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The Prospective Clinical Observational Study on Assessment and Evaluation of Serum Fucose as Biomarker in Cervical Cancer.

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ABSTRACT

Cervical cancer is one of the most common cancers among women worldwide. It mostly affect in low and middle-income countries, with most women dying in the prime of life. Early diagnosis of cervical cancer helps in overall management of disease. The present Study was undertaken to validate diagnostic value of Fucose. The main objective of the study is to investigate the possible clinical usefulness of serum Fucose in diagnosing cancer patients by estimating and comparing the Fucose levels in healthy individuals and in cervical cancer patients. This study was carried out on total 80 subjects which including 25 healthy individuals as control group and 55 cervical cancer patients cases as case group. Among them 44 cases are with various clinical stages (stage I, stage IIA, stage IIB, stage III) the significant. The serum fucose level was estimated my using winzler method. Significant elevation ($p < 0.001$) was observed in levels of serum Fucose in cervical cancer patients as compared to the healthy control. The statistical difference between stages values of serum Fucose in cervical cancer shows significant difference $P < 0.005$. The results suggest that evaluation of these markers would be useful in assessing early detection of cancer. In order to reduce mortality and to manage morbidity due cervical cancer and also to improve patient's Quality of life. Fucose biomarkers can be an additional tool for diagnosis along with other diagnostic procedures.

Keywords: Cervical cancer, Fucose, biomarker, winzler.

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INTRODUCTION

Globally cervical cancer is one of most common cause of cancer related deaths and it is the second largest cancer killer of women in low and middle-income countries, with most women dying in the prime of life. Most of cervical cancers begin in the cells lining of cervix. These normal cells of the cervix first gradually develop pre-cancerous changes that turn into cancer. Several terms used to describe these pre-cancerous changes, including cervical intraepithelial neoplasia (CIN), squamous intraepithelial lesion (SIL), and *dysplasia*. (Eifel PJ *et al.*, 2008). About 80% to 90% of cervical cancers are squamous cell carcinomas. Cancer is a disorder of cellular behavior which is characterized by alteration of serum glycoconjugates which is composed of carbohydrate and protein. The fucose is one of the carbohydrate moiety which is the terminal sugar in most of glycoproteins. It plays important role in cell-cell interaction, development of cell adhesion, malignant transformation and metastasis. Physiologically, fucose level is present in low concentration in serum but increased in various cancers which indicating their usefulness in diagnosis and monitoring therapy.

MATERIALS AND METHODS

The study was conducted in Department of Oncology of St. Ann's General and Cancer Hospital a secondary care hospital with the consent and under the supervision of Dr. K. V. Raghavaiah MD (RT), Radiation Oncologist, St. Ann's General and Cancer Hospital, Fatima nagar, Kazipet, Warangal, AP, India. This study was approved by Human Ethical Committee, Kakatiya Medical College, Warangal, A. Pand written informed consent was obtained from every participant. The study subjects were selected randomly in the age group ranging in between 20 to 70 years. The study sample consisted of total 80 subjects, including 25 healthy individuals as control group and 55 cervical cancer patients as case group. Exclusion criteria included liver diseases, hypertension, diabetes, pregnancy, renal problems, TB, viral diseases like HIV, etc.

Blood samples were collected by venipuncture and transferred to sterilized plain tubes and allowed to clot at room temperature. The serum was separated by centrifugation at 3000 rpm for 15min. fucose was measured according to the winzler method by using cystine hydrochloride reagent, absorbance was read at 490nm using spectrophotometer.

Statistical analysis

The results were expressed as mean \pm SD. unpaired t- test was used to assess statistical significance in serum Fucose between cervical cancer patients as case group and healthy individuals as control group. P value <0.001 was considered as highly significant and p value <0.05 were considered as significant. One way analysis of variance (ANOVA) was applied to study the statistical significance between various stages of cancer.

RESULTS

The mean serum Fucose level in 25 healthy subjects was 3.384 ± 0.1226 mg/dl, whereas in 55 cervical cancers patient was found to be 9.733 ± 0.1765 mg/dl. And when compared was statistically significant ($p < 0.001$) (Table 1, figure 1).

Table 1: Comparison of Serum Fucose levels between normal subjects and cervical cancer patients (mean \pm SD; n= 80)

Groups	No	Mean \pm SD	P value	95%Confidence interval
control	25	3.384 \pm 0.1226	<0.0001	-6.897 to
case	55	9.733 \pm 0.1765	<0.0001	-5.801

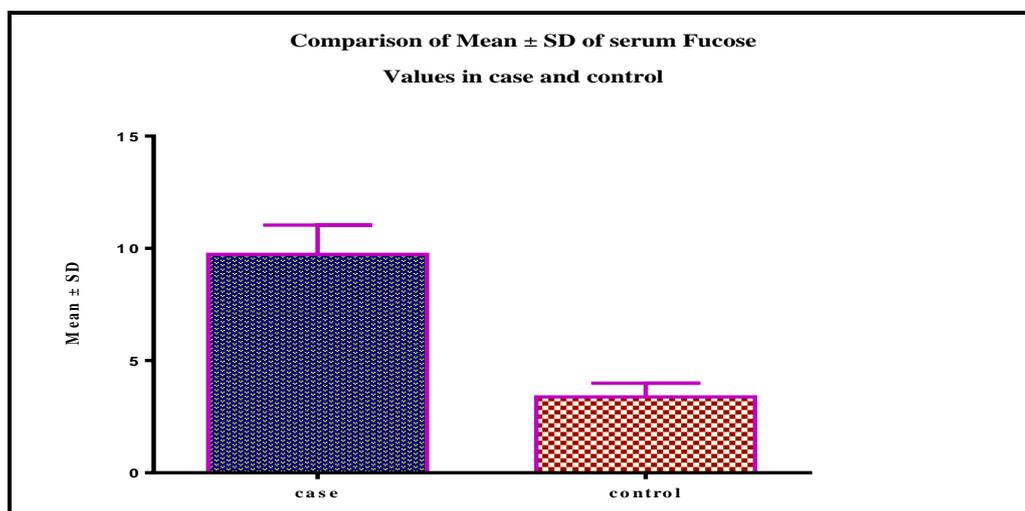


Fig 1: Comparison of serum Fucose level between normal healthy subjects and cervical cancer patients (mean \pm SD; n= 80).

The Fig.1 shows the levels of serum Fucose in cervical cancer patients and normal healthy individuals. Serum Fucose was statistically higher in serum of cervical cancer patients as compared to the apparently healthy individuals.

Distribution of patients according to age wise

Total 55 patients of cervical cancer were divided into age wise according to class interval; details were summarized in Table 5, Fig 7. In overall patients the highest percentage patients are of age group in between 30 to 40 years old.

Age(years)	No. of patients	Percentage (%)
20-30	7	16.3
30-40	17	30.9
40-50	15	27.2
50-60	10	18.1
60-70	6	10.9

Table 2: Age specific distribution of patients

Age specific distribution

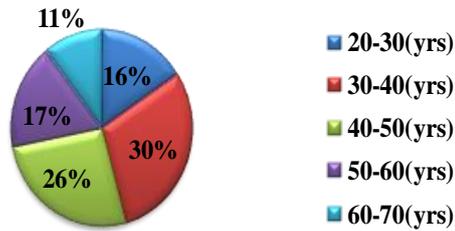


Fig 2: Age specific distribution

Stage wise distribution

Among 55 cervical cancer patients 44 patients are identified with stages by reviewing the patient’s case records. Remaining cervical cancer patients were not identified with stages. A summary detail of stage wise distribution among 42 cervical cancer patients was shown in table 3, fig 3.

Stage	Percentage (%)
I	11.9
II A	26.19
II B	28.57
III	35.71

Table 3: Stage wise distribution of cervical cancer patients

Stage wise distribution of cervical cancer patients

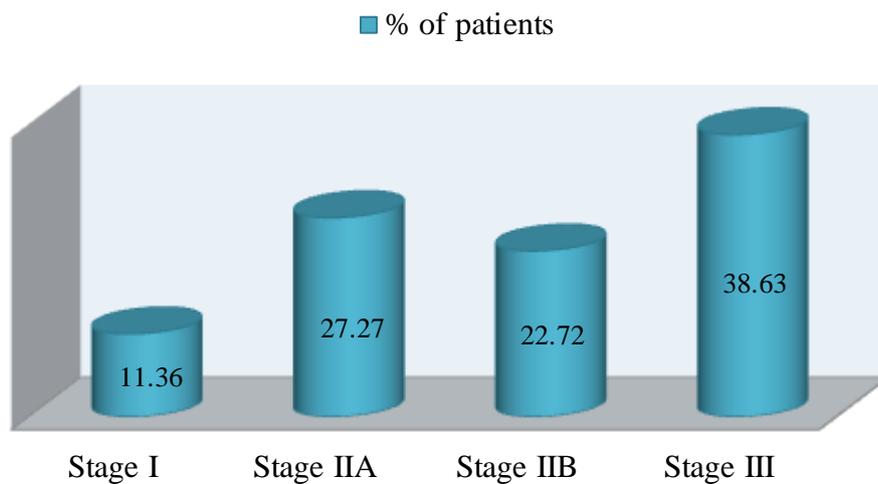


Fig 3: Stage wise distribution of cervical cancer patients

Table 4 shows the levels of serum Fucose in patients with various clinical stages of cervical cancer. The levels of serum Fucose were gradually increase from stage I to stage III cervical cancer patients as compared to healthy individuals. (Fig 4) The statistical difference between stages values of serum Fucose in cervical cancer shows significant difference $P < 0.005$.

Stage	Mean \pm SD
I	8.440 \pm 0.2839
II A	9.417 \pm 0.2956
II B	10.17 \pm 0.3612
III	11.01 \pm 0.3683

Table 4: Serum Fucose levels in various stages of cervical cancer (mean \pm SD; $n = 44$).

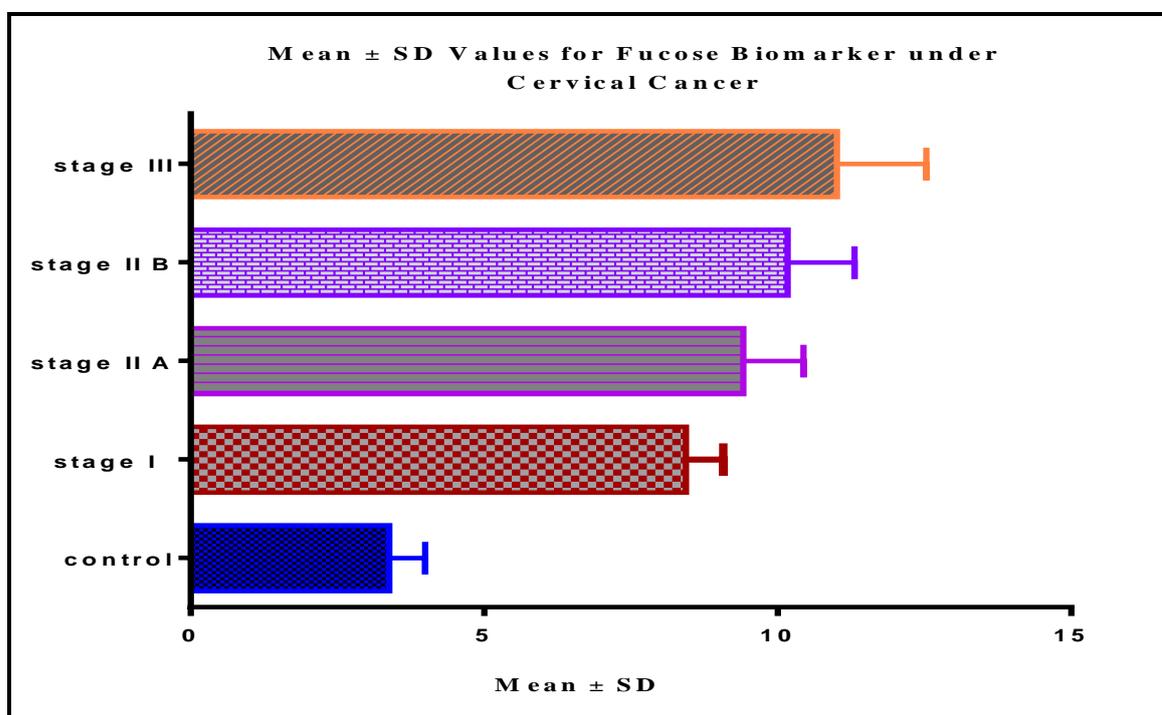


Fig 4: Comparison of serum Fucose levels in between stages of cervical cancer patients and control group(mean \pm SD; $n = 44$).

DISCUSSION

Cervical cancer is one of the most common gynecological cancers recognized nowadays. Its early detection helps to provide a good quality of life for patients. During the past years, several studies have conducted identified potential biomarkers in various cancers. Cancer cell synthesize a wide variety of biochemical products it can be detected in body fluids. It helps in detecting the cancer. Numerous observations indicate the glycoproteins are often elevated in cancer patients while compare with normal. Various views have been expressed by authors regarding the rise in glycoprotein. Glycoproteins are essential for cell- cell communication and they are found on the surface of all cells and some

are released into blood fluids (Dennis JW *et al.*, 1999). The carbohydrate structure of glycoprotein altered in many pathological conditions. (Manoharan *Set al.*, 2005).

In the present study a significant rise of serum Fucose in cervical cancer patients was observed when compare with normal healthy individuals. Similarly higher serum Fucose levels compared with control have been observed by previous studies.

Parwani RN *et al* observed same result in oral squamous cell carcinoma patients threefold rise in the levels of serum Fucose when compared with healthy individuals. And also observed that there was no relationship of serum Fucose level with age the findings was similar to present study. Shetlaret *et al* suggests that tissue proliferation cause for increase in serum Fucose. It has been documented that increase fucosylation levels contribute to increase several abnormal characteristics of tumor cells like uncontrolled tumor growth, decreased adhesion.

Rise in serum Fucose level is not specific for only cervical cancers, the elevated serum Fucose levels also reported in various other conditions like brain tumor (Manjula S *et al.*,2010), oral cancer (Manoharan S *et al.*,2005), oral squamous cell carcinoma (Parwani RN *et al.*, 2011), ovarian, endometrial cancer (Subramanyam D *et al.*,2012).In the present study the levels of serum Fucose were gradually increase from stage I to stage III cervical cancer patients as compared to healthy individuals. The statistical significant difference was between stages values of serum Fucose in cervical cancer patients. It correlates with the previous study. Manoharan S *et al* in his study it shows that the statistically significant difference of fucose levels was observed in between stages of oral cancer patients.

CONCLUSION

Cervicalcancer is a curable disease early screening has considerably reduced morbidity and mortality from the disease. Tumor marker detection plays an important role in the clinical oncology and it would be very useful to find biochemical marker or tumor marker in suspecting the cancer at early stage. Fucose is terminal sugar in most of glycoprotein elevated levels of fucose have been reported in cancer and other diseases. It would be very useful to suspect the cancer at early stage. There was progressive elevation in mean serum Fucose in cervical cancer patients as compared with healthy controls. By the Estimation of serum Fucose in cervical cancer patient's cases helps in understanding it's effective and significant role in the treatment and promoting fucose as an effective biochemical biomarker in conjugation with other diagnostic procedures. And also it is cost-effective technique. Highest percentage of cervical cancer patients are of age group in between 30 to 40 years old. There was no relation of serum Fucose level with age. Advanced stage patients of cervical cancer were more compare to early stages and the serum Fucose level was increased in advanced stages. Analysis of the serum Fucose biomarkers can be an additional tool for diagnosis along with other diagnostic procedures it helps full in early detection of cancer in order to reduce mortality and to manage morbidity due cervical cancer and also to improve patient's Quality of life.

Drawback: This study was confined to only one area and fucose levels were elucidated to only one type of cancer.



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