



RESEARCH ARTICLE

SCREENING FOR DEPRESSION IN CANCER PATIENTS RECEIVING RADIOTHERAPY: AN INSTITUTIONAL EXPERIENCE

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ABSTRACT

**Introduction:** Esophageal carcinoma is an uncommon malignancy accounting for approximately 1% of all malignancies, 6% of all GI malignancies (1). Its distribution across the world is variable. Esophageal cancer is the 8th most common cancer worldwide & 6th leading cause of death worldwide.

**Aim of the study:** To determine the outcomes of the definitive management of thoracic esophageal cancer using chemoradiotherapy or radiotherapy, at our institute during the period between 20011 and 2014.

**Material and Methods:** This is a Retrospective study done at our institute from January 2011 and May 2012 patients who received radiotherapy (RT) alone or chemoradiotherapy (CT+RT) for the treatment of carcinoma esophagus.

**Conclusion:** Our study shows that chemoradiotherapy yields significant survival benefit over the radiotherapy alone in the definitive management of patients with T1-3 N0-1 esophageal tumor, who did not undergo surgery. While the overall survival of the entire cohort (N=185) was 13.9 months, chemoradiotherapy offered a survival advantage of 11.6 months over radiotherapy alone (median survival in the CT+RT versus RT alone groups was 19.1 and 7.5 months, respectively). The overall survival rate (OS) at 1 year following treatment was significantly better in the combined chemoradiotherapy group when compared with RT alone group (56% versus 24%).

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INTRODUCTION

Depression is a serious problem in cancer patients. The diagnosis of cancer results in intense psychological distress, ranging from sadness, anger, grief, which is normal response on learning the cancer diagnosis to "Major Depressive Disorder" (M.D.D). Which, is never normal. It is a significant complication that must be addressed. (Anne F. Gross et al., 2007) The effects of depression in cancer patients are increased psychological distress subjective perception of pain, decreased adherence to treatment and quality of life, increased suicidal ideation and attempts, prolonged hospital stay, increased family distress, and worse prognosis. (Santhosh K. Chaturvedi and Yosuke Uchitomi, 2012) predisposes to morbidity and mortality and desire for hastened death (mostly in terminally ill). (Anne F. Gross et al., 2007) After the diagnosis of cancer, various factors which make the patient prone to depression are the diagnosis of cancer disease itself, treatment related factors

like whether patient receiving chemotherapy, radiotherapy, or hormonal therapy and tumor factors like site of disease and, early disease or metastatic disease (stage of tumor). And personal issues like marital status, a supportive family, financial stability and education, a history of substance abuse, past or present history of MDD contributes to the rates of depression. Age and severity of illness are inversely related to psychological adjustment finally personal attributes like positive coping styles (Anne F. Gross et al., 2007). The need of this study is to know the depressive rates. Among our hospital patients and what clinical factors and personal factors of patients are contributing to these rates. Knowledge of these personal, clinical factors and the rates are helpful to identify which patients will become non adherent to treatment, and factors increasing morbidity and mortality and which patients will be having suicidal ideation and patients having difficulty in coping. The correction of these factors by treating oncologist increase the compliance to treatment (reduce dropouts while on treatment), reducing costs of health care, increases communication between doctor and patients, by decreasing morbidity patients will have shorter stay at hospital. Total of 145 patients are screened with good performance status and

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biopsy proven cases of malignancy and who are screened positive on depression scale and willing to take a psychiatric treatment is referred to psychiatrist for further evaluation.

### Aim of the study

1. To study the prevalence of depression in cancer patients receiving radiotherapy
2. To assess the association and prevalence of clinical, socio demographic risk factors involved in causing depression.
3. To know the feasibility of screening for depression in cancer patients by radiation oncologist at MNJ institute of oncology and regional cancer center. Hyderabad.

## MATERIALS AND METHODS

With aims and objectives in view the study is conducted at RADIOTHERAPY DEPARTMENT MNJ institute of oncology and regional cancer center. Hyderabad. Total of 145 cases, with biopsy proof of malignancy and considered for radiotherapy treatment during the period of October 2012 to September 2014 was taken for study.

**Type of study:** - Exploratory descriptive study.

### Inclusion criteria:-

1. Age >21 years of both gender.
2. Performance status ECOG:-0-2
3. Patients with stage I-IV (where applicable.)
4. Patients screening to be performed before/within 2 weeks of treatment for first diagnosis of any tumor type.
5. Patients with a preexisting diagnosis of depression.
6. Patients receiving psychotropic medication.
7. Patients may have had or be in combination therapy with chemotherapy hormonal therapy or immunotherapy along with radiotherapy.

### Exclusion criteria:-

1. Age > 70 years.
2. Performance status ECOG>2.
3. Patient considered suicidal and psychotic or otherwise unfit for study participation by cancer staff clinical judgment.
4. Any prior treatment received for tumor except for breast and gastrointestinal tumor where adjuvant radiation is the mainstay of treatment.

In this study patients are randomly selected; not considering to which site of cancer and stage of cancer the patients belong. After obtaining that the patients are Histo-pathologically confirmed case of malignancy and confirming they are not suicidal and able to understand and can answer the questionnaire are taken for further administration of semi structured intake proforma and depression screening tool PHQ2. The elaborate intake proforma consists of preliminary data regarding age, sex and hospital registration number and clinical and socio-demographic details. The detail clinical factors like performance status, site of cancer, stage of cancer, histo- pathology report (HPE) and type of radiation treatment patient receiving. The socio-demographic details includes marital status, the living companion of patient and education, occupation, monthly family income, and stratification of these

three respectively into Kuppaswamy scale<sup>42</sup>, and details regarding alcohol, smoking, gutka/tobacco chewing and past psychological history, if diagnosed with depression what type of treatment taken. Finally the screening tool is administered.

### Description of tools

#### Patient health questionnaire:-2.43

The PHQ2 enquires about the frequency of "depressed mood" and "anhedonia" over the past two weeks Table 1.

**Table 1.**

Over the past 2 weeks, how often have you been bothered by any of the following problems?	Not at all	Several Days	More than Half the Days	Nearly Every Day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed or hopeless	0	1	2	3

The PHQ2 includes the first two items of the PHQ9.

In illiterate patients the questionnaire and scores are read and report is taken by the clinician. In literate patients who are able to read and write English the English version of the PHQ2 is used and in patients who can read and, write in TELUGU language the TELUGU version of PRIME-MD, Validated by PFIZER, COMPANY<sup>44</sup> by taking first two questions used.

### Scoring

PHQ-2 score ranges from 0-6. according to Kroenke K, Spitzer RL, Williams identified optimal cutoff score of 3 for screening purposes and stated that a cut point of 2 would enhance sensitivity, where as a cut point 4 would improve specificity and with  $\geq 3$  the sensitivity is 83% and specificity 92% for major depression and concluded the construct and criterion validity of the PHQ2 make it an attractive measure for depression screening. The purpose of the PHQ2 is not to establish final diagnosis or to monitor depression severity, but rather to screen for depression in a "first step" approach. Patients who screen positive should be further evaluated with PHQ-9 or any gold standard measures to determine whether they meet criteria for depressive disorder Reducing depression evaluation to two screening questions enhances routine inquiry about the most prevalent and treatable mental disorder.

### Analysis of Data

The data is analyzed by using SPSS Ver.19, software and chi-square tests and P-value are calculated to know the statistical significance. Table 2

### Age distribution

In this study majority number of patients belongs to 51 to 60 age group, minimum age is 21 and maximum age is 70 years, the mean age is 47.92 and standard deviation 11.801. The highest levels of depression rates are seen in 31- 40 years and lowest level is 61-70 years. The data is statistically non – significant.

### Sex wise distribution

The Incidence of Depression in male is 58.6 % and in female 47.5%. Males are more depressed than Females Chi – square is

1.81 and P-value is 0.175 and there is no statistical significance between gender and depression.

**Table 2.**

Variable	No. Of patients(n)	Percentage (%)
<b>Age</b>		
21-30	15	10.3
31-40	32	22.1
41-50	31	21.4
51-60	49	33.8
61-70	10	12.4
<b>Gender</b>		
Male	58	40
Female	87	60
<b>Marital status:-</b>		
Married	124	85.5
Widower/widowed	21	14.5
<b>Living companion</b>		
Alone	8	5.5
Spouse	33	22.8
Spouse, kids &Others	104	71.7
<b>Education level:-</b>		
Illiterate	83	57.2
Literate	62	42.8
<b>Occupation:-</b>		
Not engaged in work	49	33.8
Engaged in work	96	66.2
<b>Monthly family income:-</b>		
1.<1600	26	17.9
2.1601-4809	35	24.1
3.4810-8009	45	31.0
4.8010-12019	15	10.3
5.12020-16019	7	4.82
6.16020-32049	14	9.60
7.>32050	3	2.00
<b>Socio Economic class:-</b>		
Upper(I)	4	2.8
Upper middle(II)	12	8.3
Middle/lower middle(III)	37	25.5
Lower/upper lower(IV)	62	42.8
Lower(V)	30	20.7
<b>Addictions:-</b>		
Alcoholism:-		
No	99	68.3
Yes	46	31.7

**Table 3. Incidence of depression in different age groups**

Age	Number of Depressed Patients	Percentage of Depressed patients (%)
21-30	9/15	60
31-40	20/32	62.5
41-50	13/31	41.9
51-60	26/41	53.1
61-70	7/18	38.9

Chi-square: - 4.31, P-Value: - 0.365

### Marital Status wise Distribution

The depression rates in married patients are 52.4% and in widower/widowed group is 47.6%. The number of patients in married group are more, n = 65 and number of patients with depression in widower or widowed group are less, n = 10 and the data is statistically non – significant.

### Living companion wise distribution

The number of patients living with spouse kids and others representing joint family are more, there by resulting in more depression rates. Even the numbers of patients are less in patients living alone. But the depressive rates are 50%. The number of patients living with spouse, are n = 15, and the depression incidence is 45.5% and the Chi- square is 0.72, p-value is 0.6.

### Education level wise Distribution

The depression rates are high in literate patients 61.3% and in illiterates the rates are 44.6 % and the p-values is significant 0.046, Chi – square is 3.97.

### Occupation wise Distribution

The highest prevalence is seen in patients not engaged in any kind of work than in patients engaged in kind of work 49%. The number of patients more in employed group (n = 47), Chi-square is 0.87 and P-value is not significant.

### Alcoholism wise Distribution

Depression rates are high in patients with alcohol abuse 63% than in patients without any alcohol abuse 46.5% and the P-value is non-significant.

### Smoking wise Distribution

Depression rates are high in patients without any smoking abuse 63.2% than in patients with smoking abuse and P-value is non-significant. Usually the habit of smoking in patients after diagnosis pre disposes to depression. There by increasing morbidity. In this study the patients with smoking habit found to have less depression levels.

### Gutka/Tobacco wise Distribution

The Prevalence of depression in patients without any gutka or chewing habit is 60.4% than in patient having this substance abuse is 47.4%. The tobacco high levels of depression without having taking Gutka is similar to the smoking habit where the depression levels are high. Chi-square: 2.17 P-Value: 0.14 statistically non – significant.

### Socio economic status wise Distribution

The highest depression rates are seen in Class II with 66.7% and Class III 54.1%, the majority of Indian patients belongs to Low socio economic status and lower / middle / upper class. P-Value: 0.62. Statistically non – significant.

### Site of Cancer wise Distribution

In this study highest prevalence of depression are seen in head and neck cancer patients 64.2% and second highest prevalence are seen in 52.4% of breast Cancer and lowest rates are seen in gynecological cancer are 30.6%. The P- value is highly significant and is 0.013. The site in “other” group comprises gastro intestinal and genitourinary malignancy.

### Stage wise Distribution

The highest depression rates are seen in stage IV 66.7% and Second highest is seen in stage II, Stage I has lowest percentage of depression and the P- value is statistically significant.

### PHQ2 scores wise Distribution

The PHQ2 minimum score is „Zero“ and Maximum score is „Six“ mean is 2.72 and standard deviation is 2.11. The percentages of patient correlating with different score values maximum number of patients are net score of „Zero“ are 31 and lowest group of patients have net criteria for score of 4.

## DISCUSSION

Depression in cancer patients is a serious comorbid condition when identified after diagnosis of malignancy. The patients

can be diagnosed with depression spectrum disorders or with major Depression disorder (MDD). The anxiety and depression are seen in radiotherapy patients before initiation of RT but anxiety dissipates after initiation of treatment but depression continuous more over as it proved in many studies pre-treatment depression condition predicts post treatment depression rates. As the RT is local treatment it induces, from skin reactions to mucositis and facial disfigurement due to swellings and ulcers especially in head and neck cancer patients and diarrhoea, pain abdomen in pelvic RT in gynaecologic patients etc. Make the RT patients to prone for intense psychological stress and there will always be the issue of whether the disease is cured or not, or it is recurred. The burden of the physical symptoms due to the disease and various stress factors like whether having family support, income, and knowledge of the patient about disease, and in patients with high risk behaviour problems like substance abuse and finally treatment related factors like chemotherapy, surgery, hormonal therapy influence the presence or absence of depression rates.

Hence depression affects quality of life, adherence to treatment, psychological morbidity, and mortality, and in some patient's suicidal ideation. This study aimed to identify the association prevalence factors and overall rates, the correction of these factors leads to better patient outcome. The study is done at Radiotherapy department, MNJIO/RCC, Hyderabad and the patient are randomly selected after biopsy proof and the PHQ2 tool is administered along with intake proforma. The PHQ2 tool used in this study is an ultra-short screening tool that have high sensitivity and inexpensive and can be administered in busy clinical.

#### Comparison of age distribution in various studies

The literature linking age of the adult cancer patient to depression varies widely. In a study by William.F.Pirl, titled the evidence report on occurrence, assessment and treatment of depression in cancer patients—that the depression rates are low in younger age group. According to Kimberly Miller and Mary Jane Massie, depression rates are high in younger age and are a risk factor for depression. (Kimberly Miller and Mary Jane Massie, 2010) According to Pandey older patients have less depression. In our study highest depression rates are seen in 31-40 years of age group and second highest in 21-30 years age patients, when compared to the older age patients and this study is similar to Kimberly Miller and Mary Jane Massie study.

#### Comparison of Sex Distribution

The prevalence rates of depression in relation to gender vary widely but the majority of studies reporting “No Gender Difference”. In a “Monograph “titled gender difference in pain, fatigue and depression in patients with cancer by Christine Miaskowski. They evaluated a total nine studies, with seven publications and two unpublished studies from the group were identified for gender difference in the prevalence of depression rates, in five of the prevalence studies found no gender difference in depression rates, the other two studies reported high prevalence in women. The studies in which no gender difference seen are by Aass et al. (1997); Ciarmella and Poli, (2001) and one study where high prevalence of depression in women is reported by de Leeuw et al. (2001) and Christine Miaskowski t concluded it is impossible to draw definite

conclusion regarding gender difference in the prevalence or severity of depression.<sup>47</sup> In another Monograph by Massie titled „Depression in Cancer“<sup>48</sup>, concluded that there is no gender difference.<sup>48</sup> In our study males are more depressed with prevalence of 58.6 % this is in accordance with study by Pandey et al<sup>46</sup>, reported high rates of depression in male patients. Finally in a study by „Given and Colleague“<sup>49</sup> found an interaction between age and gender on the level of depression measured using the centre for epidemiological studies depression scale (CES-D). For men as age increased by two years, depression decreased by 0.33 units, whereas for women as age increased by one year depression increased by 0.16 units.

#### Comparison of marital status in various studies

In a study Nauman A Jadoon et al. assessment of depression and anxiety in adult cancer out patients a cross sectional study found no relationship between marital status and psychological morbidity.<sup>50</sup> In a study by Aizer A.A et al named, “Marital status and survival in patients with cancer reported a survival benefit in cancer patients who are married than unmarried and marriage provides a social support that have a potentially significant impact on cancer detection, treatment, and survival.<sup>51</sup> In our study the depression rates in married patients are high, but is statistically non-significant and is similar to study by Nauman A Jadoon and the high rates might be due to large patient number in this group.

#### Comparison of Socio Economic Status

The socio economic status of the Indian patients differ from the west. The studies connecting socio economic status to the depression is spouse the low socio economic status patients have less financial support less education, leading to less depression. In the study by Chintamani et al. reported as compared to the results of the studies conducted in the developed world, the Indian counter parts of breast cancer patients showed lower anxiety and depression levels. This can be probably attributed to their low socio economic status (most patients in this study were in lower middle and lower class according to the Kuppuswamy scale) consequently leading to lower education status, Being an uneducated and not having much knowledge about the nature of disease they were suffering led to care free attitude towards illness.

In this study high depression rates are seen in upper middle and lower middle class. The rates in upper middle are 66.7 % and second highest being in lower middle class 44.1 %. These rates seen in lower middle class are similar to study by the Chintamani et al.

#### Comparison of Alcoholism in various studies

The alcoholic abuse rates are 63.1% in a pilot study named alcoholism, depression and abnormal cognition in head and neck cancer by McCaffrey JC, Weitzner M, et al and 26.1% patients met the criteria for depression. In another study by Kugaya A, Akechi et al prevalence, predictive factors and screening factors for psychological distress in patients with newly diagnosed head and neck cancer, alcohol dependence rates are 33.6 % and alcohol abuse rates are 6.5 % and 16.8% have met criteria for adjustment disorder or major depression. Which are the lowest levels reported.

## Comparison of Smoking and Depression among various studies

Tobacco usage is the most common risk factor for development of cancer particularly head and neck, 85 % of head and neck cancer patients are related to tobacco usage, other cancer associates with smoking is lung and bladder. Cigarette smoking places individuals with cancer history at a risk of multiple health problems than in a growing body of evidence that smoking following cancer diagnosis has a negative input on cancer treatment efficiency, like radiotherapy, chemotherapy and treatment related complications and side effects, cancer recurrence and second malignancy and overall survival 55. In a study by Kugaya A, Akechi the nicotine dependence rates are 32.7% and 16.5% had an adjustment disorder or major depression. In a study by Duffy SA, Terrell JE et al, „effect of smoking, alcohol and depression on the quality of life of head and neck cancer““ patients 35 % had smoking and 44 % screened positive for depressive symptoms.

## Comparison of Various studies in patient using Gutka

The use of gutka or chewing tobacco is largely prevalent in India and is less common in western countries. The literature connecting gutkachewing and depression is sparse. In our study the depression rates in gutka chewing patient are 47.4 % and the P- value is non-significant. And this substance abuse is causative agent for many cancers like head and neck.

## Comparison of site of Cancer

### Head and Neck cancer

In a study titled psychological distress (depression and anxiety) in people with head and neck cancers by Kate A Nielson et al. that the preliminary studies showed, that patients diagnosed with head and neck has elevated levels of psychological distress, further more that 40 % - 66 % of patient meet the criteria for psychiatric diagnosis. In this research they showed post treatment depression was significantly associated with pre-treatment depression ( $r = 0.55$ ,  $p < 0.001$ ) and concluded, that rates of depression in patients with head and neck increase after cancer treatment, with a third of patients experiencing clinically significant symptoms of depression after radiotherapy and the prevalence of mild to severe depression was 15 % before treatment and 31 % after treatment. In a study by Duffy SA, Terrell JE et al, 44 % of screened positive for significant depressive symptoms in head and neck cancer patients.<sup>56</sup> In our study the depression rates are (64.2%). The high rates of depression might be due to large number of patients and as it is a screening method, the number of false positive case detection will be high, further studies by Gold standard methods are required and these rates might also be due to high symptom burden and advanced stage of presentation and in some cases younger age of presentation.

### Breast Cancer:

In a review by Jessie R Fann titled, „Major depression after breast cancer: epidemiology and treatment that breast cancer patients receiving chemotherapy have high rates of depression than patients not receiving chemotherapy and patients undergoing surgery also had high rates of depression. In many of the studies breast cancer depression levels are rated as

second most common levels. 58 in this study the levels are much higher than other studies the reason might be that the screening is carried out in patients after surgery and chemotherapy and finally coming for RT and Indian women will have much family responsibilities leading to constant worry and increased psychological morbidity. According to Massie, the prevalence of depression in breast cancer patients are 46% and the present study prevalence is 52.4%

## Gynecologic cancer

The most common type of gynaecologic malignancy seen in India is cervical cancer. In this study all the patients are cervical malignant patients. According to Rohan Dilip Mendosa and Prakash Appaya the gynaecological cancer patient's psychological morbidity is less studied. In their study the reported rates of depression are 42.5%. In a study by Evans and colleagues the depressive rates of gynaecological patients is 23%. In this study the prevalence of depression is 30.6% the prevalence is less as compared to study done in INDIA by Rohan Dilip Mendosa and Prakash Appaya.

These might be due to women specifically responding to depression question and symptom burden is less compared to head and neck cancer and in this study the screening is carried out before initiation of radiotherapy, where various studies showed less depression rates at starting of RT and depression levels increased during treatment and post treatment and low levels in this study is similar to study by Evans.

## Comparison of stage of cancer in various studies

According to Kimberly Miller and MJ Massie advanced disease is a risk factor for depression.<sup>4</sup> In a study by Vodermaier et al. titled disease stage predicts post diagnosis anxiety and depression only in some types of cancer concluded that disease stage was directly associated with emotional distress, except for patients with breast cancer.<sup>61</sup> In our study all patients are non-metastatic even though the patients have presented in advanced disease, lowest levels are seen in stage I patient with 16.7 % and highest levels are seen in stage IV 66.7 % and the data is statistically significant, with p-value of 0.045. and is similar to Kimberly Miller and MJ Massie that advance disease is risk factor for depression. In our hospital majority of patients presents in advanced and metastatic stages and the larger number of patients seen in stage IV, may also be the reason for high levels of depression in the stage IV patients.

## Comparison of overall prevalence of depression in various studies

In research by Zabora et al the overall prevalence of distress is 35.1%. (Zabora et al., 2001) The prevalence rates of depression according to Massie (2004) are 0-38% for, „Major depression““ and for „depression spectrum syndrome““ 0%-58%.<sup>47</sup> The depression rates by Pandey et al are (mean).<sup>45</sup> In this study total of 145 patients studied, the overall depression rates are 51.7%, the number of patients met the criteria of cut out score of  $\geq 3$  on using PHQ2 tool are 73. These high prevalence rates are due to screening procedure which is highly sensitive sometimes resulting in false positive rate. But as the studies proved the ability of these scale to identify depression in busy clinic in which the treating oncologist will have a less time to evaluate by standard method and hence routine screening can be carried out by using this



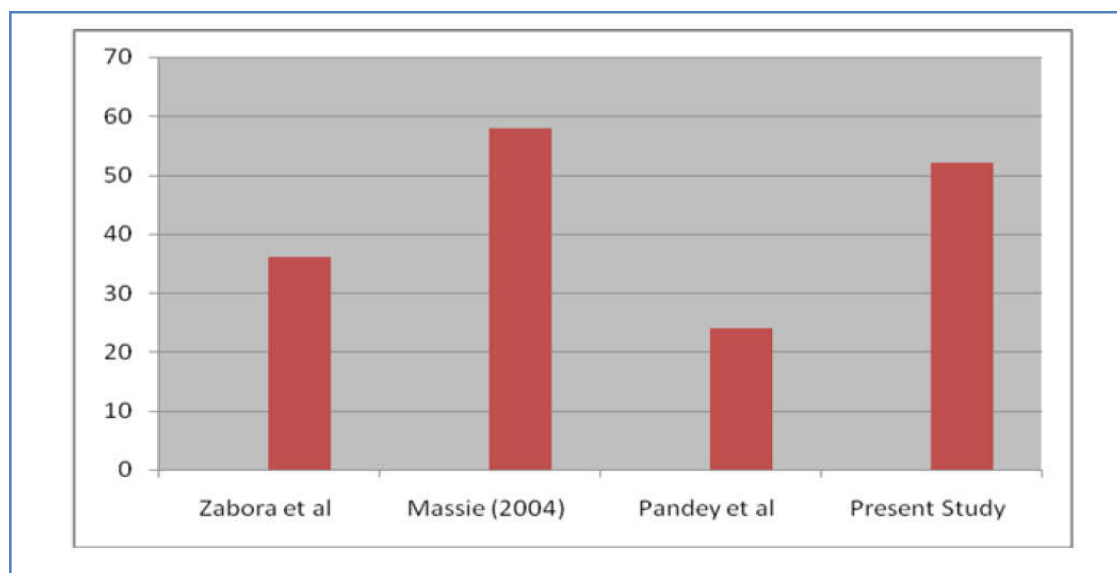


Figure 1.

scale to identify the patient with psychological morbidity, immediately after diagnosis and various time points during treatment. The prevalence of depression in this study is similar to study by Massie (2004).

#### Study limitations

Patient selection was done from one government hospital which may not reflect the various community of patients suffering with cancer. The subjects taken into the study were those who were taking treatment provided by government at free of cost and those patients who are taking treatment at their expenses were not studied. Even though precautions were taken to minimize examiner bias, chances still present as rater and investigator are the same. This study aimed for screening for depression only but patients will have a spectrum of disease from adjustment disorders, anxiety, and mild to severe depression and hence these results are to be confirmed by gold standards psychological measures. The short screening tools are prone for high false positive rates hence the high rates seen in this study might be to this reason. Yet these rates are to be confirmed against gold standard methods. The study conducted in this hospital is a large referral center where very advanced stage cancer patients are referred limiting the study to these locally advanced stages patients when compared to early stage patients. The PHQ2 tool still to be validated separately in INDIAN patients.

#### Summary

Highest levels of depression are seen in 31-40 years age group and lowest levels of depression are seen in 60-70 years age group. Incidence of depression is more in literate patients (61.5%) with statistical significant P-value. Incidence of depression in patients with alcoholism, smoking, gutka, showed high prevalence, but these results were not statistical significant. Cancer patients with unemployment had high rates of depression 57.1%. Patients living with joint family had higher rates of depression when compared to patients living with spouse alone, but the results did not reach statistical significance. Patients with "EARLY STAGES" of cancer showed low depression and "ADVANCED STAGE" patients have high depression rates and the data is statistically

significant. Highest levels of depression are seen in HEAD AND NECK cancer patients with prevalence of 64.2%. Second highest levels of depression are seen in BREAST Cancer patients 30.6%. Lowest levels are seen in GYNECOLOGICAL Cancer patients 30.6%. None of the patients studied had past psychological history.

#### Conclusions

- The overall prevalence of depression in the study patients is 51.7%
- Site of cancer is an important predictor of depression
- Education level of patient seems to be a crucial determinant of depression in Indian patients.
- The stage at which the patient presents may predict rate and severity of depression
- Cancer patients who were unemployed patients had higher depression rates.
- The risk factors like substance abuse were more prone for depression.
- Depression screening can be done by a radiation oncologist using simple screening tools like PHQ2.

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