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Research Article

A study of coagulation profile in patients with cancer in a tertiary care hospital

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Introduction

The complicated process of cancer triggers many physiological systems like vascular endothelial functions and hemostasis, which signifies the increased risk of thrombosis, which triggers thromboembolic events resulting in increased mortality and morbidity [1-3]. Tumorigenesis contributes by activation of coagulation around the perivascular region [4].

Patients with cancer of the gastrointestinal tract, pancreas, and lung are more prone to hypercoagulability [5]. Previous studies on breast cancer have also shown a hypercoagulable state with increased tissue factor, fibrinogen, prothrombin time (PT), Activated partial thromboplastin time (APTT) [6-8]. In patients with colorectal cancer, D-dimer levels correlate with tumor cells' invasion at the time of surgery [9]. These findings are explained by the fact that the inflammatory response is associated with neoplasia by changing the protein metabolism or venous stasis. Procoagulants, including tissue factor, phospholipid PS (phosphatidylserine) secreted by tumor cells, are assumed to promote angiogenesis and tumor cell growth. In Disseminated intravascular coagulation (DIC) due to the consumption of platelets and clotting factors V and VIII, fibrinogen decreases in quantity in blood circulation [10].

Relation of prognosis and coagulation tests for various tumors have been reported, but the concurrence of cancer and coagulation abnormality has not been reported so far. The risk in patients with malignancy has been discussed in various studies but shows conflicting results. Prandoni, et al. [11-13]. did not find any association between patients with cancer and those without cancer. This study aims to correlate the coagulation profile with the frequently encountered cancers and help the clinicians detect DIC at an early stage and manage the patients at different cancer stages.

Methods

This is a Laboratory-based observational study done at RL Jalappa hospital and research center in the Kolar district of Karnataka. A total of 252 patients were retrospectively included. Data regarding the coagulation parameters and histopathological diagnosis, including malignancy, were collected from the Central diagnostic research laboratory (CDLS) using Laboratory information system software. Ethical clearance was taken from Institutional Ethics Committee. Patients diagnosed with malignancy proved either with trucut biopsy of the primary lesion or metastatic site or from resected specimens, between June 2018 to June 2020 on histopathology were included retrospectively, and those who received oral/parenteral anticoagulants or those with a history of thrombosis within the last three months were excluded from the study. For histopathological diagnosis, tissue sections (2-3 mm) were deparaffinized and stained on Hematoxylin and eosin. Hemoglobin, total leukocyte counts, platelet count, were done on Sysmex XN-550, and pretreatment PT, APTT, and INR were done on Erba Manheim ECL 412 were collected for analysis. Cut off for hemoglobin of 12 mg/dl was selected to categorize the patients irrespective of their gender, into two low and normal groups. Similarly, patients with total leukocytes of more than 11000 cells/cumm were categorized into the elevated group instead of normal.

Data were entered into Microsoft Excel datasheet and analyzed using SPSS 22 version software. Categorical data are represented in the form of frequencies and proportions.

Chi-square test was used as a test of significance. Continuous data were represented as mean and standard deviation. The independent t-test was used as a test of significance to identify the mean difference. p - value < 0.05 was be considered statistically significant.

Results

252 patients diagnosed with malignancy were included, with the median age of diagnosis of 57 years, ranging from 16 to 75 years. The most common type of malignancy found in this study was squamous carcinoma of the oral cavity (32.9%), followed by cervical malignancy (18.6%) and breast (13.1%), gastrointestinal tract (9.5%). Other types were cancers of the endometrium, kidney, pancreas, lung, penis, ovary, and salivary gland. The control group matched with age and sex but without a history of malignancy. Median PT value was calculated for cases and control groups and found to be 14.4 seconds and 14.1 seconds, respectively. Similarly, the median APTT value was 36.8 seconds and 36.2 seconds for cases and control groups, respectively. Coagulation tests included PT, APTT, International normalized ratio(INR), and platelet count, showed significant differences between control and case groups with ($p < 0.05$). Although the patient group had more increased PT cases, it was not statistically significant ($p = 0.09$). In cases with cancer, the median value of hemoglobin was 11.7 g/dl and ranging from 5.1 to 15.7 g/dl, and in controls, the median value of hemoglobin was 13.1 g/dl with a range of 11.2-15.7 g/dl. On comparing both the groups of cases and controls, subjects with cancer showed decreased hemoglobin, but the difference was not statistically significant ($p = 0.1$). In cancer cases, the median value of total leukocyte count was 7.66 thousand and ranging from 3.5-15.6 thousand/cumm, and in controls, the median value of total leukocyte count was 6.8 thousand/cumm, ranging from 4.6-10.5 thousand/cumm. Comparing both the groups of cases and controls, subjects with cancer showed increased leukocyte count with significant differences statistically ($p < 0.05$). The median value of platelet count in the control group was 210 x 10^3/cumm with a range of 166-252 x 10^3/cumm, and in subjects with cancer, 210 x 10^3/cumm with a range of 166-252 x 10^3/cumm. When comparing these groups, cases showed thrombocytosis, and the difference was significant ($p < 0.05$) statistically (Table 1).

Discussion

Three processes in physiological systems linked to each other are hemostasis/fibrinolysis and angiogenesis but remain silent under normal conditions. However, with the tumor formation, these mechanisms lead to the expansion of tumors and also causes invasion of tumor [10]. During the study, hemoglobin was slightly lower in subjects with cancer than in the control group, but the difference was not statistically significant. Anemia is due to inflammation/chronic disease, blood loss depending on the site may be also common (e.g. stomach, bladder, uterina and cervical carcinoma). Similar findings were observed in a study done by Rickles, et al. [14]. on breast cancer patients. Total leukocyte count in this study was lower in subjects with cancer than controls though it was non-significant statistically. The platelet count was significantly higher ($p < 0.05$) in patients with malignancy compared to the control group. Thrombocytosis in cancer patients is due to compensation of DIC, which is similar to the findings of a previous study done by Kirwan, et al. [15]. done on breast cancer patients. A significant difference ($p < 0.05$) was found in PT between cases and controls. PT was found to be higher in cancer patients as compared to normal controls. A significant difference was found when comparing the INR in cases and the control group. Both raised PT and INR indirectly reflects an ongoing consumption of coagulation assays through the exaggerated fibrinolytic process.

Our analyses are consistent with the study conducted showing the significant difference between patient and control group concerning coagulation parameters, which involve fibrinogen, APTT, and INR [15,16]. In conclusion, almost all coagulation tests show significant differences in patients with cancer. The current study supports the importance of raised plasma PT, APTT, and INR as a DIC predictor. As PT, APTT, and INR tests are neither time consuming nor expensive, this proposal appears to be compatible with routine practices and deserves further meta-analysis.

Table 1: The values of coagulation profile in patients with cancer and healthy controls.

Coagulation profile	Cases (n = 252)		Control (n = 100)		p value
	Median	Range	Median	Range	
PT (seconds)	14.4	11.4-29.9	14.1	10.9-15.7	0.09
APTT (seconds)	36.8	12.5-81.7	32.2	24.2-36.7	< 0.05
INR	1.125	0.82-1.64	1.01	0.8-1.12	< 0.05
Platelet (x10^3/cumm)	290	45-520	210	166-252	< 0.05

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