2012 v1. 0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11. Lyon, France: International Agency for Research on Cancer; 2013. Visit: <http://globocan.iarc.fr>.
6. Stortecky S, Suter TM. Insights into cardiovascular side-effects of modern anticancer therapeutics. *Curr Opin Oncol* 2010; 22:312-7
7. CAT. Whitehead S. Prostate cancer: the most common cancer among men in England. 2010
8. Franks LM. Latent carcinoma of the prostate. *J Pathol Bacteriol* 1954;68(2): 603-16
9. Ashutosh Kumar Dubey*, Umesh Gupta, Sonal Jain Breast Cancer Statistics and Prediction Methodology: A Systematic Review and Analysis jun 2015;2.
10. DeSantis CE, Fedewa SA, Goding Sauer A, et al. Breast cancer statistics, 2015: Convergence of incidence rates between black and white women. *CA Cancer J Clin*. 2016; 66: 31-42.
11. Drukteinis JS, Mooney BP, Flowers CI, et al. Beyond mammography: new frontiers in breast cancer screening. *Am J Med*. 2013; 126: 472-479.
12. Siegel RL, Miller KD, and Jemal A. Cancer Statistics, 2017. *CA Cancer J Clin*. 2017; 67: 7-30.
13. Maffini MV, Soto AM, Calabro JM, et al. The stroma as a crucial target in rat mammary gland carcinogenesis. *J Cell Sci*. 2004; 117: 1495-1502.
14. Sonnenschein C, and Soto AM. Carcinogenesis explained within the context of a theory of organisms. *Progress in biophysics and molecular biology*. 2016; 122: 70-76.
15. Qian BZ, and Pollard JW. Macrophage diversity enhances tumor progression and metastasis. *Cell*. 2010; 141: 39-51.
16. Dumars C, Ngyuen JM, Gaultier A, et al. Dysregulation of macrophage polarization is associated with the metastatic process in osteosarcoma. *Oncotarget*. 2016; 7: 78343-78354
17. Polyak K. Breast cancer: origins and evolution. *J Clin Invest*. 2007; 117: 3155-3163.
18. Basse C, and Arock M. The increasing roles of epigenetics in breast cancer: Implications for pathogenicity, biomarkers, prevention and treatment. *Int J Cancer*. 2015; 137: 2785-2794
19. Al-Hajj M, Wicha MS, Benito-Hernandez A, et al. Prospective identification of tumorigenic breast cancer cells. *Proc Natl Acad Sci U S A*. 2003; 100: 3983-3988
20. Molyneux G, Geyer FC, Magnay FA, et al. BRCA1 basal-like breast cancers originate from luminal epithelial progenitors and not from basal stem cells. *Cell Stem Cell*. 2010; 7: 403-417.