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Status of Various Clinical Attributes and Electrolytes in Oral Cancer Patients from Pakistan

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ABSTRACT

Cancer is a lethal disease and its incidences has been increasing day by day. The survival rates of the cancer patients are lesser due to lack of its awareness, available health facilities and other many socioeconomic conditions to treat it. Various abnormal metabolic and ionic changes occur in throat and mouth cancer patients than healthy persons. In this experiment, with average 36-42 years aged 21 throat and 24 mouth cancer patients were selected to analyze the changes in complete blood counts (CBC), liver functional tests (LFT) and electrolytes. Among the patients, Hb (g/dL) decreased and PLT (10^8/µL) increased significantly in both typed cancer patients than normal healthy persons. Higher ALP and bilirubin levels were observed high ($p \leq 0.05$), while ALT and urea concentration remained unchanged among the patients to normals. Serum electrolytes i.e. Mg^{2+} was observed higher in patients ($p \leq 0.05$), while Cl^- and Ca^{2+} were decreased significantly in both throat and mouth cancer patients. The K^+ mildly increased non-significantly remained within the reference ranges. Changes in biosynthesis of metabolites induces electrolyte imbalanced condition as well as the alterations in HB and PLT may also be caused by imbalanced nutrition-based factors. By early careful monitoring of such indicators in the cancer patients could play a preventive role in cancer disease prognoses.

KEY WORDS: CANCER PATIENTS, ELECTROLYTES, SERUM, CBC, LFTS, PLATELETS.

INTRODUCTION

In the world, the 2nd largest human killer disease is cancer with 25 % of total deaths per year including Pakistan and it has been elevating in numbers continuously (Jemal et al., 2010; Simard et al., 2012; Moore, 2013; Torre et al., 2016; Murray et al., 2020). New cancer incidences are increasing in Asian Pacific regions, while survival rates remained lesser due to lack of cancer awareness, lake of health facilities and other many socioeconomic conditions (Hanif et al., 2009; Begum et al., 2012; Cao et al., 2017; Ashaq et al., 2021). The cancer is the multi-factorial condition of organs or bodies, which have lost the control on their growth with excessive cell proliferation (Weinberg, 1996; Schmelzle and Hall, 2000; Chan and Steven, 2021). The causative cancer agents are originated with mutual sharing of multiple environment and genetic factors (Knox, 2010; Parsa, 2012; Yadav and Khodke, 2015; Caruso et al., 2021; Singh et al., 2021).

The environmental exposure on inters or intra-cellular are developing cancer gradually. Available preventions may be adopted against the accomplished factors, which are actively involved in disruption of cellular signaling pathways (Yadav and Khodke, 2015; Huang and Ping-Kun, 2020). Major priority is still prevention

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of carcinogenic exposures (Anetor et al., 2008; Rudel et al., 2014; Felter et al., 2021), while particular genetic pre-dispositions are more susceptible than others. Like as people with genetic alterations in BRCA1, BRCA2 and p53 locus have lost the abilities to suppress irregular cell growth (Bièche and Lidereau, 1995; Ingvarsson, 1999; Hilton et al., 2002; Narod and Foulkes, 2004; Colonna and Amanda, 2016; Ababou, 2021).

Meanwhile, a number of factors including gene locus, drugs, environment, industrial pollution, chemicals, radiation, food additives, diet, changed life style could be source to contribute in cancer disease process. Even individuals are living in the same environment and in some individual the cancer develop while not in others. The phenomena could be inherited genetic susceptibility for cancer (Douglas and Wildavsky, 1983; Lichtenstein et al., 2000; Hu et al., 2021). Natural chemicals of human diet appear to be major cause of DNA damage (Ames, 1979). In spite of that many studies are emphasizing that cumulative effects of chemicals among the individuals are acting with different path-ways. These chemicals and their related systems among the cells, tissues and organs could be plausibly conspire in the process to induce tumorigenesis and then ultimately into malignancies (Casey et al., 2015; Hu et al., 2015; Narayanan et al., 2015; Mwila et al., 2021).

The electrolyte disturbance might be involved in the mediation of cancerous micro-environment for the pro-carcinogenic outcomes. The role of dysregulation of electrolytes-homeostasis is the most recognized feature, which enable the induction, maintenance and progression of cancer (Woolf et al., 2016; Kamanga and Zhou, 2017; Robey et al., 2017; Diala, 2020). The electrolytes are involved in the regulation of the many intra-cellular systems like as protein synthesis, mutagenesis and oncogenesis. These regulatory intra-cellular metallic Mg, Na, K, Cl, H and Ca ions have specific correlations with physiological and growth rates of the cells. Among the turmeric cells, the elevated concentrations of Na and Cl are observed but Mg and K ions remain normal.

The regulation of Na and Cl concentrations have got prime importance to control their concentrations in both normal and tumor cells (Kopec and Groeger, 1988; Cameron and Smith, 1989; Varghese et al., 2021). It has been considered that many metabolic changes are occurring in cancer diseased organs, while an imbalanced electrolyte character is one of them. The present study is aimed for the careful monitoring of various electrolytes in the serum of cancer patients. As it plays destructive role in cancer prognosis.

MATERIAL AND METHODS

Subjects in the study: In present study, the women participated from Nursing Civil Hospital, Mirpur Khas District are arranged into two groups. The total numbers of subjects were confirmed 45 patients and first group of 21 throat and 24 mouth cancer patients (each group divided into 4 sub-groups with 6-indviduals = 1 replicate). Each individual patient was subjected for clinical as well as biochemical analysis. Here in this study, the confirmed replicates of each category were compared for the subjects reported, ethical clearance for the present study was obtained vide letter Ethical letter No Physiol. / ERI /60 / 08.05.19.

Collection of blood samples: The fresh ten milliliters blood serum samples of selected cancer patients in fasting were collected into standard Vacutainer® plain vials [anti-coagulated with EDTA-K_2 (ethylene di-amine tetra-acetic acid-dipotassium] from each participant in the blood diagnostic laboratory. The half of each blood sample was transferred for hematological analysis and other half allowed stand at room temperature to clot. The clotted blood was centrifuged for 15 min at 3,000 rpm for 15 min and plasma/serum used for electrolyte estimation and other different biochemical analysis (Alghamdi et al., 2012; Kumar and Gill, 2018).

Hematological Analysis of Samples: A number of hematological attributes were analyzed in collected blood samples of the patients. The parameters including CBC (complete blood count), hematocrit (HCT), Hb level, mean cell Hb (MCH), MCH concentration (MCHC), mean cell volume (MCV) and red blood cell distribution width were determined with Hematology Analyzer (Model-Advia 2120, Bayer Diagnostics, USA) and the liver marker i.e. alanine aminotransferase (ALT), alkaline phosphatase (ALP), total bilirubin and creatinine and red cell distribution width (RDW) were determined with Beckman Coulter Automatic Biochemical Analyzer by following their procedure given in the manuals (Harthoorn-Lasthuizen et al., 1999; Bereket et al., 2011; Koster, 2015; Wang et al., 2017; Haq et al., 2018).

Determination of Electrolytes: Before absorption, the samples were digested by taking 0.5 ml sample in glass tubes than 3 ml crucibles (20 ml conc. HNO_3 + 40 ml H_2O_2) added. The mixture was placed at hot plate (90°C) for 2 hrs. When sample color appears a pale-yellow allow it to cool-down and 10 ml 0.2 M HNO_3 added. Its filtrate is used to run on atomic absorption spectrophotometer [Hitachi-Ltd 180-50 (Sr. #. 5721-2) with graphite furnace G-03] and ion selective electrode (ISE) methods (Transasia Bio-Medicals Ltd) for analysis of electrolytes including sodium, magnesium, calcium and chloride (Kamei et al., 1998; Kazi et al., 2006; Yadav and Khodke, 2015).

Statistical Analysis: The present study was comprised on 04 replicates per cancer patient's category. The collected data expressed as mean with standard error (St. Err.) and these analyzed with CoStat (version 3.03) CoHort software (Berkeley, USA). The significant ($p \leq 0.05$) mean values further analyzed with Duncan Multiple Range Test (DMRT) at 5 % (d Steel and Torrie, 1986; Behrens, 1997; Johnson and Bhattacharyya, 2019).

RESULTS AND DISCUSSION

The cancer prevalence has been increasing day by day, leading to acute need of care for growing population

of patients. It is essential to adopt patient-centered approach to achieve good quality care. There step-care approach (i.e. correct and timely detection) for these patients is crucial to manage the increasing severity of the disease. In present study, clinical samples of 21 throat and 24 mouth cancer patients (36-42 years aged) were subjected for various biochemical assessments including complete blood counts (CBC), liver functional tests (LFT) and electrolytes (Table 1).

Table 1. Comparative analysis of clinical attributesincluding electrolytes in patients of mouth and throat cancers to healthy persons.

#s.	Characters	Reference values	Healthy persons	Cancer patients		F-signif-icance
				Mouth	Throat	
A. Complete blood count (CBC) analysis						
01.	Hb (g/dL)	13.0-18.0	^{a}13.93±0.281	^{b}11.20±0.667	^{b}11.53±0.599	7.527^{ns}
02.	WBC (109/L)	3.50-10.0	^{b}8.100±0.158	^{a}10.55±0.790	^{b}12.300±0.579	13.87**
03.	RBC (1012/L)	3.50-5.50	^{b}4.855±0.197	^{a}5.248±0.449	^{b}3.800±0.171	6.235^{ns}
04.	HCT (%)	35.0-55.0	^{a}36.75±1.461	^{b}34.00±1.046	^{bc}32.38±0.892	3.645^{ns}
05.	MCV (fl)	75.0-100	^{a}85.90±0.938	^{ab}83.73±2.939	^{b}73.40±0.660	13.44**
06.	MCH (pg)	25.0-35.0	^{a}27.15±0.504	^{b}23.63±1.250	^{ab}26.13±0.774	4.083^{ns}
07.	MCHC (g/dl)	33.0-38.0	^{a}35.25±0.841	^{ab}34.00±0.471	^{b}33.13±0.507	2.884^{ns}
08.	RDW (%)	11.5-15.5	^{a}13.21±0.121	^{b}16.45±0.074	^{ab}15.42±0.147	3.224^{ns}
09.	PLT (108/µL)	150-400	^{a}253.8±11.24	^{b}342.0±14.14	^{c}410.3±9.801	43.74***
10.	NEU (%)	35.0-80.0	^{b}62.25±2.428	^{a}79.75±2.496	^{a}79.75±2.955	14.67**
11.	LYM (%)	15.0-50.0	^{a}31.00±1.472	^{b}48.25±1.887	^{b}52.50±2.102	28.95***
12.	MO (%)	2.00-10.0	^{a}3.250±0.479	^{b}2.250±0.250	^{b}2.000±0.000	4.500^{ns}
13.	EOS (%)	1.00-6.00	^{a}3.000±1.472	^{a}2.250±1.887	^{a}2.250±2.102	1.929^{ns}
14.	BASO (%)	0.00-0.20	^{a}0.119±0.013	^{b}0.093±0.001	^{b}0.087±0.004	5.148^{ns}
B. Liver functional tests (LFT)						
01.	ALP (UL^{-1})	36.0-141	^{a}120.5±4.444	^{b}96.75±5.360	^{c}81.50±4.330	17.24**
02.	ALT	4.0-38	^{a}20.75±1.887	^{b}12.75±1.797	^{b}15.00±1.225	6.158^{ns}
03.	BR (mg dl^{-1})	0.20-1.2	^{a}0.950±0.065	^{a}0.825±0.144	^{b}0.425±0.048	8.331^{ns}
04.	Urea (mg dl^{-1})	10.0-40.0	^{b}17.63±1.253	^{a}56.30±2.464	^{a}50.00±3.536	64.14***
05.	Crt (mg dl^{-1})	0.4-1.40	^{a}0.880±0.149	^{a}2.175±0.858	^{a}1.075±0.111	1.899^{ns}
C. Electrolyte analysis						
01.	Mg^{2+} (mg/dL)	1.50-2.10	^{b}1.761±0.085	^{a}2.188±0.035	^{a}2.228±0.049	18.55**
02.	K^{+} (mmol/L)	3.50-5.0	^{a}4.165±0.070	^{b}4.425±0.078	^{b}4.458±0.077	4.561^{ns}
03.	Cl^{-} (mmol/L)	95-108	^{a}101.8±1.071	^{b}97.70±0.615	^{b}97.00±0.221	12.84**
04.	Ca^{2+} (mg/dL)	8.10-10.2	^{a}9.248±0.129	^{b}8.638±0.098	^{b}8.633±0.097	10.56*

CBC: Complete blood count, RBC: Red blood cells, Hb: Hemoglobin, MCV: Mean corpuscular volume, HCT: Hematocrit, MCH: Mean carpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW: Red cell distribution width; NEU: Neutrophillus, MO: Monocytes, EOS: Eosinophillus, LYM: Lymphocytes, BASO: Basophillus, WBC: White blood cells, PLT: Platelets, ALP: Alkaline phosphatase, ALT: Alanine aminotransferase, BR: Bilirubin, Crt: Creatinine, Mg+2: Magnesium, K+: Potassium, Cl-: Chloride, Ca+2: Calcium.

Note: The data shown in table is mean of four replicates expressed as mean ± SE. The Duncan's Multiple Range (DMR) test calculated at 0.05 % significance ($p \leq 0.05$).

As in table 1, results showed that means of red cell indices in both mouth and throat cancer patients likely to MCV (83.73±2.939 fl and 73.40±0.660 fl; $p \leq 0.05$), MCH (23.63±1.250 pg and 26.13±0.774 pg; non-significant) (34.00±0.471 pg and 33.13±0.507 pg; non-significant) and MCHC (34.00±0.471 g/dl and 33.13±0.507 g/dl; non-significant) observed lowered respectively than healthy control person. The mean values of red cell distribution width (RDW) observed higher in the patients than healthy persons but non significantly. The hematological tumors have observed in close relation with malnutrition, changes in microenvironment and disturbances in erythropoiesis, while RDW levels symbolize the functional survival of abnormal RBC (red blood cell) (Mantovani et al., 2008; Lee et al., 2014; Huang et al., 2016; Matsui et al., 2021).

From other CBC parameters, the WBCs, lymphocytes and neutrophil showed higher concentrations in both typed cancer patients than healthy controls. Due to a fact that neoplasms are associated neutrophilia, so demarginating neutrophils are normally tumor cells which are occupying the vascular spaces. These are killed by $CD8^+$ cytotoxic T-lymphocyte without prior sensitization, while for evading immunity, there is downregulation of class 1 MHC (major histocompatibility complex) molecule's expression (Warren et al., 1994; Swigut et al., 2004; Mwimanzi et al., 2017). There the lymphocyte count observable either elevated or depressed. The platelet counts also found higher in cancer patients than healthy control (Table 1).

From the results of liver function tests, the blood urea is a sensitive indicator of abnormal renal functions. Its levels from control to patients were increased (Chauhan, Yadav, Kaushal, & Beniwal, 2016). The serum creatinine (Crt) level is further considered as more sensitive over urea for kidney function and it is observed increased ($p > 0.05$) in patients (Devi, 2015). Meanwhile, increased levels of serum uric acid among the cancer patients (Iseki et al., 2001; Zhu and Cao, 2012; Nincevic et al., 2019) associated renal insufficiencies (Hunsicker et al., 1997; Iseki et al., 2001; Rapa et al., 2020). Activities of serum alkaline phosphatase (ALP) observed significantly lower than healthy persons.

In other studies, the observed parameter was found between the normal ranges (Stieber et al., 1992; Van Hoof et al., 1992; Ray et al., 2017). Similar trend in data also observed total bilirubin levels (Liu et al., 2014). For alanine aminotransferase (ALT), data showed lower ALT in both typed cancer patients than healthier ones but between the normal ranges. The ALT is a sensitive indicator but lack in specificity for hepatocellular injury as it is also in muscles and kidneys (Söderberg et al., 2010; Weber et al., 2019).

he data about the serum electrolytes, the Mg^{2+} levels observed significantly higher from the healthy persons (1.761 ± 0.085 mg/dL) in the mouth (2.188 ± 0.035 mg/dL) and throat (2.228 ± 0.049 mg/dL) cancer patients, while non-significant increase in K^+ level found among the patients. The serum chloride levels in normal healthy controls were 101.8 ± 1.071 mmol/L, whereas 97.70 ± 0.615 mmol/L and 97.00 ± 0.221 mmol/L in mouth and throat cancer patients respectively. The statistically significant low chloride (Cl) levels were observed in serum of cancer patients from healthy controls but values remained within the reference ranges (McAndrew et al., 2021). Alea et al., (2017) group found that serum levels of Ca^{2+} was significantly decreased in patients in comparison to control group (Thompson, 2010; Doshi et al., 2012; Ephraim et al., 2014). The electrolyte imbalance causes additional risk factor in cancer patients. The prior detection of electrolyte levels night be helpful for the clinicians to manage the cancer prognosis and their proper monitoring (Berghmans et al., 2000; Capdevila et al., 2018; Fassnacht et al., 2018).

CONCLUSION

We have concluded in present study that the imbalanced attributes of CBC, LFTs and electrolyte contents impose additional health risk factors in cancer patients. Their prior detection among the patients might be helpful for the clinicians to manage the cancer prognosis and their proper monitoring. This study of bio-content's analysis may be a helpful diagnostic tool in terms of minimizing the imbalanced characters in patients with different supplements.

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