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Original Research Article

Coagulation Profile of Cancer Patients in a Tertiary Care Hospital Located in North Bihar

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Abstract

Introduction: Cancer patients exhibit marked derangements in hemostatic system, which leads to increased risk of thrombosis and hemorrhage. They are more prone to develop a hypercoaguable state or chronic DIC. With the spread of malignancy fibrin production and fibrinolysis are both increased, with elevated platelet, tumor microparticles and D dimer levels. Deep vein thrombosis and pulmonary embolism can have disastrous consequences. By analysing the BT, CT, PT & APTT and other coagulation parameters the morbidity and mortality can be reduced.

Materials and Methods: All patients with proven cases of malignancy were included with healthy controls. Venous blood anticoagulated with EDTA & Tri sodium citrate was obtained for platelet count and coagulation studies respectively. PT, APTT values and platelet counts were obtained from the patients along with comparison of control cases.

Results: In our study, most cases showed thrombocytosis (38%) compared to controls (2%), with increased Prothrombin time (90%), Activated partial thromboplastin time (58%) compared to age matched controls having PT and APTT values mostly within reference range.

Conclusion: Cancer patients exhibit deranged coagulation profiles compared to normal population. It is imperative to obtain coagulation parameters in such patients as it reflects their overall health status and risk of complications related to coagulation abnormalities. They help predict the risk of bleeding or thrombotic events.

Keywords: Prothrombin time, Activated Partial Thromboplastin time, Coagulation profile, Malignancy.

Introduction

Malignancy is characterized by a derangement of the hemostatic system which predisposes cancer patients to both thrombosis and hemorrhage. Both thrombosis and haemorrhage are more likely to occur in people with cancer because of the hemostatic system disturbances caused by the disease. Hematological malignancies have a thrombotic incidence comparable to that reported in solid tumours with a high risk of thrombosis, hence thrombotic events are now understood to represent serious consequences

for patients with both types of cancer. Acute leukaemia is a disease characterised by a wide range of hemostatic consequences, including bleeding and uncompensated disseminated intravascular coagulation (DIC).[1]

In 1865, Armand Trousseau first identified a clinical link between thrombosis and a malignancy that had not yet been characterised. Patients with cancer are more likely to develop a hypercoagulable condition or chronic DIC due to the disease's propensity to stimulate blood coagulation. In cancer patients, abnormalities in one or more coagulation tests are widespread, even in the absence of obvious thrombotic and/or hemorrhagic symptoms. Fibrin production and fibrinolysis, as shown by laboratory testing, has been shown to increase in tandem with the spread of malignancy.[2] Elevated levels of circulating microparticles (MP) shed by tumour cells and platelets, as well as high levels of prothrombin fragment 1+2 [F1+2], fibrinopeptide A [FPA], thrombin-antithrombin complex [TAT], and D-dimer, are some of the minor hemostatic modifications that have been found.[3,4] However, tumour development and metastasis are intertwined with hemostatic proteins and responses.[4]

Blood clot activation in cancer has a complicated and multifaceted aetiology. However, the development of clot-promoting characteristics by tumour cells is a characteristic of malignancy.[5] By virtue of these characteristics, the clotting cascade is initiated, and thrombin and fibrin are produced, while platelets, leukocytes, and endothelial cells are stimulated to display their cellular procoagulant traits. In particular, factors that are rich in matrix metalloproteinases (MPs) and angiogenic growth factors (NGFs) are emerging as key facilitators of tumour growth.[4] A decade ago, researchers uncovered a complicated situation in which oncogenic processes promote the procoagulant conversion of tumour cells, expanding our understanding of how tumours spread and metastasize.[6]

Although both arterial and venous thrombosis are possible in cancer patients, thrombotic venous occlusions have received greater attention. When compared to the general population, the risk of having venous thromboembolism (VTE) is up to seven times higher in this group.[7] Due to advances in oncology, increased administration of thrombogenic treatment, and an ageing population, this incidence has increased in recent years. Finally, thrombosis may be the first indicator of a malignant condition, appearing months or even years before cancer is diagnosed clinically.[8]

Cancer patients are at a higher risk of thrombosis due to a number of variables, including general risk factors like inactivity, old age, and surgery, and cancer-specific risk factors including the kind of cancer, the stage of illness, and the treatment being used. Multiple recommendations have been published by worldwide scientific associations to aid doctors in the prevention and treatment of thrombotic and hemorrhagic events in cancer patients.[9,10]

The current study's goal is to identify risk factors for thrombo-hemorrhagic symptoms in in patients with malignancies by analysing their bleeding time (BT), clotting time (CT), prothrombin time (PT), and activated partial thromboplastin time (APTT), among other coagulation parameters.

Materials & Methods

This case control study was conducted in Department of Pathology, MGM medical college & LSK hospital, Kishanganj, Bihar from December 2020 to November 2022.

Sample size – We employed the convenience sampling method to recruit consecutive patients who satisfied the inclusion criteria.

The following formula was employed for computing the sample size of the present study at a 95% confidence level, which was calculated from the formula below.

$n = z^2 pq/ \alpha^2$

where,

n = the sample size, z = the standard normal deviation equivalent to 95% level of confidence.

The value attained from the normal distribution is 1.96.

p = 6.3% (0.063)

q = (1 – p) = (1 – 0.063) = 0.937

α = allowable error is set at 5% (0.05).

$n = (1.96)^2 \times 0.063$ x (1-0.063)/$(0.05)^2$

n = 90.67 + 10% attrition (10% of n)

n = 90.67 + 9.067 = 99.737 ≈ 100

Therefore, total 100 cases were taken along with 100 cases were included as control from apparently healthy individuals.

Inclusion Criteria

Hematological, Cytological and histopathological proven cases of Malignancy with healthy controls.

Exclusion Criteria

Present study does not include patients with co-morbid conditions that could affect coagulation profile, or patients using certain medication like heparin other anticoagulant and those with history of coagulation disorders.

Ethics committee clearance and consent: The study was taken clearance from institutional ethical committee and oral consent also will be obtained from the study subjects.

Data collection: All the patients diagnosed with cancer were subjected to the tests for coagulation profile. Clinical data namely age, sex, site of organ, histological type of malignancy was collected from the patients. Simultaneously blood samples were collected from healthy individual for coagulation profile.

Study variables

For platelet count and Hb: Venous blood anticoagulated with ethylene diamine tetra acetic acid (EDTA) was preferred.

For PT and APTT: Venous blood anticoagulated with Trisodium citrate was taken.

Platelet poor plasma: Coagulation studies required platelet poor plasma (ppp).

To obtain (ppp), blood samples was centrifuged at 3000-4000 revolutions per minute for 15 to 30 minutes.

Statistical Analysis

Continuous variables was analysed by independent student t test depending on the data normality. Categorical data will be analysed by EpiCalc 2000, as appropriate. A p value of <0.05 was considered to be statistically significant. Data was analysed by SPSS 21.0 version.

Results & Observation

During this study period, a total 100 cases along with 100 healthy controls were evaluated.

In the case group, 4 cases (4.0%) showed thrombocytopenia, 38 cases (38.0%) showed thrombocytosis & remaining 58 cases (58%) showed normal range of platelets count.

While, in the control group, 18 cases (18.0%) showed thrombocytopenia, 2 cases (2.0%) showed thrombocytosis & remaining 80 cases (80%) showed normal ange of platelets count.

The chi-square value for the comparison of platelet count between the case group and the control group is 44.8163with a p-value of less

than 0.0001. This indicates that there is a statistically significant difference in the distribution of platelet count between the case group and the control group.

Table 1: Distribution of Platelet count among case & Control Group

Platelet count $\times 10^3$ /mm3	Case Group(n=100)		Control Group(100)	
	No	**%**	**No**	**%**
<1.5	4	4.0	18	18.0
1.5 – 4.0	58	58.0	80	80.0
>4.0	38	38.0	2	2.0
Statistical inference	**Chi-square value- 44.8163 P Value- <0.0001**			

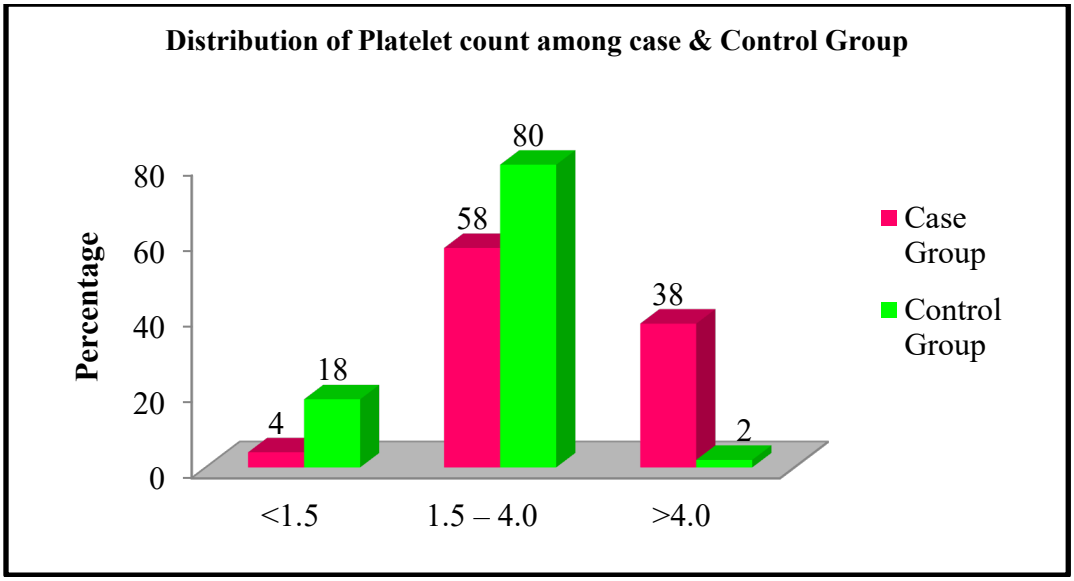

Figure 1: Distribution of Platelet count among case & Control Group

The present study showed, in the case group, 10 cases (10.0%) had a PT between 12 to 15 seconds, while 90 cases (90.0%) had a PT greater than 15 seconds. In the control group, 98 cases (98.0%) had a PT between 12 to 15 seconds, while only 2 cases (2.0%) had a PT greater than 15 seconds. The chi-square value for the comparison of PT between the case group and the control group is 155.87 with a p-value of less than 0.0001. This indicates that there is a statistically significant difference in the distribution of PT between the case group and the control group.

Table 2: Distribution of Prothrombin Time among case & Control Group

Prothrombin Time (Sec)	**Case Group(n=100)**		**Control Group(100)**	
	No	**%**	**No**	**%**
12 – 15	10	10.0	98	98.0
>15	90	90.0	2	2.0
Statistical inference	**Chi-square value- 155.87; P Value- <0.0001**			

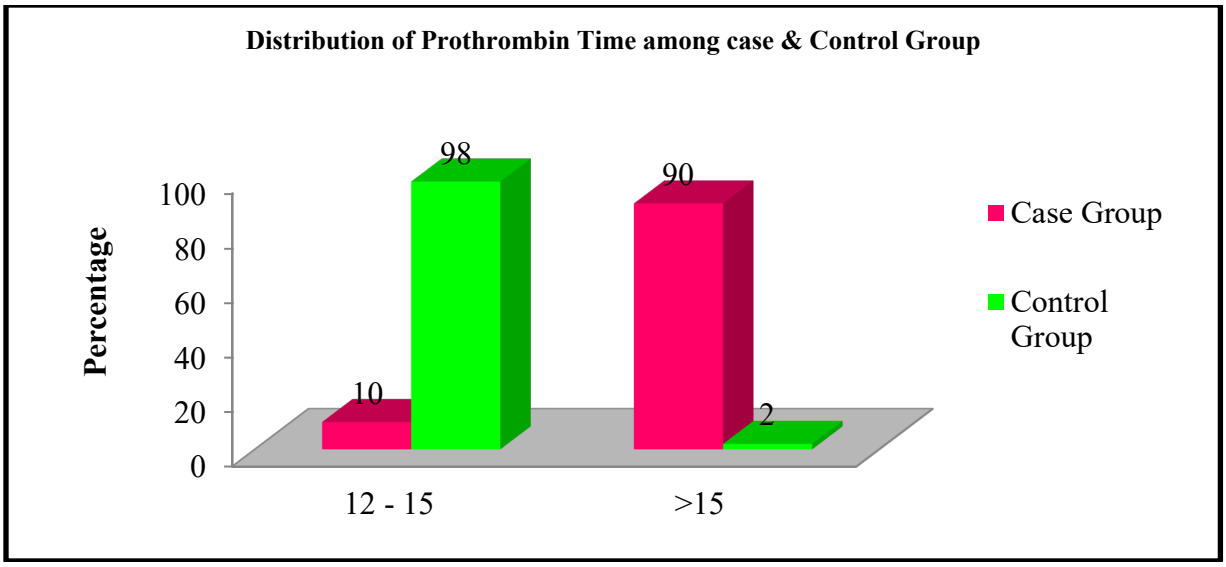

Figure 2: Distribution of Prothrombin Time among case & Control Group

In the case group, none of the individuals had an aPTT less than 25 seconds, while 42 cases (42.0%) had an aPTT between 25 and 35 seconds, and 58 cases (58.0%) had an aPTT greater than 35 seconds. In the control group, 2 case (2.0%) had an aPTT less than 25 seconds, while 96 cases (96.0%) had an aPTT between 25 and 35 seconds, and 2 case (2.0%) had an aPTT greater than 35 seconds.

The chi-square value for the comparison of aPTT between the case group and the control group is 75.3971with a p-value of less than 0.0001. This indicates that there is a statistically significant difference in the distribution of aPTT between the case group and the control group.

Table 3: Distribution of Activated Partial Thromboplastin Time among case & Control Group

aPTT (Sec)	Case Group(n=100)		Control Group (100)	
	No	%	No	%
<25	0	0.0	2	2.0
25 – 35	42	42.0	96	96.0
>35	58	58.0	2	2.0
Statistical inference	**Chi-square value- 75.3971; P Value- <0.0001**			

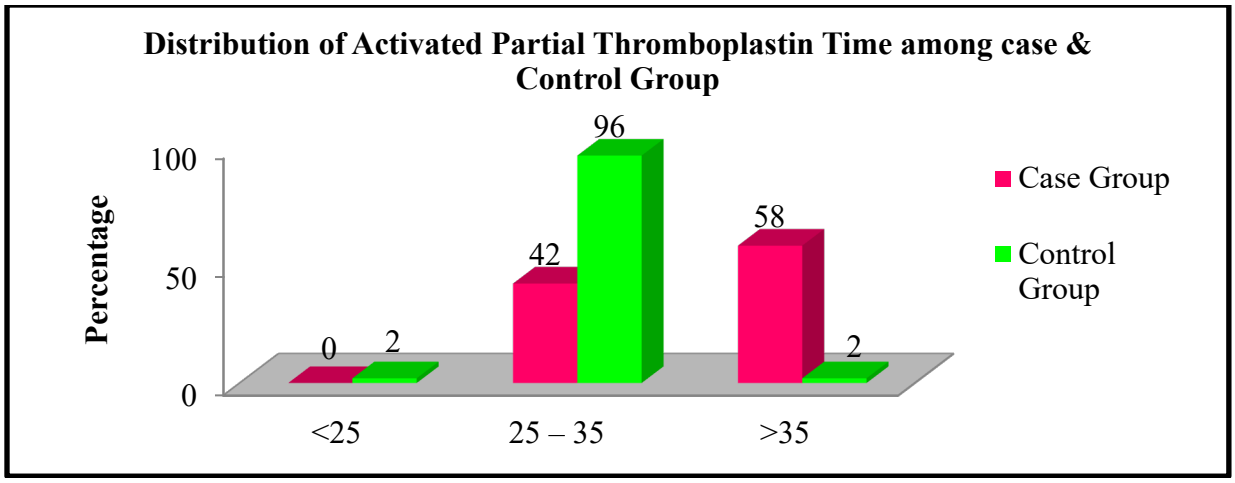

Figure 3: Distribution of Activated Partial Thromboplastin Time among case & Control Group

In our study, the results indicate that there were significant differences between the case and control groups in terms of their prothrombin time (p=0.023), aPTT (p=0.001), and platelet count (p=0.006), with the case group having longer prothrombin time and aPTT, and a lower platelet count than the control group. However, there were no significant differences between the two groups in terms of their bleeding time (BT) and clotting time (CT) (p>0.05 for both parameters).

Table: 4: Mean Difference of Coagulation parameters among case and Control group

Coagulation Parameters	Case Group(n=100)		Control Group (100)		p Value
	Mean	SD	Mean	SD	
P. Time (Sec)	17.45	±1.24	14.12	±1.09	0.023
aPTT (Sec)	49.45	±2.49	32.11	±3.45	0.001
Platelet count (×10^3 /mm3)	4.34	±0.41	2.35	±0.99	0.006
BT(Min)	2.02	±0.56	1.89	±0.41	0.411
CT(Min)	4.21	±0.45	3.26	±0.44	0.214

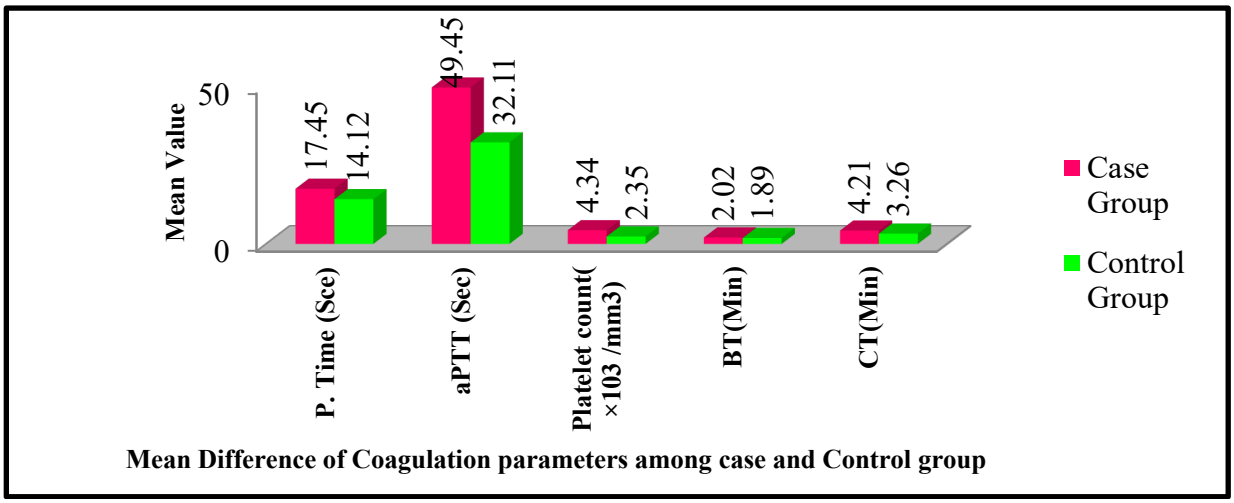

Figure 4: Mean Difference of Coagulation parameters among case and Control group.

Discussion

The study is important as cancer patients are known to have an increased risk of developing blood clots, which can lead to complications such as deep vein thrombosis and pulmonary embolism. Understanding the coagulation profile of cancer patients can help in the early detection and management of these complications, which can ultimately improve patient outcomes. The study focuses on patients with malignancies and evaluates changes in haemostatic-clotting parameters, which are relevant to the study population.

In our study we found significant differences between case and control group Prothrombin time values (p=0.023), Activated Partial Thromboplastin Time (p=0.001) and platelet count (0.006). most cases showed an increase in PT and APTT (90% and 58%) respectively compared to age matched controls. Thrombocytosis was observed in most cases (38%) compared to control cases (2%).

These findings were similar to studies conducted by Choudhury R *et al* [11], who found significant derangement in coagulation parameters in malignancy cases. Study conducted by Khichariya *et al*[12] showed increased aPTT values which was statistically significant ($p<0.05$). According to Turna *et al* [13], there was a marked lengthening of PT in cancer patients compared to control values. Karagoz *et al* [14] reported increased platelet counts in cancer patients compared to controls ($p<0.00001$).

Conclusion

Cancer patients have higher levels of platelet count, prothrombin time (PT), and activated partial thromboplastin time (aPTT) compared to normal healthy controls. These differences were found to be statistically significant (with p-values < 0.05).

The coagulation profile in cancer patients can provide valuable information about their overall health status and the potential risks of complications related to coagulation abnormalities. Increased platelet count, prolonged prothrombin time (PT), and activated partial thromboplastin time (aPTT) are common findings in cancer patients, and these parameters can help predict the risk of bleeding or thrombotic events.

Coagulation abnormalities are known to play a critical role in the pathogenesis and progression of cancer. Disruption of blood coagulation can impair metastasis, and hypercoagulable states can contribute to thrombotic complications, such as deep vein thrombosis and pulmonary embolism, which are a significant cause of morbidity and mortality in cancer patients.

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