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THE EFFECT OF ORAL CURCUMIN ON SOLID TUMORS OF PATIENTS IN REFERENCE TO CLINICAL PARAMETER AND BIOCHEMICAL MARKERS

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ABSTRACT

Background: There are numerous malignancies afflicting the human body and are characterized by fast growth, invasiveness and metastatic potential. There are various treatment methods such as – surgery, chemotherapy, radiation therapy and most recently, immunotherapy that have been routinely used. However, these treatment modalities are associated with significant morbidities and can sometimes, cause mortality, also. However, there is a need to channelize alternative treatment options such as use of plant extracts to minimize this side – effect.

Objective: The aim of this comparative study was to analyze effectiveness of oral curcumin when used in solid tumor patients in relation to clinical parameters along with biochemical markers. Objective included-a) observe patient's demographic data, b) investigate solid tumor, c) identification of effectiveness of oral dosage and d) evaluation of its overall effects on weight, behavioral changes and adverse drug reaction.

Methods: A total of 40 patients diagnosed with solid tumors were included in the study. Oral curcumin (500mg) was administered to the patients along with other chemotherapy and supportive agent. The recorded responses were grouped under the following categories- a) improvement in markers, c) deterioration in condition despite curcumin use and d) No improvement were seen and patients were in stable condition.

Result: The highest incidence of solid tumor of cancer was noted in patients between 46 to 50 years age range while extremely significant between ($P<0.0001$) in improvement in all clinical condition (appetite, pain, vomiting and weight) were observed in all the studied type of cancer. Although, none of the analyzed biochemical markers showed any statistically significant difference ($P=1.000$) in improvement.

Conclusion: Although there were significant improvement observed in studied clinical parameters, no significance was seen in biochemical markers. It can be concluded that large sample sized should be studied to critically evaluate the advantages of using curcumin in drug therapy

Key Words

To study the effects of oral curcumin on solid tumor patients in reference to clinical parameter and biochemical markers.

INTRODUCTION

Cancer is the uncontrolled growth of body cell. They are of 2 types of Cancers Benign and malignant

Benign – This kind of cancer generally located at one place and cell of this tissue don't spread.

Malignant – This kind of cancer cell arises and spread from one part to other part of the body. Cancer is uncontrolled growth of abnormal cells within body. There are approximately 200 varieties of cancers. Any stimulus which causes normal cells to behave abnormally can result in cancer. Cancer symptoms are nonspecific and comprise of –fatigue, weight loss, pain, cutaneous changes, abnormal bleeding, continuous coughing, change in voice, pyrexia, swellings or tissue growths. Tumors are the one of the important cause responsible for the most of the death in world. The chemistry behind the uncontrolled division of the cancer cell is still being studied. The different solid tumors are classified according to the part that is involved for that tumor i.e. Carcinoma, Sarcomas, lymphomas, Melanoma.

Type of cancer: Cancers are divided according to the part they affected- Solid tumors are the one of the important cause responsible for the most of the death in world. The chemistry behind the uncontrolled division of the cancer cell is still being studied. The different solid tumors are classified according to the part that is involved for that tumor i.e. Carcinoma, Sarcomas, Lymphomas, Marlanoma.

Etiology and risk factor:-

There are many causes that are associated with various cancers. But some researcher had found some of the factors as the main possible cause for this cancer this includes:

1) **Modifiable risk factors**: These factors include as follows

i. **Smoking**- Researcher had found that the nitro derivative present in the smoke is responsible for the most of cancers and it acts as carcinogen.

ii. **Alcohol**- Researcher had found that the drinking alcohol in large qty on daily basis led to pancreatic cancer.

iii. **Diet –** It has been found that those who consume red meat on regular basis are more prone to pancreatic cancer because of the nitro so derivative present in the red meat that stimulate the cell to act as oncogene as compared to the cancer compared

iv. Obesity: this is another cause for developing some cancer because of decreased metabolism rate and various other factors and genes that are provoked due to it.

2) Non-modifiable risk factors:-

These have been classified as follows

i. **Gender:** Some cancer cases are most prevalent in males as compared to females and vice versa. For example, Prostate cancers among males and Breast cancer among females.

ii. **Age:** Old aged persons are more prone to cancer as their immune system is quite weak to detect these malignant cells and less efficiency of body to detect any changes in normal cellular growth.

iii. **Mutation**: This is the wide spread cause for various cancers. Person, who is frequently exposed to some conditions like U.V rays exposure, has to face genetic mutation which led to cancer. E.g. Skin cancer mostly of cases is found in Australia.

iv. **Family history**: Person with family history of any cancer also possesses some traits which led to development of cancer in future.

v. **Infection**: Infection by some of the bacterial and viral agents also led to development of the cancer because they enhanced the effect of carcinogen conveyed through any other environmental sources. E.g. H. pylori infection led to development of the pancreatic cancer.

vi. **Diabetes mellitus**: It has been found by some researchers that the diabetes mellitus is another cause of developing pancreatic cancer.

vii. **Races**: some cancers are more prevalent in some races as compared to others. For e.g.: African American is more prone to pancreatic cancer as compared to Asian American.

REVIEW OF LITERATURES

Curcumin and its preparation have been used to treat various types of tumors. Many analogues have been synthesized and are used directly alone or in combination with the other compounds. This compound generally inhibits the various biomarkers present in cell signaling pathway that are responsible for the cell differentiation and uncontrolled division. This review highlights the various curcumin combinations that had been given to control the various biomarkers responsible for uncontrolled division of cell. [Wu etal.1990] demonstrated that the curcumin up regulated the expression of the biomarker TCF21 that was found to be responsible for various cancer especially lung cancer. They displayed that the curcumin down regulate the expression of DNMT1 which in turn up regulated the level of the TCF21 in H1299 cell line that prevent tumor growth. [Kakarala et al 1995] used curcumin and piperine combination to target the mesosphere formation, aldehyde dehydrogenate and Wnt signaling responsible in the breast cancer. They endowed that the curcumin and the piperine combination were able to inhibit these three biomarkers (5-10μM). They concluded that this combination in future could use to treat the various other cancers.

Reported that curcumin could act against this cancer.

Materials AND METHODS

All patients of solid tumor were included in this study. Patients were grouped in 4 groups.

Group 1: Early cancer patients.
Group 2: Advanced cancer patients (Palliative chemotherapy has been done).
Group 3: Surgery and radiotherapy patients.
Group 4: Most advanced cancer patients.

Total 40 cases of solid tumor were included in this study from 2019-2020 (admitted/operated/ chemotherapy/radiotherapy) in Prankur Hospital and Cancer Research Center, Mahipura, Saharanpur (U.P.). The patients from indoor and outdoor OPD were included in this study. The markers were tabulated, according to the type of tumor. The data was recorded in table form and analysis process was done as per standard statistical methods.

Biochemical parameter - Following parameter were performed –

➢ CBC level (Complete blood count) ➢ LFT level (Liver function test) ➢ CEA level (Carcino embryonic antigen) ➢ Alpha feto protein Clinical parameter:

Following parameter was included:

➢ Weight ➢ Work performance ➢ Appetite

Other cooperative drug used in this study: i. Cyclophosphamide – 120 mg/m2 ii. Cisplatin -80 mg/m2 iii. Doxorubicin -70mg/m2 iv. Paclitaxel -200 mg/m2

Calculation of body surface: Body surface area (BSA) has been used in many measurements in medicine including the calculation of drug dosage and the amount of capsule to be administered orally. Since direct measurement is difficult, many formulae have been published to estimate

BSA. There are various formulas such as:- **i**. Du Bois formula: BSA= 0.007184 X W0.425 X H0.725 **ii.** Mosteller formula: BSA= 0.016667 X W0.5 X H0.5 **iii**. Haycock formula: BSA = 0.0235 X W0.5378 X H0.3964 **iv**. Gehan and georage formula: BSA = 0.0235 X W0.51456 X H0.42246 **v.** Boyd formula: BSA = 0.03330 X W (0.6157-0.0188 X LOG 10(W) X

H0.3 **vi**. Fujimoto formula: BSA = 0.008883 X W0.444 X H 0.663 **vi**. Takahira formula: BSA = 0.007241 X W 0.425 x H 0.725 **vii.** Shlich formula: BSA = 0.000975482 x W0.46 x H 1.08 (Women) BSA = 0.000579479 X W 0.38 X H 1.24 (Men)

Note: - In this study, Du Bois Formula has been used.

RESULTS

Total 40 cases of solid tumor were included in this study from 2019-2020 (admitted/operated/ chemotherapy/radiotherapy) in Prankur Hospital and Cancer Research Center, Mahipura, Saharanpur (U.P.). On comparing the above data given in table the majority of patient had recovered and showed improvement in biochemical markers on giving curcumin with the other chemotherapeutic drugs. It has been deduced that more than 50% of patients had been recovered using this curcumin whereas 10% of the patients had shown no improvement and are in detoriation condition.

Total number of patients = 40

Early cancer patients = 10

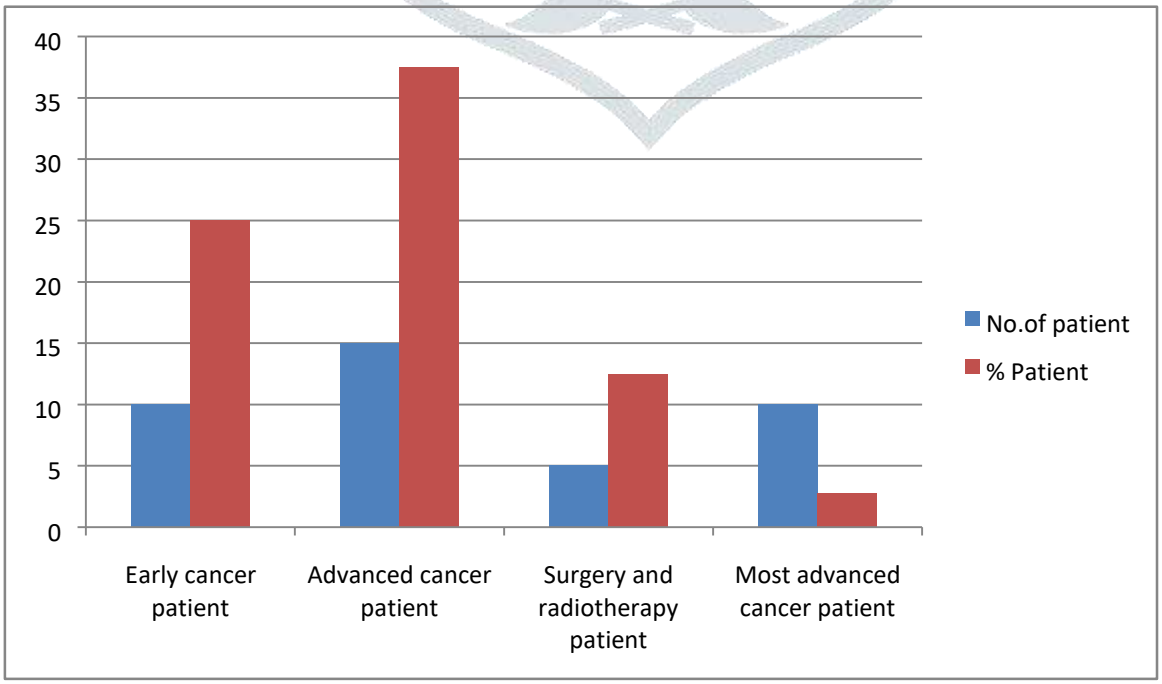
Advanced Cancer patients = 15

Surgery and radiotherapy patients = 5

Most advanced cancer patients = 10

Table Types of cancer

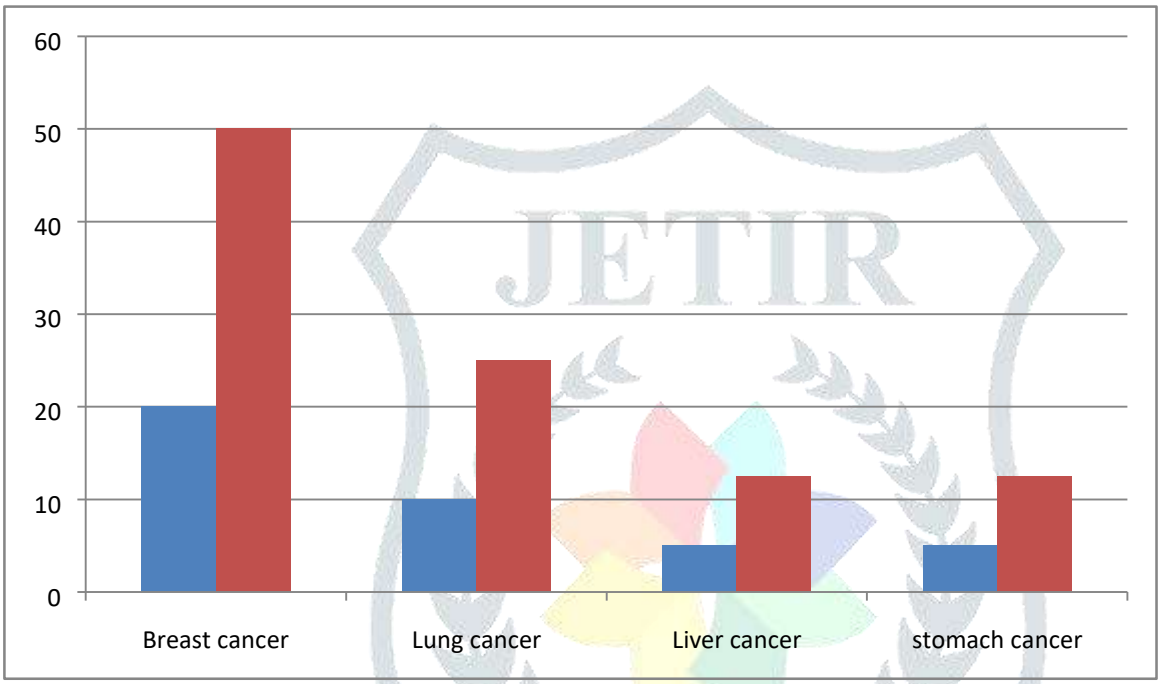
S.N.	Type of cancer	No. of patient	Patients %
1.	Early cancer patient	10	25
2.	Advanced cancer patient	15	37.5
3.	Surgery and radiotherapy patient	05	12.5
4.	Most advanced cancer patient	10	25



Graph 4. Graph showing % of patients in different type of cancer

7. No. of breast cancer patients, lungs cancer, liver cancer, stomach cancer.

S.N.	Name of disease	No. of patients	Percentage
1.	Breast cancer	20	50%
2.	lung cancer	10	25%
3.	Liver cancer	05	12.5%
4.	Stomach cancer	05	12.5%



Graph 5. Graph showing total number of breast cancer, lungs cancer, stomach cancer, liver Cancer patients

8 Percentage of appreciable improvement in clinical and biochemical markers after given Curcumin

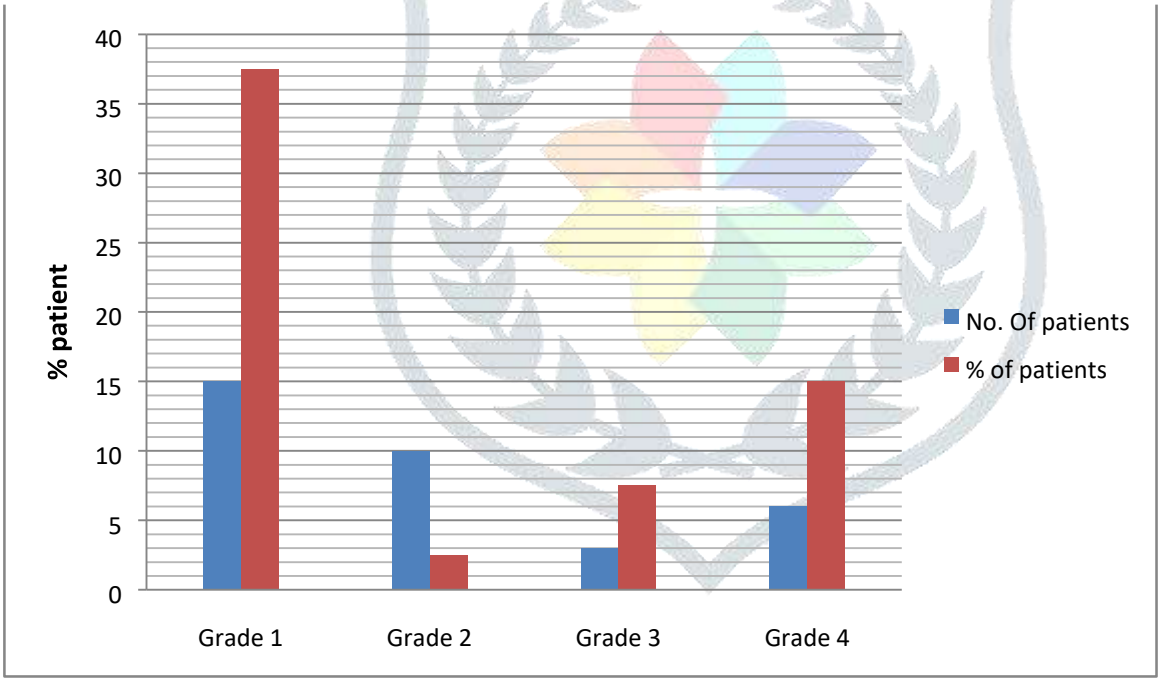
Group 1 -Early cancer patient

Group 2 –Advanced cancer patient

Group 3-Surgery and radiotherapy patient

Group 4- most advanced cancer patient

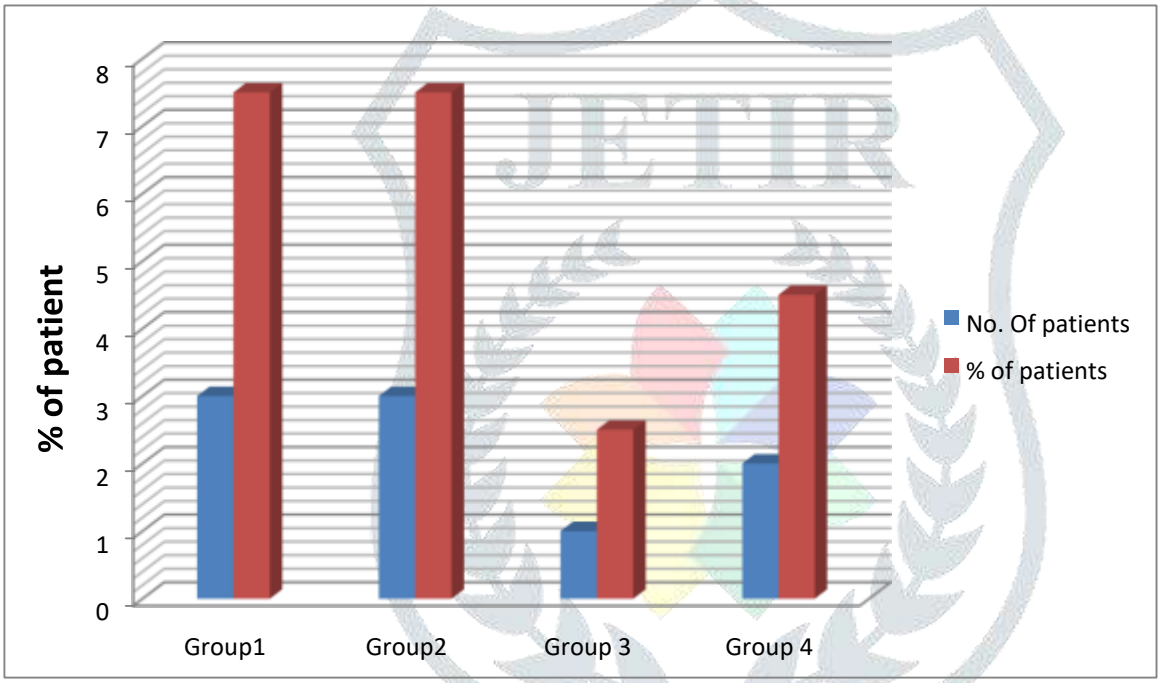
S.N.	Grade	No. of patients	% of patients
1.	Group 1	15	37.5%
2.	Group 2	10	25%
3.	Group 3	03	7.5%
4.	Group 4	06	15%



Graph 6. Graph showing % of most appreciable improvement in clinical and biochemical markers.

9. Percentage of evaluated improvement in markers.

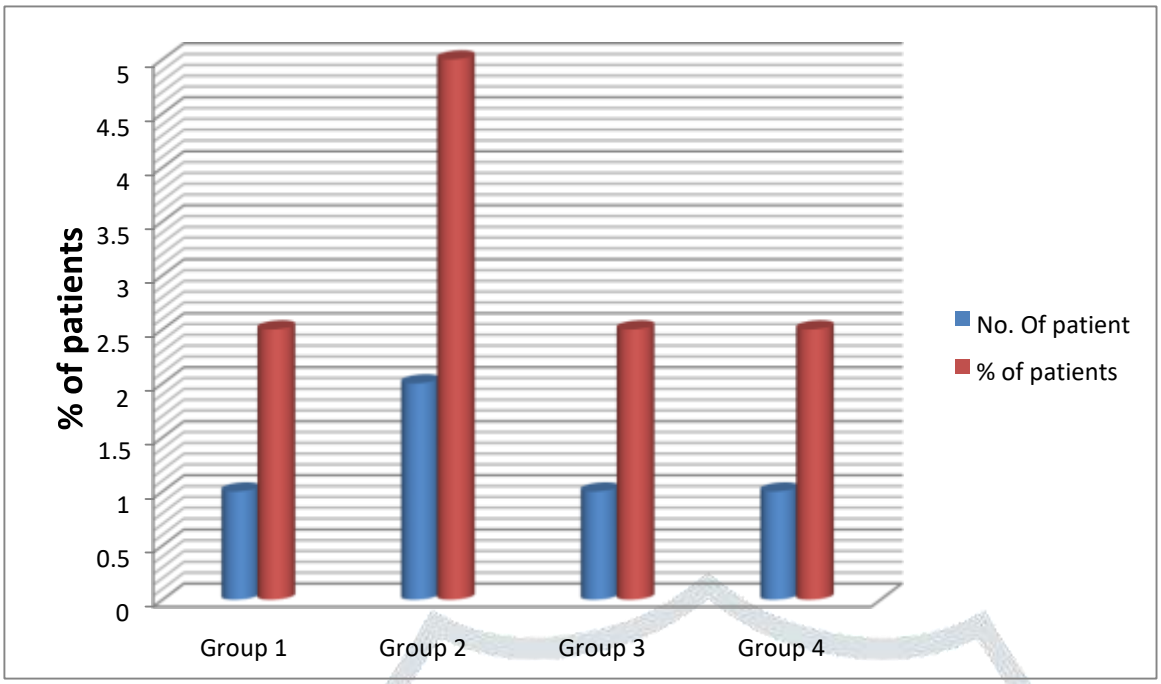
S.N.	Grade	No. of patients	% of patients
1.	Group 1	3	7.5
2.	Group 2	3	7.5
3.	Group3	1	2.5
4.	Group 4	2	5



Graph 7. Graph showing the % improvement in evaluated markers.

10 Percentage of patients in deterioration condition inspite of curcumin use.

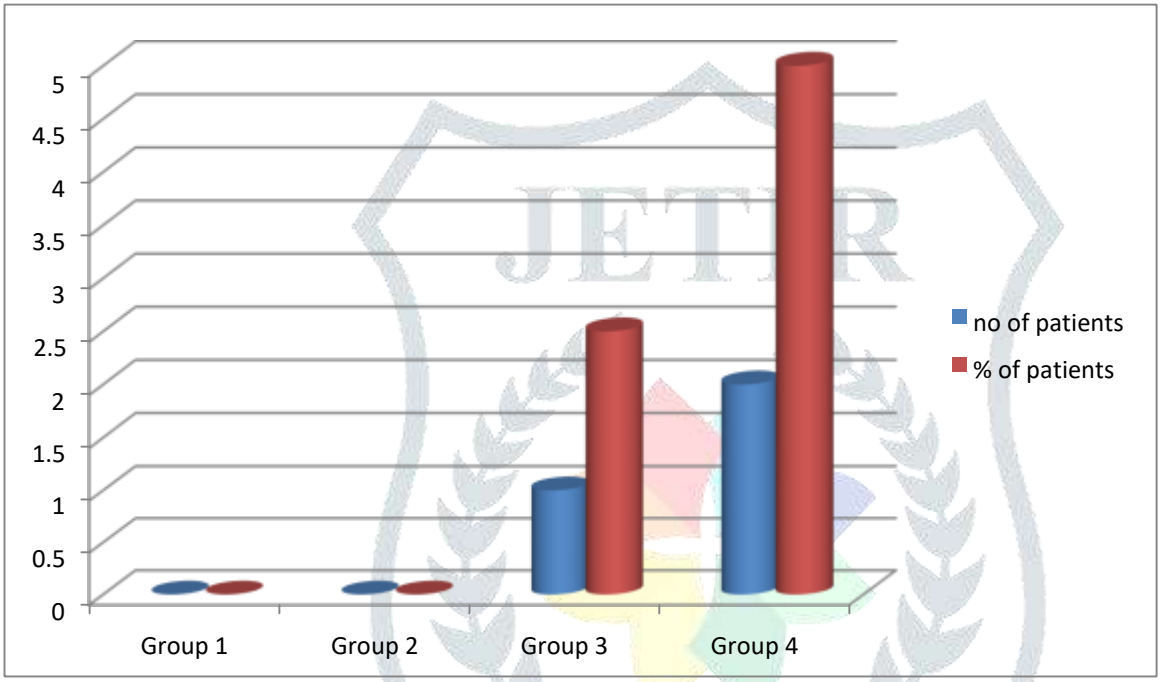
S.N.	Grade	No. of patients	% of patients
1.	Group 1	1	2.5
2.	Group 2	2	5
3.	Group3	1	2.5
4.	Group 4	1	2.5



Graph 8. Graph showing the % improvement in deterioration condition inspite of arcumin.

Table 11. No improvement and patients is in stable condition.

S.N.	Grade	No. of patients	% of patients
1.	Group 1	0	0
2.	Group 2	0	0
3.	Group3	1	2.5
4.	Group 4	2	5



Graph 9. Graph showing the no improvement% after given curcumin and patients is in stable.

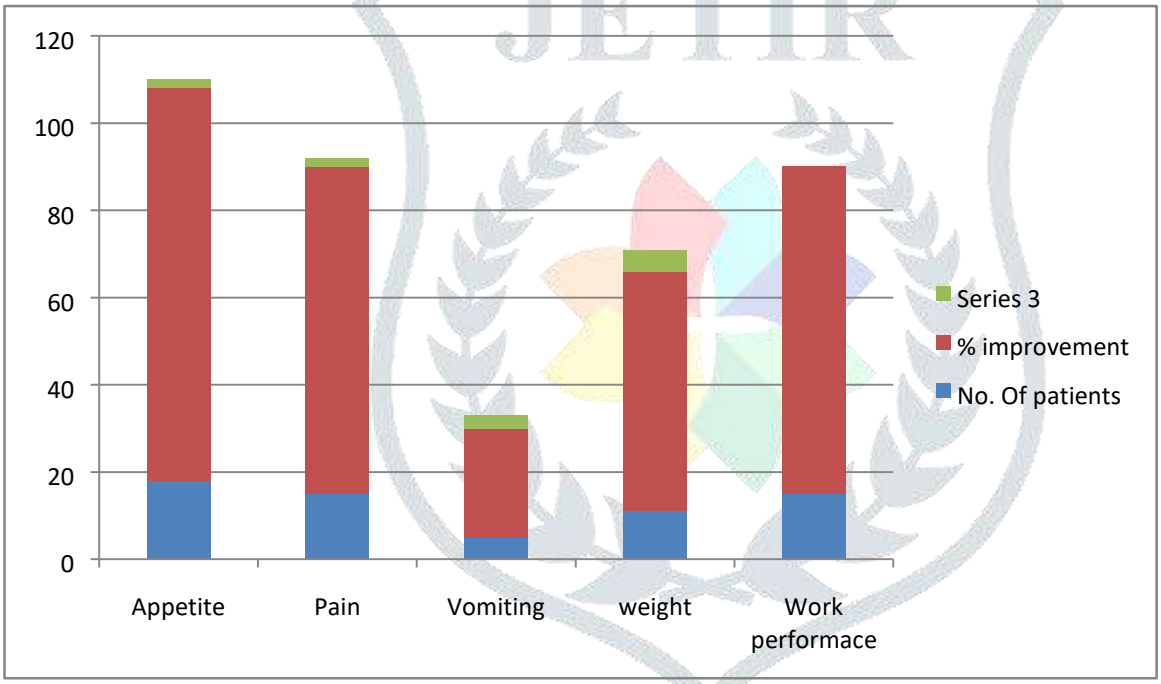
On comparing the above data given in table the majority of patient had recovered and showed improvement in biochemical markers on giving curcumin with the other chemotherapeutic drugs. It has been deduced that more than 50% of patients had been recovered using this curcumin whereas 10% of the patients had shown no improvement and are in detoriation condition.

12. Clinical improvement in breast cancer:

Total no of patients = 40

No. of breast cancer patients =20

S.N	Clinical parameter improvement		
	Clinical parameter	**No. of patient**	**% improvement**
1.	Appetite	18	90
2.	Pain	15	75
3.	Vomiting	05	25
4.	Weight	11	55
5.	Work performance	15	75



Graph 10. Graph showing % improvement in clinical parameter of breast cancer.

In case of clinical parameters majority of patients had shown improvement in all tested parameter which again enlightens the efficacy of curcumin in curing the various secondary factors associated with chemotherapy and cancer.

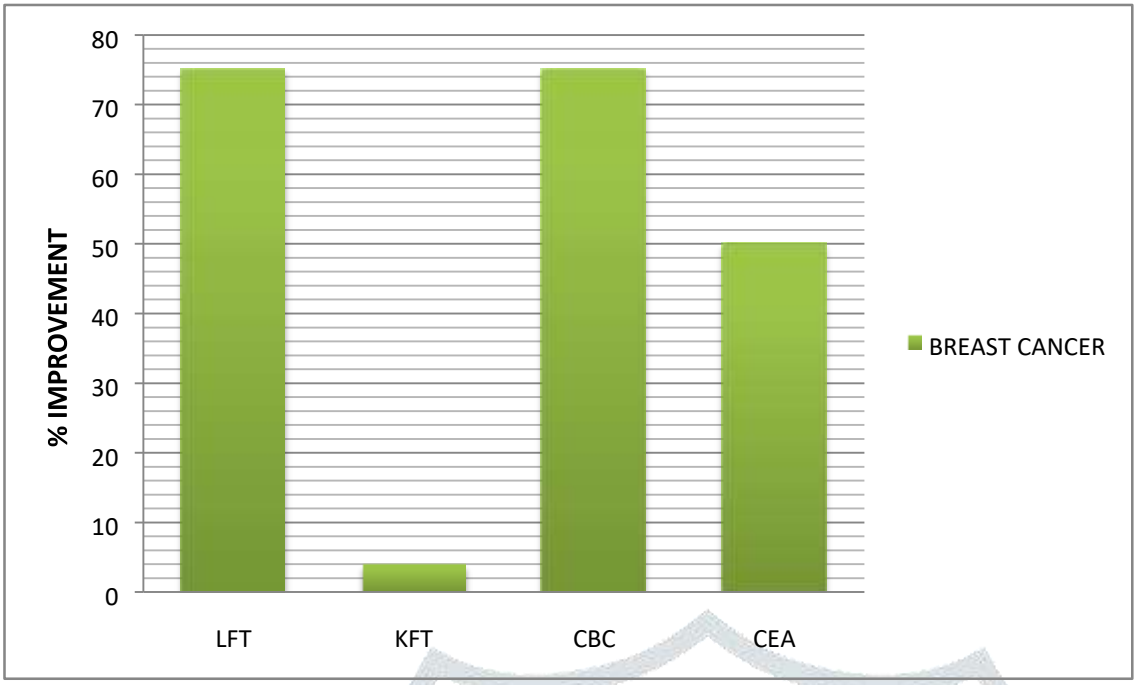
Table13. Biochemical improvement in Ca. breast:

Total number of patients =40

No. of Ca breast patients= 20

S. N.	Biochemical markers improvement			
	Name of biochemical markers		**No of patients**	**Patients %**
1.	Liver function test	i. Bilirubin total	10	50%
		ii. Blood sugar	00	0%
		iii. Protein improvement	15	75%
2.	Kidney function test	i. Blood urea	00	0%
		ii. Uric acid	00	0%
		iii. Sodium	00	0%
		iv. Potassium	00	0%
		v. Chloride	00	0%
3.	Complete blood count test	i. Hemoglobin	15	75%
		ii. Leucocyte	10	50%
		iii. Neutrophils	05	25%
		iv. Eosinphils	00	0%
		v. Monocyte	02	10%
		vi. Basophils	01	05%
		vii. RBC‟s	15	75%
	CEA Level		10	50%

13. Patients displayed improvement in biochemical parameter of breast cancer.



Graph 11. Graph showing % improvement in biochemical parameter of breast cancer

LFT-Liver function test

KFT-Kidney function test CBC-Complete blood count

CEA-Carcinoembryonic antigen.

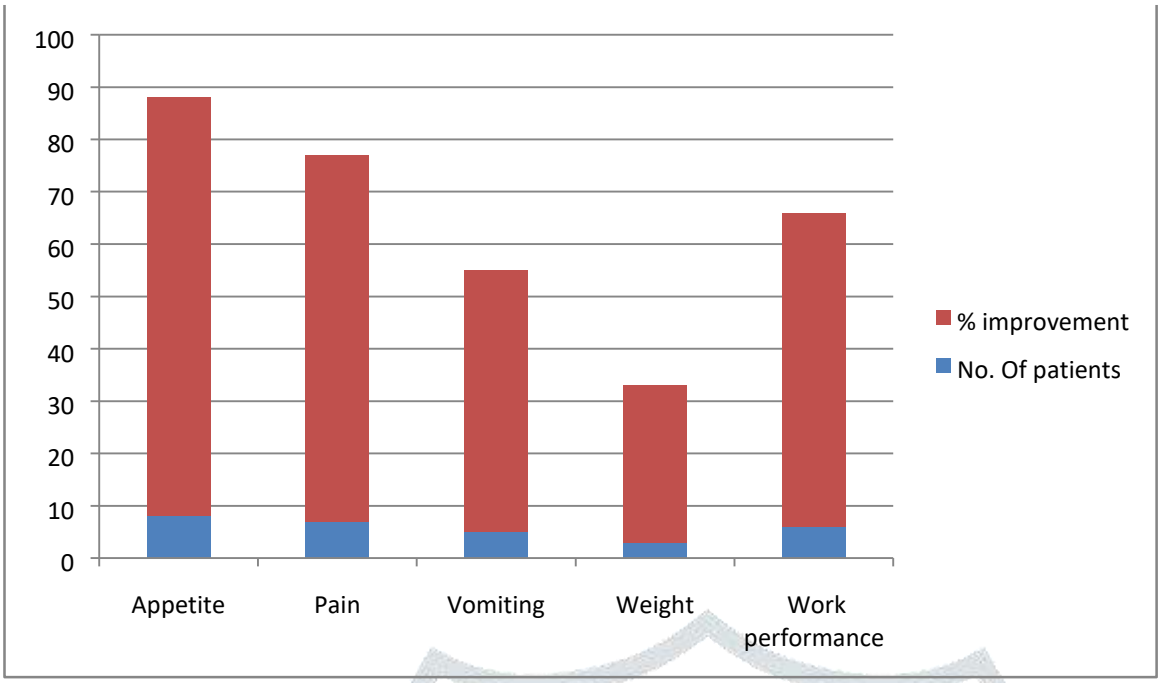
As we can deduce from the graph, in this studied parameter, maximum patients had been recovered even in case of breast cancer. This clearly enlightens the importance of the curcumin in treating the biomarkers expressed in the liver cancer also.

Table14. Clinical improvement in lungs cancer;

Total no of patients = 40

No of Ca lung cancer= 10

S.N.	**Clinical parameter improvement**		
	Clinical parameter	**No. of patient**	**% improvement**
1.	Appetite	08	80
2.	Pain	07	70
3.	Vomiting	05	50
4.	Weight	03	30
5.	Work performance	06	60



Graph 12.Graph showing % improvement in clinical parameters of lung cancer

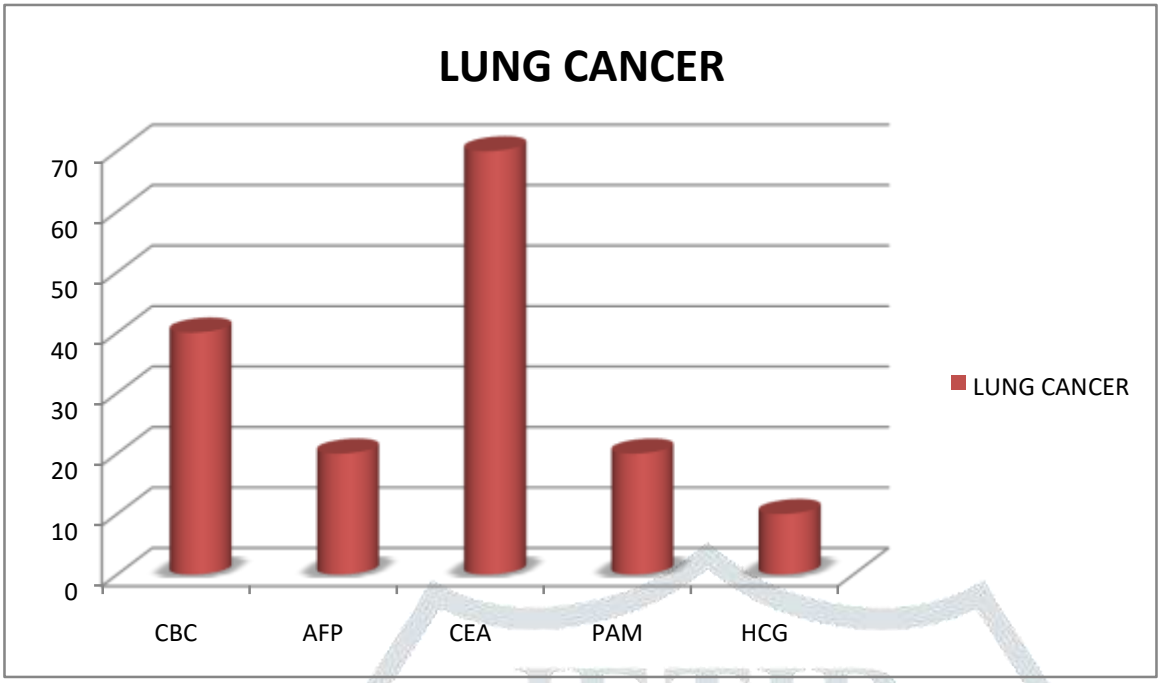
Table15. Biochemical improvement in Ca. lung:

Total number of patients =40

No. of Ca lungs patients = 10

S.No.	Biochemical markers improvement			
	Name of biochemical markers		**No of patients**	**Patients %**
1.	Complete blood count test	i. Hemoglobin	04	40%
		ii. Leucocyte	02	20%
		iii. Neutrophils	00	0%
		iv. Eosinphils	00	0%
		v. Monocyte	00	0%
		Vi Basophils	02	20%
		Vii RBC‟s	03	30%
2.	Alpha feto protein test	------	02	20%
3.	CEA level	-------	07	70%
4.	Pregnancy associated alpha maco globulin (PAM)	------	02	20%
5.	Human chronic Gonadotropin (HCG)	------	01	10%

Table15. Patients displayed improvement in biochemical parameter of lung cancer.



Graph 13. Graph showing % improvement in biochemical parameter of lung cancer.

CBC-Complete blood count

AFP- Alpha feto protein

CEA- Carcinoembryonic antigen

PAM- Pulse amplitude modulation

HCG- Human chorionic Gonadotropin

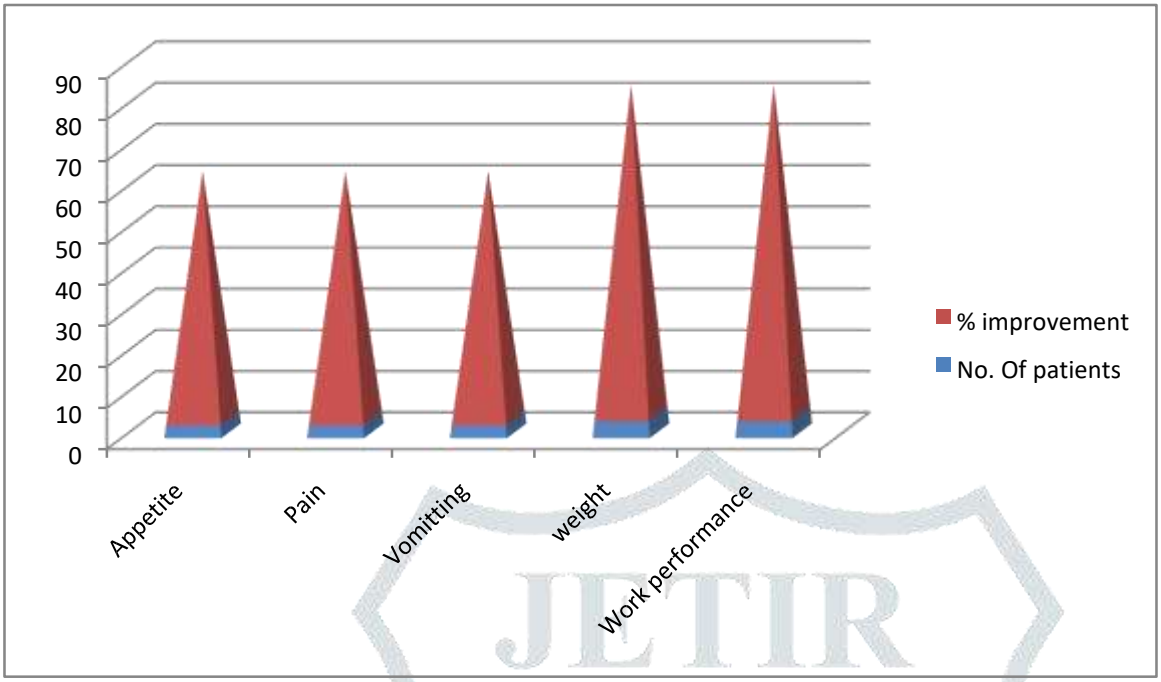
Graph 15 clearly demonstrated that maximum no. of patients had shown improvement in their CEA level and CBC level which is mainly responsible for lungs cancer.

Table16. Clinical improvement in liver cancer:

Total no of patients = 40

No of liver cancer= 05

S.N.	**Clinical parameter improvement**		
	Clinical parameter	**No. of patient**	**% improvement**
1.	Appetite	03	60
2.	Pain	03	60
3.	Vomiting	03	60
4.	Weight	04	80
5.	Work performance	04	80



Graph 14. Graph showing % improvement in clinical parameter of liver cancer.

Table17. Biochemical improvement in liver cancer.

Total no of patients = 40

No of Ca liver patients = 05

S.N.	Biochemical markers improvement			
	Name of biochemical markers		**No of patients**	**Patients %**
1	Liver function test	iv. Bilirubin total	01	20%
		v. Blood sugar	02	40%
		vi. Protein improvement	03	60%
2.	Complete blood count test	viii. Hemoglobin	04	80%
		ix. Leucocyte	02	40%
		x. Neutrophils	00	0%

		xi. Eosinphils	00	0%
		xii. Monocyte	00	0%
		xiii. Basophils	02	40%
		xiv. RBC‟s	03	60%
3.	Alpha feto protein test	----	02	40%

Table17. Patients displayed improvement in biochemical parameter of liver cancer.

Discussion

Current study is an observational analysis of solid tumor cases which under wentchemotherapy from a period of 15 December 2019 to 20 June 2020. The following 40patients were considered for study in Prankur Hospital and Cancer Research Center .In our study 20 males and 20 females were selected for the study. These patients were given curcum in and then analyzed for the appreciable clinical and biochemical improvement.

Curcumin (diferuiloylmethane) is poly-phenolic compound that is derived from Curcuma longa. It has non-toxic and therapeutic properties such as- anti-oxidative, analgesic, anti-inflammatory along with antiseptic and anti-carcinogenic activities. Numerous biological pathways that have central role in mutagenesis, oncogenetic expressions, cell-cycle regulation, apoptotic mechanisms, tumor formation and metastatic pathways. Thus, its anti-proliferation role and inhibitory role on transcription factors: NF-ƙβ along with down-stream gene products which include c-myc, Bcl-2, NOS, Cyclin-D1, TNF-α, various , interleukins etc. in addition to modifying various growth factor receptors and cell adhesion molecules which are responsible for tumor growth, angiogenetic patterns and metastasis (Wilken et al, 2011). Oral curcumin is tolerated well by patients. Inspite of its limited absorptive capacity, it has numerous biological activities in patients suffering from cancer. Dhillon et al, 2008 demonstrated its positive effects on patients diagnosed with pancreatic carcinoma. A total of 40 patients were recruited in this study of which 10 suffered from early cancer while 15 were in advanced stages. 10 patients were in highly advanced stages and 5 patients underwent surgery and radiotherapy.

a) Gender distribution: Equal numbers of male and female patients (n=40, each) were selected for the study (table 2). b) Age distribution related to percentages of cases: No cancer cases were found in 20

to 25 a 26 to 50 years age ranges. 2.5% each of subjects suffering fromcancer belonged to 31 to 35 years, 36 to 40 years and 66 to 70 years age groups. 17.5% belonged to 41 to 45 years category; highest numbers of cases (25%) were observed in 46 to 50 years age-ranged patients followed by 51 to 55 years (22.5%), 56 to 60 years age-range comprised of 12.5% patients while 7.5% cases belonged to 61 to 65 years and above 71 years age-range, respectively (table 3). c) Dietary comparison: Majority of studied cases consumed a non-vegetarian diet (72.5%) when compared to vegetarian (27.5%) (Table 4). However, no statistics could be applied as data was too small. d) Comparison between improvements observed in various clinical and biochemical markers following curcumin administration: 37.5%, 25.5%, 7.5% and 12.5% of patients belonged to groups 1, 2, 3 and 4, respectively (table 5). On application of unpaired T-test, an extremely significant P value (less than

0.0001) was obtained (Table 20). e) Comparison of evaluated improvements in markers: Groups 1, 2, 3 and 4 contained 7.5%, 7.5%, 2.5% and 5% patients, respectively who demonstrated improvement on evaluation pf markers (table 6). On applying unpaired T-test, an extremely significant P value (<0.0001) was obtained (Table 20).

Concussion

Our result displayed that curcumin can act as boon when given in combination with these chemotherapeutic agent in controlling the biomarker and other clinical parameter expression. It had also found in this study that curcumin treatment can cure these biomarker expressions in any stage of cancer and breast cancer patients when treated with theses curcumin had shown tremendous recovery in their biomarkers as compared to other cancer.

CEA level has improved in more than 50% in breast cancer patients which clearly demonstrate the effectiveness of the curcumin. Similarly, tremendous improvement in complete bold count had been shown in patients with breast cancer. Current study was done to evaluate effects of curcumin on types of cancers, following conclusion were drawn:

 Highest incidence of cancers was noted in 45 to 50 years age group.

 An extremely significant improvement (P<0.0001) in all clinical condition

(appetite,pain, vomiting and weight) were observed in all cancer types.

 However, biochemical markers did not reveal any significant improvement (

P=1.000)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