ORIGINAL RESEARCH

To compare various biomarkers in head and neck squamous cell carcinoma pre and post treatment

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Abstract

Introduction: In India, head and neck cancer is the commonest cancer in men and in both sexes.In most cases, due to extensive loco-regional involvement, poor general condition of the patient, or co-morbid conditions, curative treatment is not possible. Aims & Objectives: To know serum Magnesium levels in patients of head and neck squamous cell carcinoma before and after treatment. Data & Methodology: This study was conducted in the Department of Biochemistry in collaboration with Department of Radiotherapy, Pt BD Sharma Post Graduate Institute of Medical Sciences, Rohtak, India. For the completion of the study, 30 newly diagnosed patients with HNSCC, and 30 age and sex matched healthy individuals were taken. Chi-square and t-test were applied to know the association and comparison between case and control group respectively. Results: The subjects were categorized into three groups such asgroup A- Pretreatment cases, group B- Post-treatment cases and group C- Controls. Plasma glucose in group A was 84.73 ± 2.97 (57-115)mg/dL. Plasma glucose in group B was 103.46 ± 5.15 (61-171) mg/dL whereas group C plasma glucose was 84.73 ± 2.97 (57-115) mg/dL. p value between group A and group B was 0.001. It was found significant difference between cases before and after treatment in glucose levels. The levels in cases before treatment were found significantly different from controls regarding ALT, Albumin, total protein and TBIL with p values 0.015, 0.020 respectivelyConclusions: It was found highly significant difference between case and control groups especially for LDL, Protein and Calcium wise classification respectively.

Keywords: EDTA vacutainer, LDL-C, HDL-C, Chronic disease

INTRODUCTION

Head and neck cancers rank as the sixth most common cancer worldwide and represent a serious challenge for the health community. The typical tumor is a squamous cell carcinoma (SCC) with variable grade of differentiation (from well to undifferentiated); it predominantly affects males in their fifth to sixth decade of life. The estimated annual burden of head and neck squamous cell carcinomas (HNSCC) is about 650,000 cases and the rate of death is approximately 50%.[1]

The incidence of head and neck (HNSCC) has remained stable or even declined since the late 1980s because of a gradual decrease in typical risk behaviors. Despite this, SCCs occurring in the oro-pharyngeal (OP) region (particularly in the tonsils and base of the tongue) have increased from 2-3% to 5.5% of all HNSCCs in the United States of America and other countries. [2,3]

Globally, head and neck cancer is the 7th most common cancer. But in India, it is the most common cancer in men as well as in both sexes. In India in the year 2012, incidence and deaths related to cancer (excluding non-melanoma skin cancers) were 1014,934 and 682,830 respectively. Population based cancer registry in India projects that the number of tobacco related cancer and head and neck cancer would be 3, 16,734 and 2, 18,421, respectively, by 2020. Incidence and deaths related to head and neck cancer were 145,087 and 105,247 respectively.[2]Squamous cell carcinoma constituted about 90% of all head and neck carcinoma cases.[4]

Head and neck cancers (HNCs) affect the upper aero digestive tract and are one of the most common cancers worldwide.[5] With 77,000 cases diagnosed per year, HNCs are the second most common cancers in the Indian population.[6]While smoked tobacco and alcohol are the major causative factors for HNC worldwide, smokeless tobacco, betel nut, and Epstein–Barr virus are etiological agents responsible for it in the Asian population.[7]

In India, head and neck cancer is the commonest cancer in men and in both sexes.In most cases, due to extensive loco-regional involvement, poor general condition of the patient, or co-morbid conditions, curative treatment is not possible. Therefore, the relevance of aggressive treatment in non resectable locally advanced head and neck cancer has been questioned. Response of inoperable locally advanced head and neck cancer to aggressive treatments including chemo-radiotherapy is poor and is associated with significant treatment related toxicities. The intent of treatment in such cases is to improve the quality of life of the patients keeping their socioeconomic condition in mind and judiciously utilizing the precious resources for curable conditions[8].

The main objectives of this study are: To know the serum Magnesium levels in patients of head and neck squamous cell carcinoma before and after treatment. To know Comparison of three groups (A, B & C) by applying appropriate statistical analysis, such as chi-square, t-test etc.

MATERIAL AND METHODS

The present study was conducted in the Department of Biochemistry in collaboration with Department of Radiotherapy, Pt BD Sharma Post Graduate Institute of Medical Sciences, Rohtak. For the study, 30 newly diagnosed patients with HNSCC and 30 age and sex matched healthy individuals were enrolled. Detailed history was taken from the patient for presenting chief complaints and risk factors of cancer. Diagnosis was established with help of detailed history, clinical examination, radiological and histopathological examination. Staging was done according to American Joint Committee on Cancer 2010 criteria.[9]Written informed consent from

the patient was collected to participate in the study. Follow up nature of the study was also explained to the patients.

Inclusion Criteria :
Newly diagnosed histopathologically proven adult patients with HNSCC before starting any treatment irrespective of age, sex and staging of the disease.

Exclusion Criteria :
1. Patients suffering from any other chronic disease (renal, hepatic, endocrinal, malignancy) that could affect study participation or confound data interpretation.
2. Patient on any medication/ supplements.
3. Lactating and pregnant females.

Methodology:
Six mL of venous blood sample was collected in a plain red capped vacutainer and four mL of blood sample in EDTA vacutainer under all aseptic precautions from all the patients at the time of diagnosis and at completion of treatment. Samples were collected in a similar way from healthy controls also. Blood samples were processed within one hour of collection. Serum was separated by centrifugation at 3000 rpm X 5 minutes after clotting. Sample was analyzed for routine biochemical investigations (liver function tests, renal function tests, glucose and lactate dehydrogenase) and complete haemogram the same day and was stored at -20^0C for estimation of IL-6 in batches subsequently.

A total of 30 cases and 30 healthy subjects were enrolled in the study. All the participants were subjected to detailed history-taking as per proforma. Clinical profile was tabulated as per the master chart. The subjects were categorized into different groups as follows: group A-Pretreatment cases, group B- Post-treatment cases and group C- Controls.

RESULTS AND OBSERVATIONS
In this section, univariate and bivariate tables as well as appropriate statistics were applied to present the data.

Table1 Age in years of cases and controls

	Controls	**Cases**
Mean age	54.63±8.07 years	53.37±9.12 years
Range	43-72 years	36-74 years
p value	0.57	

The mean age of HNSCC cases was 54.63±8.07 years and among controls, it was 53.37±9.12 years, with a range of 43-72 years for cases and 36-74 years for control. The difference was statistically not significant as p value was more than 0.05.

Table2 Site-wise, Stage and complaints wise distribution of HNSCC patients.

Parameter	**Different parameter of cancer**	**Number**	**Percentage**
Location of cancer in cases	Ca Larynx	11	36.7%
	Ca Oropharynx	10	33.3%

	Ca base of tongue	6	0.20%
	Ca Tonsil	3	0.10%
Stage wise cancer	stage 4	11	36.7%
	stage 3	19	63.3%
Complaints	Difficulty in swallowing	8	26.7%
	Pain throat region	12	40.0%%
	Hoarseness of voice	8	26.7%
	Swelling in neck	2	6.0%

Table2 showssite-wise, Stage and complaints wise distribution of HNSCC in patients. Out of 30 HNSCC patients, carcinoma larynx was the most common type with 11 patients (36.7%) followed by 10 patients of Ca Oropharynx (33%), 6 patients of Ca base of tongue (20%) and 3 patients of Ca Tonsil (10%). In case of stage wise classification, Out of 30 patients, 11 presented in stage IV (36.7%) whereas 19 (63%) presented in stage 3. No patients presented in early stages i.e. stage I and II.

In case of complaint, out of 30 patients, 8 patients (26.7%) had difficulty in swallowing, 8 patients had hoarseness of voice. Twelve out of 30 HNSCC patients complained of pain in throat region (40%). Only 2 cases (6%) presented with neck swelling.

Table 3. Risk factors (smoking, alcoholism and tobacco use) in HNSCC in cases and controls

Risk factor	Cases	Controls
Smoker	28(93.3%)	25(83.2%)
Non Smoker	2(6.7%)	5(16.6%)
Alcoholic	20(66.7%)	15(50%)
Non Alcoholic	10(33.3%)	15(50%)
Tobacco user	25(83.3%)	10(33.3%)
Tobacco non user	5(16.6%)	20(66.7%)
Both alcoholic and smoker	15(50%)	15(50%)

Table3 shows Risk factors (smoking, alcoholism and tobacco use) in HNSCC in cases and controls.Out of 30 HNSCC patients, 28 (93.3%) were smokers and 2 (6.7%) were nonsmokers. 20 (66.7%) were habitual of alcohol and 10 were nonalcoholic (33.3%). 25 (83.3%) patients were Tobacco users and 5(16.6%) were non-tobacco users. 15 (50%) cases were both alcoholic and smoker.

Table 4.Glucose levels in group A, group B and group C

Groups	Mean ± SD	Range
Group A	84.73 ± 2.97 mg/Dl	57-115 mg/dL
Group B	103.46 ± 5.15 mg/dL	61-171 mg/dL
Group C	100.46 ± 2.94 mg/dL	75-137 mg/dL
p values between groups		
p value between group A and B		0.001
p value between group C and B		0.616

p value between group A and C	0.0004

Table 4 indicates glucose levels in group A, group B and group C. Plasma glucose in group A was 84.73 ± 2.97 (57-115) mg/dL. Plasma glucose in group B was 103.46±5.15 (61-171) mg/dL. While in group C plasma glucose was 84.73±2.97 (57-115) mg/dL. p value between group A and group B was 0.001. Hence significant difference was found in cases before and after treatment in glucose levels. p value between group B and group C was 0.616 (not significant). p value between group A and group C was 0.0004. Hence cases before treatment had significantly low glucose values than controls.

Table 5Lipid profile (mg/dL) in group A, group B and group C.

	Lipid profile Analyte	Mean	Range	p values	
1.	TC-group A	173.17±7.01	85-233	Between group A & B	*0.045*
	TC-group B	149.6±6.93	56-228	Between group C & B	*0.028*
	TC-group C	127.47±7.04	57-235	Between group A & C	*0.0001*
2.	TG-group A	142±11.38	46-309	Between group A & B	0.128
	TG-group B	189.03±24.52	36->500	Between group C & B	*0.017*
	TG-group C	120.8±12.42	53-305	Between group A & C	0.213
3.	VLDL-C group A	29.03±2.29	9-62	Between group A & B	0.162
	VLDL-C group B	37.77±4.91	7-140	Between group C & B	*0.017*
	VLDL-C group C	24.20±2.48	11-61	Between group A & C	0.158
4.	LDL-C group A	106.27±5.41	50-169	Between group A & B	*0.0028*
	LDL-C group B	85.47±4.80	35-152	Between group C & B	*0.077*
	LDL-C group C	72.73±5.21	19-129	Between group A & C	*<0.0001*
5.	HDL-group A	37.9±1.78	16-66	Between group A & B	*0.0015*
	HDL-group B	29.57±1.66	2-44	Between group C & B	*<0.0001*
	HDL-group C	30.53±1.49	15-46	Between group A & C	*0.002*

Table 5shows Lipid profile (mg/dL) in group A, group B and group C.Total cholesterol in group A was 173.17±7.01 (85-233) mg/dL, total cholesterol in group B was 149.6±6.93 (56-228) mg/dL, while in group C total cholesterol was 127.47±7.04 (57-235) mg/dl. Triglycerides in group A was 142±11.38 (46-309) mg/dL, triglycerides in group B was 189.03±24.52 (36-500) mg/dL, while in group C triglycerides was 120.8±12.42 (53-305) mg/dl. Very low density lipoprotein-cholesterol (VLDL-C) in group A was 29.03±2.29 (9-620) mg/dL, VLDL-C in group B was 37.77±4.91 (7-140) mg/dL,while in group C, VLDL-C was 24.20±2.48 (11-61) mg/dL. Low density lipoprotein-cholesterol (LDL-C) in group A was 106.27±5.41 (50-169) mg/dL, LDL-C in group B was 85.47±4.80 (35-152) mg/dL, while in group C, LDL-C was 72.73±5.21 (19-129) mg/dL. High density lipoprotein-C (HDL) in group A was 37.9±1.78 (16-66) mg/dL,

HDL-C in group B was 29.57±1.66 (2-44) mg/dL, while in group C, HDL-C was 30.53±1.49 (15-46) mg/dL.

In case of total cholesterol, the levels of group A and B were significantly different with p value of 0.045. p value between group B and C was 0.028 (significant) while between group A and C was very highly significant (p value <0.0001). In case of Triglycerides, The levels of group A and B were statistically not different with p value of 0.128. p value between group B and C was 0.213 (not significant) while between group A and C was significant (p value 0.017). In case of low density lipoprotein-cholesterol (LDL-C),The levels of group A and B were significantly different with p value of 0.003. p value between group B and C was <0.0001 (highly significant) while between group A and C was significant (p value 0.077).

In case of high density lipoprotein-cholesterol (HDL-C),difference in means of group A and B was statistically significant with p value of 0.0015. p value between group B and C was 0.002 (highly significant) while between group A and C was very highly significant (p value <0.0001).

Table 6 Liver function tests in group A, B and C

	Liver function tests	Mean± SD (IU/L)	Range (IU/L)	p values	
1.	AST-group A	35.83±7.34	15-240	Between group A & B	0.120
	AST-group B	24.9±1.96	8-54	Between group C & B	0.836
	AST-group C	25.47±1.92	8-60	Between group A & C	0.181
2.	ALT-group A	22.53±1.26	12-40	Between group A & B	*<0.0001*
	ALT-group B	14.03±0.82	4-27	Between group C & B	0.440
	ALT-group C	15.93±2.29	7-60	Between group A & C	*0.015*
3.	A:G-group A	1.07±0.05	0.4-1.6	Between group A & B	0.895
	A:G-group B	1.08±0.05	0.8-1.9	Between group C & B	0.350
	A:G-group C	1.14±0.04	0.7-1.8	Between group A & C	0.282
4.	ALB-group A	3.64±0.12g%	2-4.6	Between group A & B	*0.0004*
	ALB-group B	2.98±0.12 g%	0.6-3.8	Between group C & B	*0.042*
	ALB-group C	3.29±0.08 g%	2-3.9	Between group A & C	*0.020*
5.	TP-group A	7.19±0.14 g%	5.6-9.1	Between group A & B	*<0.0001*
	TP-group B	5.88±0.25 g%	1.2-7.5	Between group C & B	0.222
	TP-group C	6.26±0.17 g%	3.8-8.5	Between group A & C	*<0.0001*
6.	TBIL-group A	0.34±0.03mg%	0.1-0.9	Between group A & B	*0.008*
	TBIL-group B	0.23±0.02 mg%	0.1-0.7	Between group C & B	*0.003*
	TBIL-group C	0.14±0.01mg%	0.0-0.3	Between group A & C	*<0.0001*

Table 6 shows liver function tests in group A, B and C. Aspartate aminotransferase (AST) in group A was 35.83±7.34 (15-240) IU/L, AST in group B was 24.9±1.96 (8-54) IU/L, while in group C, AST was 25.47±1.92 (8-60) IU/L. Albumin globulin ratio (A:G Ratio) in group A was 1.07±0.05 (0.4-1.6), A:G Ratio in group B was 1.08±0.05 (0.8-1.9)., while in group C, A:G Ratio was 1.14±0.04 (0.7-1.9). Albumin (ALB) in group A was 3.64±0.12 (2-4.6) g%, ALB in group B was 2.98±0.12 (0.6-3.8) g%, while in group C, ALB was 3.29±0.08 (2-3.9) g%. Total protein (TP) in group A was 7.19±0.14 (5.6-9.1) g%, TP in group B was 5.88±0.25 (1.2-7.5) g%, while in group C, TP was 6.26±0.17 (3.8-8.5) g%. Total bilirubin levels (TBIL) in group A were

0.34±0.03 (0.1-0.9)mg%, TBIL in group B was 0.23±0.02 (0.1-0.7) mg%, while in group C TBIL was 0.14±0.01 (0.0-0.3) mg%.

In case of ALT enzyme, the levels of group A and B were very highly significantly different with p value of <0.001. p value between group B and C was 0.015 (significant) while between group A and C was not significant (p value 0.440). In case of albumin, the levels of group A and B were very highly significantly different with p value of 0.0004. p value between group B and C was 0.020 (significant) while between group A and C was also significant (p value 0.042).

In case of total Protein, the levels of group A and B were very highly significantly different with p value of <0.0001. p value between group B and C was <0.0001 (very highly significant) while between group A and C was not significant (p value 0.22). In case of total Bilirubin, the levels of group A and B were highly significantly different with p value of 0.008. p value between group B and C was very highly significant p <0.0001, while between group A and C was also highly significant (p value 0.003).

Table7. Kidney function tests in group A, group B and group C

	Kidney function tests	Mean ± SD (mg%)	Range	p value	
1	Urea-group A	25.43±2.14	7-58	Between group A & B	0.243
	Urea-group B	28.63±1.34	17-43	Between group C & B	*0.000*
	Urea-group C	21.33±1.36	10-41	Between group A & C	0.112
2	CREAT-groupA	0.92±0.04	0.7-1.7	Between group A & B	0.589
	CREAT-group B	0.96±0.05	0.2-1.6	Between group C & B	0.469
	CREAT-group C	1.33±0.51	0.6-1.6	Between group A & C	0.426
3	UA-group A	4.38±0.63	2.3-22	Between group A & B	0.992
	UA-group B	4.38±0.23	2-6.8	Between group C & B	0.737
	UA-group C	4.21±0.45	2-16	Between group A & C	0.820

Table7 shows Kidney function tests in group A, group B and group C. Urea levels in group A were 25.43±2.14 (7-58) mg%, urea levels in group B were 28.63±1.34 (17-43) mg%, while in group C, urea levels were 21.33±1.36 (10-41) mg%. Creatinine (CREAT) in group A was 0.92±0.04 (0.7-1.7) mg%, CREAT in group B was 0.96±0.05 (0.2-1.6) mg%, while in group C CREAT was 1.33±0.51 (0.6-1.6) mg%. Uric acid (UA) in group A was 4.38±0.63 (3-22) mg%, UA in group B was 4.38±0.23 (2-6.8) mg%, while in group C, UA was 4.21±0.45 (2-16) mg%.

In case of blood Urea, difference in levels of group A and B was not significant with p value of 0.243. p value between group B and C was 0.112 (insignificant) while between group A and C was highly significant (p value 0.0003).

Table 8 Serum amylase, calcium and phosphorus in group A, group B and group C

	Analyte	Mean± SD (IU/L)	Range	p value	
1.	AMY-group A	98.12±30.53IU/L	1.5-964 IU/L	Between group A and B	0.744
	AMY-group B	88.27±11.02IU/L	12-213 IU/L	Between group B and C	*0.013*
	AMY-group C	58.1±3.19 IU/L	24-87 IU/L	Between group A and C	0.202
2.	CA-group A	8.95 ±0.03mg%	6.9-9.8 mg%	Between group A and B	*0.0001*
	CA-group B	7.95±0.05 mg%	3.5-9.7 mg%	Between group B and C	*0.006*

	CA-group C	6.24±0.50 mg%	0.2-8.6 mg%	Between group A and C	*<0.0001*
3.	PH-group A	3.95±30.53 mg%	3.1-5.0 mg%	Between group A and B	*0.003*
	PH-group B	3.52±11.02 mg%	2.6-4.7 mg%	Between group B and C	0.060
	PH-group C	3.27±3.19 mg%	2.1-4.2 mg%	Between group A and C	*<0.0001*

In case of S. Uric acid, the levels of group A and B were not different with p value of 0.992. p value between group B and C was 0.820 (not significant) while between group A and C was insignificant (p value 0.737).

Table 8 shows Serum amylase, calcium and phosphorus in group A, group B and group C.group A had amylase levels as 98.12±30.53 (1.5-964)IU/L, group B amylase levels as 88.27±11.02 (12-213)IU/L and group C amylase levels as 98.12±30.53 (1.5-964)IU/L. Group A had calcium levels as 8.95±0.03 (6.9-9.8)mg/dL, group B had calcium levels as 7.95±0.05 (3.5-9.7) mg/dL, while group C calcium values as 6.24±0.50 (0.2-8.6) mg/dL. Group A had phosphorus levels as 3.95±30.53 (3.1-5.0) mg/dL,group B had phosphorus values of 3.52±11.02 (2.6-4.7) mg/dL, while group C had phosphorus as 3.27±3.19 (2.1-4.2) mg/dL.

In case of total Calcium, the levels of group A and B were very highly significantly different with a p value of 0.0001. p value between group B and C was <0.0001 (highly significant) while between group A and C was significant (p value 0.006). In case Phosphorus, the levels of group A and B were very highly significantly different with a p value of 0.003. p value between group B and C was <0.0001 (highly significant) while between group A and C was significant (p value 0.060)

DISCUSSION

Thirty newly diagnosed histopathologically proven HNSCC cases and thirty age and sex matched healthy controls were enrolled. Cases were followed up after six weeks ofchemoradiation.Cases before &after treatment, and controls were categorized as group A, B and C respectively. The results were analyzed from the three groups and compared statistically.

Mean age of HNSCC cases in present study was 53.37±9.12 years, with a range of 36-74 years. Mean age of group C was 54.63±8.07 years, range being 43-72 years. This age is lower than as mentioned by Sasaki et al, according to whom oral squamous cell carcinoma is more common in men between the sixth and eighth decades of life,and the incidence of oral SCC in young age varies between 0.4% and 6.6%.[10] A study reported most common age group at presentation to be 61-70 years (32.2%) in India. A number of other researchers also found the highest incidence to be in sixth decade (31.13%),[11-13] with mean age of 62.6 years for women and 68.8 years for men. With a shift of lifestyle towards modernization and increased exposure to risk factors (pollution, food additives and preservatives), with each passing day, there is a trend towards involvement of younger population with most of the chronic diseases including cancer. This might be the explanation for lower age group of the subjects. Studies have shown that the disease is more aggressive with poor prognosis in young adults as compared to older age groups.[14] In contrast, some studies have not found any significant difference in survival between different age groups.[15-16]

Out of 30 patients, 11 presented in stage IV (36.7%) whereas 19 (63%) presented in stage 3. No patients presented in early stages i.e. stage I and II. This finding is in accordance with some studies which shows the poor control of this disease amongst the population.[17-18]Around 75% to 80% of patients with cancers present with late-stage incurable disease and so increased

mortality.[19] One reason for delayed diagnosis is the lack of easy access to healthcare, with one study demonstrating a delay of 67.5 days and 53.7 days in obtaining a first appointment for rural and urban patients, respectively. Other reasons included poor socio-economic status of the patient, cost of care, and high rate of illiteracy. As majority of our subjects was rural population, so there is lack of resources and awareness to present at an early stage.A study reported SCC grade I was common among 60-69 years which was also the most prevalent age group for malignancies. This inference was identical to north India where SCC grade I was common among 50-59 years which was the most prevalent age group. Similar age pattern for SCC grade II was observed. SCC grade III was reported to be common in 40-49 years in north India.[20]

The levels of ALT, Albumin, total protein and TBIL in group A and B were very highly significantly different with p value of <0.0001, 0.0004, <0.0001and 0.008 respectively. The levels in cases before treatment were different from controls regarding ALT, Albumin, total protein and TBIL with p values 0.015, 0.020, <0.0001and <0.0001 respectively. According to a report abnormal values were found in 49% patients, including elevated alkaline phosphatase in 26% and lactic dehydrogenase in 18%. Abnormal values were most commonly attributed to alcohol-related liver disease. No liver metastases were identified at initial screening. Abnormal LFTs were seen in 26% of all patients. Overall sensitivity and specificity were 45% and 75%. Seventy-five percent of patients with liver metastasis had stage IV disease at diagnosis and were more likely to have abnormal LFTs than other stages ($P = .048$). In these patients, 2.2% (8/365) had liver metastases and abnormal LFTs, whereas 1.9% (7/365) had liver metastases and normal LFTs.[21]

Plasma urea levels in group A were found to be 25.43±2.14 (7-58) mg%, in group B were 28.63±1.34 (17-43) mg%, while in group C, these were 21.33±1.36 (10-41) mg%. The difference in levels between group A and B were not significant with p value of 0.243, p value between group B and C was 0.112 while between group A and C was highly significant (p value 0.0003). Creatinine (CREAT) in group A was 0.92±0.04 (0.7-1.7) mg%, in group B was 0.96±0.05 (0.2-1.6) mg%, while in group C, it was 1.33±0.51 (0.6-1.6) mg%. Group A and B were statistically not different with p value of 0.589, p value between group B and C was 0.426 (not significant) while between group A and C was also insignificant (p value 0.469). Uric acid (UA) in group A was 4.38±0.63 (3-22) mg%, in group B was 4.38±0.23 (2-6.8) mg%, while in group C, it was 4.21±0.45 (2-16) mg%. Group A and B were not different with p value of 0.992, p value between group B and C was 0.820 (not significant) while between group A and C was insignificant with p value of 0.737.

As per some studies mild nephrotoxicity (BUN, 25 to 30 mg/dL; and/or creatinine, 1.5 to 2.0 mg/dL) was observed (38%) along with other complications like myelosuppression and mucositis. This usually reflected dehydration occurring before cisplatin administration and was reversible with hydration. As per another study, use of cisplatin for six weeks led to transient renal dysfunction in the majority, 27 patients out of 30, completed treatment and renal function returned to normal or near normal in almost all cases.[22] The present study also demonstrates some nephrotoxicity to be associated with cancer treatment as indicated by significantly increased plasma urea levels in patients of HNSCC after treatment as compared to healthy controls.

A study suggested no significant difference in levels of uric acid in patients of HNSCC. Whereas as per Dhankhar et al the levels of uric acid were found to be significantly higher in patients of head and neck cancers as compared to the levels in controls. As suggested by another study increased serum uric acid has been associated with increased head and neck cancer risk. Uric

acid in cancer patients may increase because of increased nucleic acid breakdown of cancer cells.[23] Uric acid levels in the present study were not found to differ significantly among the three groups.

Group A was found to have plasma amylase levels of 98.12±30.53 (1.5-964) IU/L, group B had amylase levels of 88.27±11.02 (12-213) IU/L and group C amylase levels as 58.1±3.19 IU/L (24-87) IU/L. Group A had calcium levels were 8.95±0.03 (6.9-9.8) mg/dL, group B had calcium levels of 7.95±0.05 (3.5-9.7) mg/dL, while group C has calcium values of 6.24±0.50 (0.2-8.6) mg/dL. Group A had phosphorus levels of 3.95±30.53 (3.1-5.0) mg/dL, group B had phosphorus values of 3.52±11.02 (2.6-4.7) mg/dL, while group C had phosphorus values of 3.27±3.19 (2.1-4.2) mg/dL. Amylase levels between group A and C were significant (p value 0.013). Calcium levels of group A and B were very highly significantly different with a p value of 0.0001 and p value between group B and C was <0.0001 (highly significant) while between group A and C was significant (p value 0.006). Phosphorus levels of group A and B were very highly significantly different with a p value of 0.003. p value between group B and C was <0.0001 (highly significant) while between group A and C was significant (p value 0.060)

The changes in serum amylase that occur when radiotherapy is given in the treatment of head and neck cancer has been studied in 41 patients, 29 treated by continuous hyperfractionated accelerated radiotherapy (CHART) and 12 by conventionally fractionated radiotherapy. The peak rise in serum amylase following the start of treatment is seen earlier and is greater in the patients receiving CHART. The serum amylase returns to normal earlier in the CHART patients so that the area under the curve is the same for both groups[24.]As per some studies hypercalcemia is a well-recognized phenomenon in squamous cell carcinoma of the head and neck, but the incidence of hypercalcemia in their study group of patients was not clear. Some other studies also had the same findings. Serine/threonine kinase-33 protein is a member of the calcium/calmodulin dependent kinase (CAMK) family, which exhibits a non-ubiquitous and low level of expression in most tissues.[25] More recently, evidence has indicated the involvement of serine/threonine kinase 33 (STK33) gene in tumorigenesis.[26] Increased phosphorus levels are suggested to meet the demand of diving tumor cells and an study suggested the correlation of increased serum phosphorus and head and neck cancers.[27]

This being a single-centre study carries some limitations, but still provides a present outlook of HNC in the state of Haryana. Head and neck cancers, if detected early, have high cure rates. So, there is an urgent need of biomarkers which can help in early detection as well as monitoring of this disease. IL-6 plays a very significant role in every aspect of cancer as observed in this study and may prove to be a valuable diagnostic and prognostic marker in patients of head and neck squamous cell carcinoma.

CONCLUSIONS & SUMMARY

Plasma glucose in group A was 84.73 ± 2.97 (57-115) mg/dl. Plasma glucose in group B was 103.46±5.15 (61-171) mg/dl. While in group C plasma glucose was 84.73±2.97 (57-115) mg/dl. p value between group A and group B was 0.001. Hence significant difference was found in cases before and after treatment in glucose levels.

Total cholesterol in group A was 173.17±7.01 (85-233) mg/dl. Total cholesterol in group B was 149.6±6.93 (56-228) mg/dl. While in group C total cholesterol was 127.47±7.04 (57-235) mg/dl. were statistically significant in cases before and after treatment.

Total protein of group A and B were very highly significantly different with p value of <0.0001. p value between group B and C was <0.0001 (very highly significant). Means of group A and B

were highly significantly different with p value of 0.008. p value between group B and C was very highly significant p <0.0001, while between group A and C was also highly significant (p value 0.003). Group A had calcium levels as 8.95±0.03 (6.9-9.8)mg/dL, group B had calcium levels as 7.95±0.05 (3.5-9.7) mg/dL, while group C calcium values as 6.24±0.50 (0.2-8.6) mg/dL. Group A had phosphorus levels as 3.95±30.53 (3.1-5.0) mg/dL,group B had phosphorus values of 3.52±11.02 (2.6-4.7) mg/dL, while group C had phosphorus as 3.27±3.19 (2.1-4.2) mg/dL. These values were statistically significant. The levels of group A and B were very highly significantly different with a p value of 0.003. p value between group B and C was <0.0001 (highly significant) while between group A and C was significant (p value 0.060).

The levels of ALT, Albumin, total protein and TBIL in group A and B were very highly significantly different with p value of <0.0001, 0.0004, <0.0001and 0.008 respectively. The levels in cases before treatment were different from controls regarding ALT, Albumin, total protein and TBIL with p values 0.015, 0.020, <0.0001and <0.0001 respectively.The rest of routine biochemical parameters were not statistically significantly different between the two groups.

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