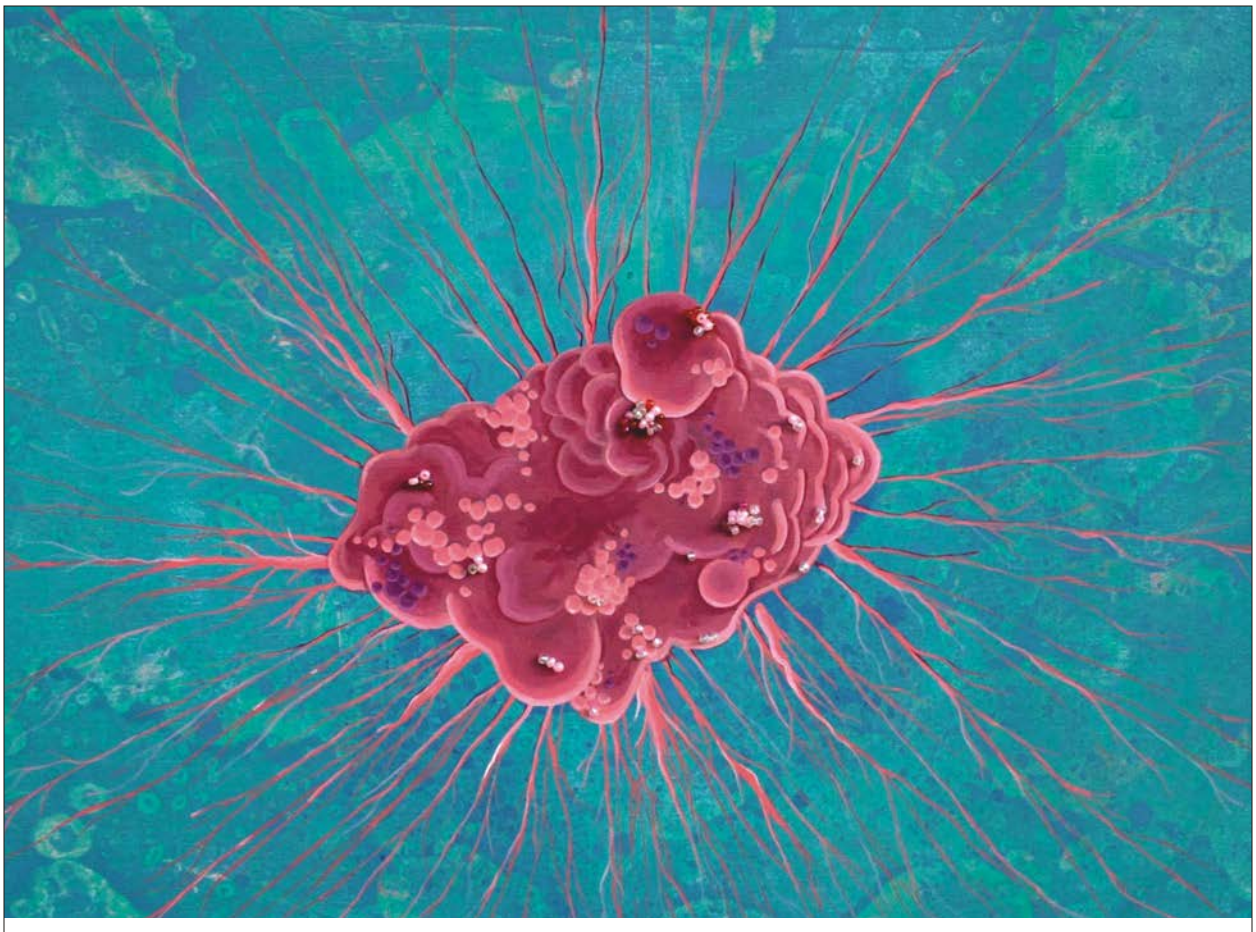

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Research Article
Haemostatic Changes in Patients with Lymphoid Malignancies on Chemotherapy in Benin City, Edo State

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Abstract

Background and Objective: The involvement of haemostasis in lymphoid malignancy is of great importance. Thrombosis may occur as a result of some lymphoid malignancies and chemotherapeutic agents used. Therefore, the study aimed to evaluate some haemostatic functional changes such as platelet counts and factor V in lymphoid malignant patients on chemotherapy to determine their clinical significance. **Materials and Methods:** It was a prospective study carried out in a tertiary hospital in Benin City, Edo State. A total of 60 patients, comprising of 20 lymphoid malignant patients on chemotherapy, 20 novel lymphoid malignant patients and 20 controls participated in the study. Factor V analysis using the one-stage method and platelet count analysis using the electronic impedance principle in the haematology analyzer was done. **Results:** The results revealed that there was a significant decrease of coagulation factor ($p<0.001$) and a significant increase in platelet count ($p<0.05$) for the comparison of novel lymphoid malignant patients and the control group. Furthermore, for lymphoid malignant patients on chemotherapy, there was a significant decrease of coagulation factor ($p<0.05$) and not significant for platelet count ($p>0.05$) compared with control. However, there was no significance for factor V ($p>0.05$) and platelet count ($p>0.05$) for lymphoid malignant patients on chemotherapy and novel lymphoid malignant patients. **Conclusion:** The results showed that lymphoid malignancy is associated with the haemostatic disorder and that chemotherapy had a therapeutic effect on the platelets and not on factor V. For effective management of the lymphoid malignant patients, there should be routine screening for all the specific single coagulation factors assay and platelet count before the commencement of the chemotherapy.

Key words: Haemostatic, factor V, platelet count, lymphoid malignancies, chemotherapy, bone marrow, metastasis

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Different malignant conditions from bone marrow cells and the lymphatic system origin are referred to as lymphoid malignancies[1]. Alteration of a gene in the bone marrow cell and lymphoid tissue at the surface area are the causes of this clonal diseases[2]. The following are Lymphoid malignancies: Acute Lymphoblastic Leukaemia (ALL), Chronic Lymphocytic Leukaemia (CLL), Prolymphocytic Leukaemia (PLL), Hairy Cell Leukaemia (HCL) and lymphomas such as Hodgkin Lymphoma (HL), Non-Hodgkin Lymphoma (NHL), myeloma, indolent lymphoma, aggressive lymphoma according to World Health Organisation[3].

The involvement of haemostasis in tumour growth, angiogenesis and metastasis is of great importance. Better interesting treatment options may occur in future as a result of the adjustment of these pathways. Few percent of all patients with malignant conditions develop thrombosis during the process of their disease as estimated by Rickles and Levine[4].

The recognition that platelets being part of the mini thrombus increases the interruption, storage of tumour cells that move around the blood vessels and abnormal proliferation of cancer was noticed about 3 decades[5,6]. Platelets contain protein factors in their α-granules in large quantities that play important role in angiogenesis such as Vascular Endothelial Growth Factor (VEGF) and are numerous in circulation[7]. Malignant patients were observed to have elevated circulating levels of this protein factor[7]. Megakaryocytes secrete VEGF which is pro-angiogenic that may provide for rapid multiplication of vascular endothelial cells[8].

Factor V or proaccelerin is a protein synthesizes mainly in the liver that converts prothrombin into thrombin. Hence, it is one of the major components and important proteins of the coagulation cascade. Factor V has a plasma half-life of 12-36 hrs and circulates in plasma as a single-chain molecule. Factor V and VIII deficiency may occur simultaneously resulting in more severe blood clotting problems[9].

In the conversion of prothrombin to thrombin, the activated factor V serves as a cofactor. Platelet plug and clot formation occur as a result of the enzyme thrombin cleave fibrinogen into fibrin which binds to and crosslinks platelets. Deficient factor V patients will have severe haemorrhage as a result of an inability to produce activated factor V. Regulation of the coagulation cascade to avoid clotting uncontrollably can be achieved by Activated Protein C (APC) inhibiting factor V thereby closing down the cascade[10].

Chemotherapy continues to serve as one of the best option therapies in treating human malignancies that have undergone metastasis and cannot be managed solely by surgical removal or radiation[11]. In the first phase of the 20th century, haematological chemotherapy was dawdling but rapidly improved during the last phase of that century by specific significant discoveries which bring a great change in the field of haematological chemotherapy for many terminal diseases. These specific significant discoveries were (a) Monoclonal antibodies advancement for the management of different malignant and non-malignant conditions, (b) Recombinant proteins and more comprehension of basic techniques of cell growth, division, differentiation, migration and cellular death, (c) Many antimetabolite and cytotoxic drugs development, (d) Tremendous development in blood product and supportive therapy permitting more intensive use of cytotoxic drug alone or in combination and (e) Sets of the rule being developed for preemptive antibiotic treatment in an immune-suppressed patient before microbiology laboratory results were available[12].

The major principles of the beginning of thrombosis linked with chemotherapy are (1) Cell-targeted treatment that damages tumour cells that will turn to produce procoagulants and cytokines, (2) A toxic effect directed towards vascular endothelium and (3) Decrease of protein C, protein S and antithrombin III[11].

The study aims to evaluate factor V and platelet count in lymphoid malignant patients on chemotherapy to ascertain the impact of such chemotherapy on them.

MATERIALS AND METHODS

Study area: The study was carried out in the Department of Haematology, University of Benin Teaching Hospital, Benin City, Edo State, Nigeria from March-August, 2017.

Methodology: The study population is composed the lymphoid malignant patients from 18 years and above. The total population of 60 subjects was divided into 3 groups as follows:

Group 1 : Twenty lymphoid malignant patients on chemotherapy
Group 2 : Twenty novel lymphoid malignant patients
Group 3 : Twenty controls (those without lymphoid malignancy)

The study was carried out in Benin City, Edo State.

Ethical approval: Ethical clearance was obtained from the Ministry of Health, Edo State Ethical Committee and oral

consent were obtained from the patients before their names were inputted into the data collection form.

Research protocol: Using aseptic precaution, 4.5 mL of venous blood were collected into a plastic tube containing 0.5 mL of aqueous tri-sodium citrate and were separated by centrifugation at 4000 rpm for 15 min to obtain citrated plasma for coagulation factor V analysis. A total of 5 mL of blood was collected into a K_3EDTA bottle for platelet count. The one-stage method was used for quantitative measurement of coagulation factor V and platelet counts were analyzed using the electronic impedance principle in an automated sysmex haematology analyzer (Sysmex KX 21, Kobe, Japan).

Statistical analysis: The data obtained were analyzed by SPSS software version 16.

RESULTS

The general demographic and clinical characteristics of lymphoid malignant patients were detailed in Table 1. The median age of all patients was 56 years (range 25-85 years). There were 19 (47.5%) males and 21 (52.5%) females in the (1:1) ratio. The lymphoid malignant patients observed were multiple myeloma 13 (32.5%), hodgkin lymphoma 12 (30%), non-hodgkin lymphoma 6 (15%) and chronic lymphocytic leukaemia 9 (22.5%).

Table 2 shows the comparison of percentage activities of factor V and platelet count between novel lymphoid malignant patients and the apparent healthy control subject, factor V ($p = 0.000$ and platelet count ($p = 0.026$). These indicate that the percentage activities of factor V were significantly decreased compared with the apparent healthy control subject. However, platelet counts were significantly increased compared with the apparent healthy control subject.

Table 3 shows the comparison of percentage activities of factor V and platelet counts between lymphoid malignant patients on chemotherapy and apparent healthy control subject, factor V ($p = 0.011$) which indicates a significant decrease in percentage activities of coagulation parameters compared with the apparent healthy control subject. However, platelet count ($p = 0.395$) did not change significantly compared with the apparent healthy control.

The data in Table 4 shows the comparison of percentage activities of factor V and platelet count between lymphoid malignant patients on chemotherapy and novel lymphoid malignant patients: Factor V ($p = 0.409$), platelet count ($p = 0.068$). It was observed that platelet count and percentage activity of factor V did not change significantly.

Table 1: Demographic and clinical characteristic of lymphoid malignant patients

Characteristics	Total of patients number	Percentage
Number of patients	40	
Ages (years)		
25-40	6	15.0
41-55	11	27.5
56-70	21	52.5
71-85	2	5.0
Gender		
Male	19	47.5
Female	21	52.5
Lymphoid malignancy		
Multiple myeloma	13	32.5
Hodgkin lymphoma	12	30
Non-hodgkin lymphoma	6	15
Chronic lymphocytic leukaemia	9	22.5

Table 2: Comparison of coagulation parameters between novel lymphoid malignant patients and control

Coagulation parameters	Non-chemotherapy	Controls	t-value	p-value
Factor V (%)	98.08±11.70	120.22±9.4	6.05	0.000
Platelet (10^3 μL^{-1})	468.65±411.64	239.85±52.27	2.42	0.026

(Apparently healthy individuals) n = 40

Table 3: Lymphoid malignant patients on chemotherapy and control

Coagulation parameters	Non-chemotherapy	Controls	t-value	p-value
Factor V (%)	103.04±22.43	120.22±9.41	2.81	0.011
Platelet (10^3 μL^{-1})	267.85±125.36	239.85±52.27	0.871	0.395

(Apparently healthy individuals) n = 40

Table 4: Lymphoid malignant patients on chemotherapy and novel lymphoid malignant patients n = 40

Coagulation parameters	Non-chemotherapy	Controls	t-value	p-value
Factor V (%)	103.04±22.43	98.08±11.70	0.844	0.409
Platelet ($10^3 \mu L^{-1}$)	267.85±125.36	468.65±411.64	1.99	0.068

n = 40

DISCUSSION

The comparison of percentage activities of factor V and platelet count between novel lymphoid malignant patients and the apparent healthy control subject were significantly decreased and increased, respectively. This confirms that malignant cells activate platelet which secretes granules that contain coagulation factors (prothrombin, fibrinogen, factor V, factor VIII), growth factors, pro-angiogenic and antiangiogenic factors that leads to proliferation and survival of malignant cells[13,14]. Generally, malignant patients have a high risk of coagulopathy as a result of tissue factors released by the malignant cells, blood vessel damage[15,16].

The comparison of percentage activities of factor V between lymphoid malignancy patients on chemotherapy and apparent healthy control subject was significant. This indicates that chemotherapy may initiate mutation in coagulation factor V that prevents activated protein C to inactivate it thereby losing its anticoagulant cofactor function with clotting mechanisms remaining active for more prolonged periods and a subsequent increase of the formation of pathological blood clots[17,18]. However, there was no significant change in platelet count. This assertion can be confirmed by a previous study in which it was observed that after completion of chemotherapy for malignant disease, serious haemorrhage complications stop completely with normal platelet count[19]. We can affirm that chemotherapy has some clinical effect in stabilizing platelet count.

The comparison of percentage activities of coagulation parameters between lymphoid malignant patients on chemotherapy and novel lymphoid malignant indicated that factor V and platelet count were not significant. These indicate that chemotherapy may escalate the general condition of the patient that can bring about haemostatic disorders[20]. This implies that chemotherapy can progress haemostatic disorder in lymphoid malignant patients. It is therefore very important to investigate coagulation profiles during chemotherapy treatment to avoid complications. More research can be done on other coagulation factors that were not captured in this study.

CONCLUSION

Our findings show that haemostatic disorders are common in lymphoid malignant patients. We also discover that chemotherapy stabilizes platelet count in lymphoid malignant patients thereby reducing the complication of thrombosis in such patients. It is therefore necessary to carry out routine screening for all the specific single coagulation factors assay and platelet count before the commencement of the chemotherapy for all the lymphoid malignant patients for effective management of the patients in the hospitals and cancer centers. Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) cannot give a specific single coagulation factor defect.

SIGNIFICANCE STATEMENT

This study discovered that critical targets of haemostatic parameters or factors in lymphoid malignancy can contribute a unique approach to lymphoid malignant treatment. This study will help researchers to uncover the critical area of haemostatic disorder and lymphoid malignancy that many researchers were not able to explore. Thus, a new theory of association of haemostatic disorder with lymphoid malignancy may be arrived at.

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REFERENCES

1. Rodriguez-Abreu, D., A. Bordoni and E. Zucca, 2007. Epidemiology of haematological malignancies. Ann. Oncol., 18: 13-18.
2. Hoffbrand, A.V., J.E. Pettit and P.A. Moss, 2001. The Genetics of Haematological Malignancies. In: Essential Haematology, Hoffbrand, A.V., J.E. Pettit and P.A.H. Moss (Eds.)., Wiley Blackwell, United States, pp: 145-161.
3. Notaro, S., D. Reimer, M. Duggan-Peer, H. Fiegl and A. Wiedermair *et al.*, 2016. Evaluating L1CAM expression in human endometrial cancer using qRT-PCR. Oncotarget, 7: 40221-40232.
4. Rickles, F.R. and M.N. Levine, 2001. Epidemiology of thrombosis in cancer. Acta Haematol., 106: 6-12.
5. Trikha, M. and M.T. Nakada, 2002. Platelets and cancer: Implications for antiangiogenic therapy. Semin. Thrombosis Hemostasis, 28: 39-44.

6. Bereczky, B., R. Gilly, E. Rásó, Á. Vágó, J. Tímár and J. Tóvári, 2005. Selective antimetastatic effect of heparins in preclinical human melanoma models is based on inhibition of migration and microvascular arrest. Clin. Exp. Metastasis, 22: 69-76.
7. Rein, B.J.D., S. Gupta, R. Dada, J. Safi, C. Michener and A. Agarwal, 2011. Potential markers for detection and monitoring of ovarian cancer. J. Oncol., Vol. 2011. 10.1155/2011/475983.
8. Wojtukiewicz, M.Z., E. Sierko, D. Hempel, S.C. Tucker and K.V. Honn, 2017. Platelets and cancer angiogenesis nexus. Cancer Metastasis Rev., 36: 249-262.
9. Huang, J.N. and M.A. Koerper, 2008. Factor V deficiency: A concise review. Haemophilia, 14: 1164-1169.
10. LaBonte, M.L., 2014. Anticoagulant factor V: Factors affecting the integration of novel scientific discoveries into the broader framework. Stud. Hist. Philos. Sci. Part C: Stud. Hist. Philos. Biol. Biomed. Sci., 47: 23-34.
11. Dragana, P., 2002. Effect of CMF-chemotherapy on blood coagulation in patients with breast cancer. Arch. Oncol., 10: 61-66.
12. Ghosh, K. and K. Ghosh, 2010. Advances in haematological pharmacotherapy in 21st century. Indian J. Hematol. Blood Transfus., 26: 30-40.
13. Mezouar, S., C. Frère, R. Darbousset, D. Mege and L. Crescence *et al*., 2016. Role of platelets in cancer and cancer-associated thrombosis: Experimental and clinical evidences. Thrombosis Res., 139: 65-76.
14. Goubran, H.A., J. Stakiw, M. Radosevic and T. Burnouf, 2014. Platelets effects on tumor growth. Semin. Oncol., 41: 359-369.
15. Prandoni, P., 2002. Cancer and thromboembolic disease: How important is the risk of thrombosis?. Cancer Treat. Rev., 28: 133-136.
16. Lee, A.Y and M.N. Levine, 2003. Venous thromboembolism and cancer: Risks and outcomes. Circulation, 107: 117-121.
17. Jadaon, M.M., 2011. Epidemiology of activated protein C resistance and factor V leiden mutation in the mediterranean region. Mediterr. J. Hematol. Infect. Dis., Vol. 3. 10.4084/mjhid.2011.037.
18. Kabukcu, S., N. Keskin, A. Keskin and E. Atalay, 2007. The frequency of factor V leiden and concomitance of factor V leiden with prothrombin G20210A mutation and methylene tetrahydrofolate reductase C677T gene mutation in healthy population of Denizli, Aegean region of Turkey. Clin. Appl. Thrombosis/Hemostasis, 13: 166-171.
19. Sallah, S. and J.Y. Wan, 2001. Inhibitors against factor VIII in patients with cancer: Analysis of 41 patients. Cancer, 91: 1067-1074.
20. Takemoto, S., Y. Shibamoto, S. Ayakawa, A. Nagai and A. Hayashi *et al*., 2012. Treatment and prognosis of patients with late rectal bleeding after intensity-modulated radiation therapy for prostate cancer. Radiat. Oncol., Vol. 7. 10.1186/1748-717x-7-87.