FREQUENCY OF INCREASED PLASMA C-PEPTIDE LEVELS IN COLORECTAL CANCER PATIENTS

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ABSTRACT

Objective: To assess the increased frequency of serum C-peptide levels in patients of colorectal carcinoma.

Study Design: Cross sectional study.

Place and Duration of Study: Combined Military Hospital, Rawalpindi Pakistan, from Jul 2018 to Jan 2019.

Methodology: A total of 100 cases of colorectal carcinoma were enrolled. Blood samples were obtained to assess C-peptide level. The C-peptide serum concentrations were deliberate through the Cobas 6000 by using the electro-chemi-luminescence immunoassay (ECLIA) method. If level of C-peptide was >2 pmol/mL, then it was noted.

Results: The mean age of all patients was 58.3 ± 5.4 years. There was a total of 136 (68%) females and 64 (32%) were males. The mean BMI of patients was 28.96 ± 12.31 kg/m². The family history of colorectal carcinoma was positive in 6 (6%) cases. The mean C-peptide level was 4.55 ± 2.37 pmol/L. There were 33 (33%) patients with raised C-peptide level while 67 (67%) had normal c-peptide level.

Conclusion: It is concluded that increased C-peptide level is high in patients with colorectal cancer.

Keywords: Colorectal cancer, C-peptide, dense energy, IGF binding protein-1.

INTRODUCTION

Cancer is the most lethal disease all over the world. Nearly about 14.1 million people have newly diagnosed cancer and 8.2 million deaths occurred due to cancerous diseases.[1,2] Colorectal carcinoma is the 3rd most common cancer diagnosed all over the world and it is the 2nd leading cause of cancer-related mortalit.[3] The development and growth of a benign adenoma to the malignant adenocarcinoma may be stimulated when mutations and epigenetic modifications occur in several genes inside the body.[4]

The frequency of cancer related morbidities and mortality are expected to raise with age and western standard of living. Junk food, obesity and sedentary lifestyle significantly affect the risk of colorectal carcinoma. Previous researches proposed that the impact of such risk factors may mediate due to increase in serum insulin level and in bioactivity of insulin-like growth factor-I.[5] The colorectal cancer had several risk factors including, the physical inactivity, obesity, dietary pattern, processed meat and the dense energy food.[6,7]

Many studies proved the types of lifestyles are significantly associated with colorectal carcinoma like

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change in insulin metabolism and associated growth factors.[8,9] Few studies found that there is significant association of serum C-peptide level and carcinoma. In few studies, increased risk of carcinoma was observed because of inappropriate adiposity.[10] Rationale of this study was to assess the frequency of increased plasma C-peptide levels in patents with colorectal cancer. There is very scarce data regarding raised C-peptide level in cancer patients. Therefore, this study would help us to get local data and we would be able to implement results in local setting.

METHODOLOGY

This cross sectional study was conducted at Combined Military Hospital, Rawalpindi, from July 2018 to January 2019 after taking permission from Institutional Ethical Review Board (IERB no.: 24125172). Sample size of 100 cases were calculated with 95% confidence level, 9% margin of error and percentage of raised C-peptide level i.e. 29% in patients with cancer.

Inclusion Criteria: Patients of either gender, aged 16-85 years with colorectal carcinoma diagnosed on biopsy were included in the study

Exclusion Criteria: Patients having cancer other than colorectal or metastasized carcinoma, patients with raised C-peptide level and taken treatment before diagnosis of colorectal carcinoma were not included.

Study participants were recruited through non-probability, consecutive sampling technique. Informed consent and demographics were noted. Blood samples were obtained by using a disposable syringe under aseptic measures. All samples were sent to the laboratory of the hospital to assess C-peptide level. The entire drawn blood samples were centrifuged and stored in ice room. The C-peptide serum concentrations were deliberate through the Cobas 6000 by using the electro-chemi-luminescence immunoassay (ECLIA) method. If level of C-peptide was >2 pmol/mL, then it was noted.

All the information was entered electronically to MS Excel sheets and analyzed by using SPSS-23. Descriptive statistics was calculated i.e. mean ± SD for numeric variables and frequency & percentage for categorical variables.

RESULTS

The mean age of patients was 58.3 ± 5.4 years. There were 68% females and 32% were males, showing more females involved in having colon cancer. The mean BMI of patients was 28.96 ± 12.31 kg/m². The family history of colorectal carcinoma was positive in 6% cases. There were 30% smokers, 37% had history of doing exercise. Out of 100 cases, 21% were using meat once a month, 55% were taking meat 3-4 times per month while 24% taking meat >4 times per month. The mean C-peptide level was 4.55 ± 2.37 pmol/L (Table).

Table: Demographic and diagnostic characteristics (n=100).

Parameter	Frequency / Mean ± SD
Age (Mean ± SD)	58.3 ± 5.4 years
Gender	
Male	35
Female	65
Body Mass Index	
<23	30
23-25	30
>25	40
BMI (Mean ± SD)	28.96 ± 12.31 kg/m²
Family History (Colorectal Cancer)	
Yes	6
No	94
Smoking Status	
Yes	30
No	70
Exercise	
Yes	37
No	63
Red Meat (Intake)	
Once a month	21
3-4 times a month	55
More than 4 times a month	24
C-peptide level (Mean ± SD)	4.55 ± 2.37 pmol/L

There were 33% patients with raised C-peptide level while 67% had normal c-peptide level shown in the Figure.
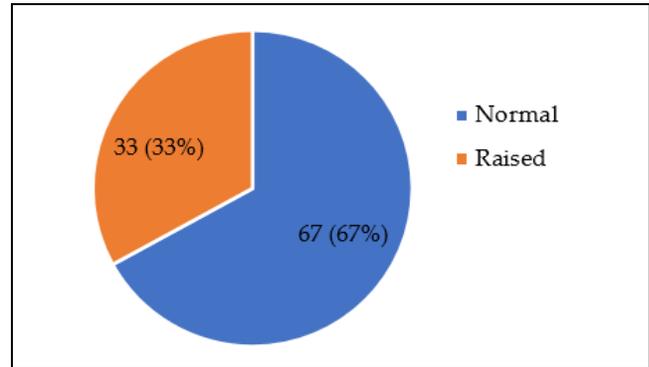
Figure: Distribution of C-peptide level.

DISCUSSION

Malignant tumors have some characteristics in common with diabetes mellitus, regarding to the variations in hormonal and cellular invulnerability. The hemoglobin A1c level reveals mean level of blood glucose during past 2-3 months. It has also been identified that prolonged high levels of high blood sugar can cause the dysfunction of cell immune-regulatory system and may disrupt the T-lymphocyte quantities. C-peptide level, insulin's concomitant, may increase because of secretion of ectopic hormone from the tissues of tumor lesion. These high levels can be examined in the blood of individuals having malignant tumors. These tumors may develop in lung, liver or colorectal in form of malignant tumors.[11] Moreover, the higher manifestation of the insulin-like growth factor-I in individuals having diabetes mellitus (type-II) may persuade an over-expression of N-myc mRNA & proteins. These can cause the dysfunction of *p*53, abnormality of cell senescence and carcinoma.[11]

In different risk factors, which are associated with type II diabetes mellitus and lung carcinoma, life-style, nutritional intake and many environmental factors have significant resemblances, proposing that type-II diabetes mellitus may amplify the hazard of the carcinogenesis inside lungs.[12] In addition to that, the levels of Hb A1c, C-peptide & insulin-like growth factor-1 are thoroughly associated with the initiation and growth of diabetes mellitus. Different studies conducted previously, have reported that diabetes mellitus can am increase the risk of developing different types of carcinomas in the body. Nevertheless, the frequency of such studies which were conducted to determine the

association among patients with diabetes mellitus and lung carcinoma is limited.[13,14]

The present study done to assess the frequency of increased C-peptide levels in colorectal cancer patients. There were 33 (33%) patients with raised C-peptide level while 67 (67%) had normal c-peptide level. Fogar *et al*, reported that percentage of raised C-peptide level i.e., 29% in patients with gastrointestinal cancer.[15] While another study found 64.5% raised c-peptide in patients with colorectal carcinoma.[16] Choi *et al*, found that the mean C-peptide level was 4.7 ± 3.1 ng/mL in patients with colorectal carcinoma and 4.2 ± 2.2 ng/mL in patients without colorectal carcinoma (p=0.10).[17]

The chief regulator in energy metabolism is insulin and the insulin elevates the IGF-1 bioactivity through the IGF binding protein (BP)-1 and BP-2 (IGFBP-2). Due to increased cell proliferation process, a tumor formation occur with insulin and IGF-1 anabolic signals.[18,19] C-peptide level was inversely related to consequent prostate cancer diagnosis, alike to association for adiposity. Fogar *et al*., found the percentage of raised C-peptide level in 29% patients with gastrointestinal cancer.[15]

Less IGFBP-I concentration and raised insulin or C-peptide concentrations are found to be correlated with high risk of colorectal carcinoma. But literature also examined the IGFBP-1 & C-peptide concerning adenomatous polyps, only known predictor of colorectal carcinoma.[16] Serum C-peptide level was also related to slight high risk of the prolonged carcinoma related morbidity and mortality in females. An identical association in C-peptide and risk of carcinoma related mortality were not detected in males.[20]

It was also suggested that metabolic syndrome shows significant rise the risk of non-cardiovascular mortality mainly in post-menopausal females but not in males. These findings proposed a gender-specific risk of carcinoma related to metabolic syndrome. Correspondingly, the association in adiposity, sexual hormones & inflammatory reactions may be associated to association in C-peptide level and carcinoma consequences in both males and females.[21] Recognizing the new ligands which can precisely target colorectal carcinoma may disentangle innovative perceptions to progress the exceptional directed treatments. Human colorectal carcinogenic cell lines are convenient pre-clinical model systems, as they thoroughly look like basic lesions to tumors.[22,23]

In another published study upon the health workers with age ranging similar to patients in our study, the serum C-peptide levels were observed highly associated with serum insulin in both; fasting & non-fasting condition. In the same study, the intra-personal for serum C-peptide was measured with four years gap was quite good. On the contrary basis in the current study, due to the lack of quality control and the imperfect long-term intra-personal association may incline the association and propose the true basic association in C-peptide and colorectal carcinoma is very strong.[24] Previous literature detects the raised risk of colorectal carcinoma related to high serum insulin and C-peptide levels. In addition, it was reported that prolonged insulin treatments were significantly related to high chances of colorectal carcinoma in patients of type 2 diabetes.

Hidaka *et al*, conducted a study to find the association of serum insulin and glucose distinctively on risk of cancer. They inspected the relationship of serum C-peptide, the substitute marker of insulin and glycated albumin, the additional steady marker of serum glucose, with risk of all-organs & organ-specific cancer after controlling the confounding effects of effect modifiers. The study was a prospective cohort, conducted on around 4,000 patients of cancer who were selected out of 33,736 individuals from a population-based cohort. These patients replied to the basic questionnaire and provided the blood samples. The patients of diabetes mellitus were excluded from the study. Data analysis was conducted on 3036 cancer patients and 3667 sub-cohort individuals. In both male and females, the highest concentrations of C-peptide were associated significantly with the high chances or risk of all-organs [Hazard ratio:1.21; 95% confidence interval: 1.02-1.42], liver [3.23; 95% confidence interval: 1.76-5.91], colon [1.73; 95% confidence interval: 1.20-2.47], kidney, renal pelvis and ureter malignancy [2.47; 95% confidence interval: 1.07-5.69], as compared to respective lowest concentrations, after adjusting for glycated albumin concentration. Amongst these C-peptide-associated malignancies, liver and colon malignancies also exhibited an augmented risk accompanying with raised glycated albumin concentrations autonomously, without C-peptide concentration. The resultant hazard ratios for liver and colon malignancies as compared to highest glycated albumin concentrations was 1.43 [95% confidence interval: 1.02-2.00] while for lowest glycated albumin concentrations was 2.02 [95% confidence interval: 1.15-3.55], respectively. Effect adjustment by gender was the only proof regarding the relationship of C-peptide with colon malignancy (p-value=0.04). Higher insulin concentrations, excluding the effect of

high blood glucose concentration, might be significant to diabetes-related carcinogenesis in malignancies of many organs. Investigation of insulin concentration flowing in the blood is an acceptable option in assessing the risk of malignancy or cancer, even in cases who do not have diabetes mellitus.[25]

LIMITATION OF STUDY

The current study limitations might include the measurement of C-peptide for only a single time could reduce the evaluation ability of linkage among long term circulating C-peptide concentration with the colorectal adenoma. The current study owes a smaller sample size that could be a reason for a probable power of the analysis and the study. Therefore, a larger study with large sample size is essential to provide more realistic and accurate perditions and results.

CONCLUSION

It is concluded from this study that It is concluded that increased C-peptide level is high in patients with colorectal cancer.

Conflict of Interest: None.

Authors' Contribution

MHS: Concept and design of study, statistics, data collection, SN: Critical revision of article, statistic, MZS: Data collection, drafting of article, HS: Data collection, drafting of article, SM: Critical revision of article, statistic, MA: Critical revision of article.

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