Biospectra : ISSN: 0973-7057, Vol. 17(2), September, 2022, pp. 211-216
An International Biannual Refereed Journal of Life Sciences

41(PS).
Plant Science

ISSN : 0973-7057

Int. Database Index: 616 www.mjl.clarivate.com

Comparative analysis of hematological profile during carcinogenesis

Deokant[a]* & Nayni Saxena[b]
[a]Department of Botany, Samastipur College, Samastipur, Bihar, India
[b]University Department of Zoology, Ranchi University, Ranchi, Jharkhand, India

Received : 13th July, 2022 ; Revised : 14th August, 2022

Abstract- Blood is a good source to measure certain hematological profile which includes Hemoglobin quantity, Total Leucocyte Count (TLC) and Differential Leucocyte Count (DLC) which reflects the alterations of certain biochemical and molecular pathways. Hematological profiles are fluctuating during normal and pathogenesis conditions and can also be correlated with development of carcinogenesis. The mean sample hemoglobin level is 8.93 gm/dL, which is significantly lower (α=0.05) than the control hemoglobin value (14.1 gm/dL). The mean sample TLC level is 23,914 per µL, which is significantly higher (α=0.05) than the control value (8,512 per µL). The mean sample neutrophil level is 20,582 per µL, which is significantly higher (α=0.05) than the control value (6,431 per µL). The mean sample lymphocyte count level is 681 per µL, which is significantly lower (α=0.05) than the control value (1,516 per µL). These alterations may lead to development of carcinogenesis or results due to carcinogenesis and may increase as cancer progresses through successive advanced stages and can be used to establish correlation between extent of alterations and stages of cancer development.

Key words: Total Leucocyte Count, Differential Leucocyte Count, Hemoglobin, Neutrophil, Lymphocyte, Carcinogenesis

INTRODUCTION

Cancer is abnormal and uncontrolled proliferation of cells, which results into different hematological changes, which may include Total Leucocyte Count (TLC), Differential Leucocyte Count (DLC) and Hemoglobin quantity alteration during carcinogenesis and can be one of the basis for cancer risk assessment. Disruption of epigenetic processes can lead to altered gene function and malignant cellular transformation. Recent advancements in the rapidly evolving field of cancer epigenetics have shown extensive reprogramming of every component of the epigenetic machinery in cancer including DNA methylation, histone modifications, nucleosome positioning and non-coding RNAs, specifically microRNA expression[1]. Global hypo methylation is a common epigenetic process in cancer (especially colon cancer), which may progressively evolve during multistage carcinogenesis.[2] Over-erosion of telomeres or telomere dysfunction in very early stages of cervical tumorigenesis might fuel transformation processes by driving chromosomal instability.[3]

Hematological malignancy is found to be associated with impaired antioxidant defense system (glutathione peroxidase and superoxide dismutase) which is correlated with arsenic toxicity because of increased reactive oxygen species which can initiate lipid peroxidation and DNA damage leading to mutagenesis, carcinogenesis and cell death.[4] 8-oxoguanine (8oxoG) and 8-hydroxydeoxy

*Corresponding author :
Phone : 9955360211
E-mail : deokant_davv@rediffmail.com

guanosine (8OHdG), biomarkers for oxidative DNA damage, in cerebral cortex microdialysate samples was determined by using capillary electrophoresis with electrochemical detection.[5] Anaemia is a common occurrence in patients with cancer especially in those who undergo chemotherapy.[6] Leukocyte migration is a key event in the inflammatory response to tumors.[7] A graded association between higher WBC and higher risk of total cancer mortality was observed.[8] DRR1 protein (tumor suppressor) is expressed in normal cells, particularly in the neurons system during embryogenesis, is involved in neuronal cell survival, and is down-regulated during neuro-blastoma carcinogenesis.[9] Differential protein expression profile between low and highly transformed epithelial ovarian cancer cell lines mimic the phenotypic changes observed during evolution of a tumor metastasis.[10] Tobacco smoking adversely affects the capacity of neutrophils to ingest microbes and so has suppressive effect on innate immune mechanism.[11]

MATERIALS & METHODS

Collection of blood samples: The blood samples were collected from patients suffering from different types of cancer and named according to the type of cancer like G.B. = Gall bladder cancer samples, B.C. = Breast cancer samples, M.M. = Medistinal malignancy samples, R.C. = Rectum cancer samples, O.C. = Oesophagus cancer samples, E.S. = Ewing sarcoma samples, C.C. = Colon cancer samples, Ov.C. = Ovary cancer samples, M.C. = Myeloblast cancer samples, U.C. = Urinal cancer samples, E.C. Endotracheum cancer samples, C.M.L. = Chronic myeloid leukemia samples, A.M.L. = Acute myeloid leukemia samples and patient number was given. The blood samples were stored at -20°C.

Hematological analysis of blood samples: A. Total leucocyte count (TLC) analysis in different test blood samples: TLC analysis in different test blood samples were performed by using Neubauer's counting chamber (Hemocytometer).[12]

B. Differential leucocyte count (DLC) analysis in different test blood samples: DLC analysis in different test blood samples were performed by using glass slides and Leishman's stain.[13]

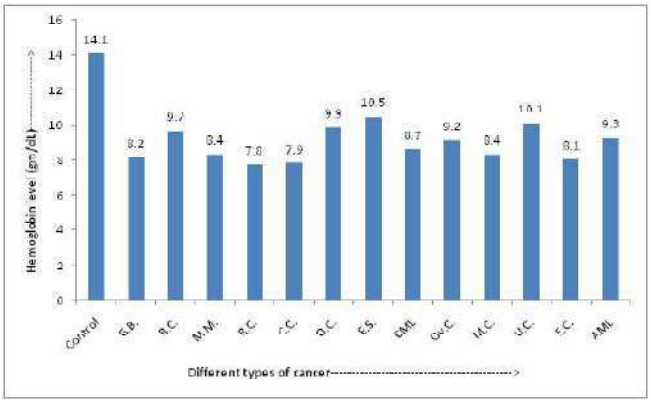
C. Quantitative hemoglobin analysis of different test blood samples: Quantitative hemoglobin analysis of different test blood samples were performed by using Sahli's hemoglobinometer.[14]

Statistical Analysis: Student's t-test was performed to compare mean values of the parameters. "P" value < 0.05 was considered to be statistically significant.

RESULTS & DISCUSSION

Table 1- The average values of hemoglobin quantities (gm/dL) measured from control and different test blood samples.

Sl. No.	Sample Type	Hemoglobin Quantities (gm/dL)
1.	$(Control)_{10}$	14.1
2.	$(G.B.)_{10}$	8.2
3.	$(B.C.)_5$	9.7
4.	$(M.M.)_4$	8.4
5.	$(R.C.)_5$	7.8
6.	$(C.C.)_5$	7.9
7.	$(O.C.)_5$	9.9
8.	$(E.S.)_4$	10.5
9.	$(CML)_7$	8.7
10.	$(Ov.C.)_4$	9.2
11.	$(M.C.)_3$	8.4
12.	$(U.C.)_5$	10.1
13.	$(E.C.)_4$	8.1
14.	$(AML)_5$	9.3



Graph 1- Diagrammatic representation of hemoglobin level in different types of carcinogenesis.

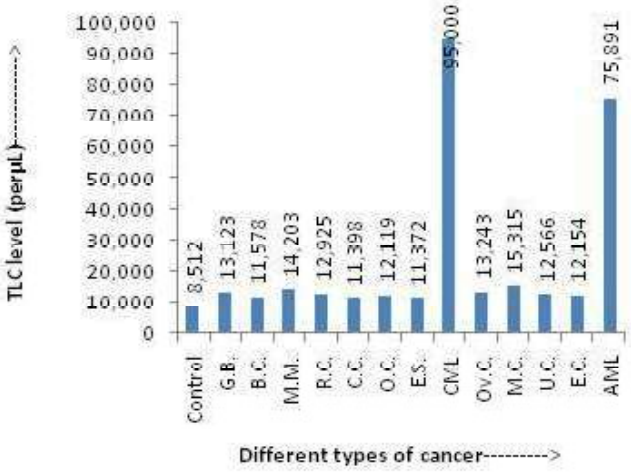
The mean sample hemoglobin level is 8.93 gm/dL, which is significantly lower (α=0.05) than the control hemoglobin value (14.1 gm/dL) (Table 1). Hemoglobin is the main protein found in blood and is required for the transport of O_2 and CO_2 in different parts of body. Anaemia is a common symptom and complication in patients with malignant tumours. In cancer patients' anaemia may occur due to blood loss or bone marrow infiltration or nutritional deficiencies or as a result of the cancer treatment itself or

due to chemical factors produced by the cancer. Chronic tumour-related anaemia is diagnosed when hemoglobin (Hb) levels are below 12 gm/dL.

The correlation between degree of increase in hemoglobin and longer progression-free survival (PFS) suggests that hemoglobin may be useful as a surrogate marker of stringent VEGF inhibition and as a predictive factor for clinical response.[15] Epoetin-α administered to patients with cancer-related anemia for up to 16 weeks resulted in significantly improved QOL (Quality of Life), increased hemoglobin levels, and decreased transfusion use in cancer patients who were not receiving chemotherapy.[16]

Table 2- The average values of total leucocytes count measured from control and different test blood samples.

Sl. No.	Test Sample	TLC (Per µL)
1.	$(Control)_{10}$	8,512
2.	$(G.B.)_{10}$	13,123
3.	$(B.C.)_5$	11,578
4.	$(M.M.)_4$	14,203
5.	$(R.C.)_5$	12,925
6.	$(C.C.)_5$	11,398
7.	$(O.C.)_5$	12,119
8.	$(E.S.)_4$	11,372
9.	$(CML)_7$	95,000
10.	$(Ov.C.)_4$	13,243
11.	$(M.C.)_3$	15,315
12.	$(U.C.)_5$	12,566
13.	$(E.C.)_4$	12,154
14.	$(AML)_5$	75,891

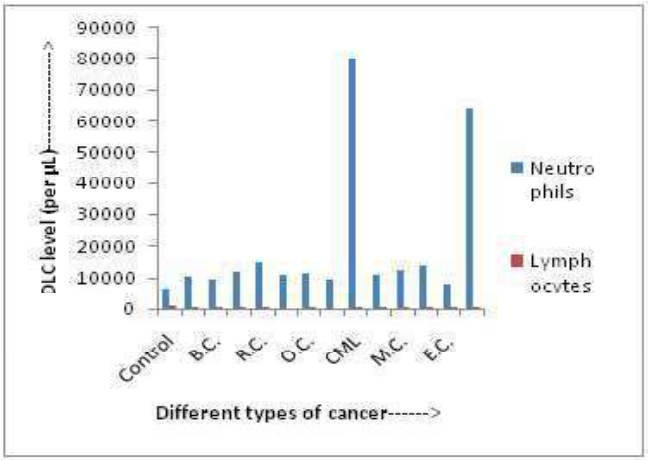


Graph 2- Diagrammatic representation of TLC level in different types of carcinogenesis

The mean sample TLC level is 23,914 per µL, which is significantly higher (α=0.05) than the control value (8,512 per µL). Higher WBC count was found to be associated with all cancer mortality. Other factors like age, sex, education, body mass index, hematocrit level, alcohol consumption, physical inactivity, smoking, weekly aspirin use, diabetes mellitus or fasting hyperglycemia status and fasting glucose levels etc. may add the risk of cancer mortality. Higher circulating WBC count is a widely available marker of inflammation and subsequent cancer mortality.[17] Host response to malignant solid tumors gives rise to systemic effects, the most frequent of which are leukocytosis, neutrophilia and lymphopenia. The ratio of neutrophil to lymphocyte counts has been suggested as a simple parameter of systemic inflammation in cancer patients. An elevated neutrophil to lymphocyte ratio is an independent prognostic factor for cancers at different sites and this parameter is a clinically accessible and useful biomarker for patient survival. Tumor cells produce soluble factors such as granulocyte colony stimulating factor, which mobilize precursor cells in the bone marrow, or other mediators that alter cell differentiation and hence increased the circulating leukocyte number.[7] Granulocytes of cancer patients had inhibited oxidative burst and had less NADPH oxidase activity that may support tumor growth and development.[18]

Table 3- The average values of differential leucocytes count measured from control and different test blood samples.

Sl. No.	Test Sample	Differential Leucocytes Count (Per µL)	
		Granulocytes (Neutrophils)	Lymphocytes
1.	$(Control)_{10}$	6,431	1,516
2.	$(G.B.)_{10}$	10,456	710
3.	$(B.C.)_5$	9,305	621
4.	$(M.M.)_4$	11,905	850
5.	$(R.C.)_5$	14,617	812
6.	$(C.C.)_5$	10,817	381
7.	$(O.C.)_5$	11,143	739
8.	$(E.S.)_4$	9, 618	297
9.	$(CML)_7$	80,243	775
10.	$(Ov.C.)_4$	10,864	827
11.	$(M.C.)_3$	12,525	709
12.	$(U.C.)_5$	13,729	644
13.	$(E.C.)_4$	8,016	658
14.	$(AML)_5$	64,323	832



Graph 3- Diagrammatic representation of DLC level in different types of carcinogenesis

Platelets and basophil counts are normal in all types of cancer. Lymphocyte counts are below normal level in all types of cancer (Table 3). TLC (Table 2), neutrophil (Table 3), eosinophil and monocyte levels are increased above normal level in all types of cancer. The mean sample neutrophil level is 20,582 per µL, which is significantly higher (α=0.05) than the control value (6,431 per µL). The mean sample lymphocyte count level is 681 per µL, which is significantly lower (α=0.05) than the control value (1,516 per µL).

In Taiwanese adults of both genders, a lower lymphocyte count is associated with cancer mortality, especially mortality from hepatoma. In Taiwanese men, higher neutrophil and monocyte counts are associated with cardiovascular mortality.[19] Lower lymphocyte counts may be due to altered cell differentiation during carcinogenesis and may support survival and proliferation of cancer cells. Cytotoxic T lymphocytes (CTLs) and NK cells, help in checking and controlling abnormal and cancer cells.

In the present investigation clear alteration has been noticed in hematological profile during carcinogenesis from normal. In hematological profile, the mean sample hemoglobin level is significantly lower (α=0.05) than the control hemoglobin value. TLC and neutrophil levels are increased above normal level in all types of cancer. Lymphocyte counts are below normal level in all types of cancer. These alterations may lead to development of carcinogenesis or results due to carcinogenesis and may increase as cancer progresses through successive advanced stages. This is a primitive study and needs further more detailed investigation to establish correlation between extent of alterations and stages of cancer development. If such correlation is established, this can be used as a successful biomarker for cancer progression and could be useful in clinical trials and in identifying patients with poor prognosis, leading to better treatment strategies. If these alterations are the possible cause of cancer, then medicines can be prescribed to minimize these alterations at earlier stages of detection. Once cancer is detected in earlier stages, it can be treated properly and cured totally. I hope this study will help doctors to detect cancer in cancer suspected persons and cure cancer patients at earlier stage in near future.

ACKNOWLEDGEMENT

Dr. Mritunjay Kumar, Medical Superintendent, Dr. (Mrs.) Chandana Banerjee, Centre Manager and Mr. Raj Kumar Gupta, Laboratory In-charge, Curie-Abdur Razzaque Ansari Cancer Institute, Irba, Ranchi, Jharkhand are highly acknowledged for providing blood samples of different types of cancer patients.

REFERENCE

1. **Sharma S., Kelly T. K. and Jones P. A. 2010.** Epigenetics in cancer, *Carcinogenesis.* **31(1):** 27-36.

2. **Chalitchagorn K., Shuangshot S., Hourpai N., Kongruttanachok N., Tangkijvanich P., Thong-ngam D., Voravud N., Sriuranpong V. and Mutirangura A. 2004**. Distinctive pattern of LINE-1 methylation level in normal tissues and the association with carcinogenesis. *Oncogene*. **23:**8841- 8846.

3. **Zhang A., Wang J., Zheng B., Fang X., Angstrom T., Liu C., Li X., Erlandsson F., Bjorkholm M., Nordenskjord M., Gruber A., Wallin K. L. and Xu D. 2004**. Telomere attrition predominantly occurs in precursor lesions during *in vivo* carcinogenic process of the uterine cervix. *Oncogene*. **23:** 7441-7447.

4. **Paul S. and De M. 2010**. Changes in anti-oxidant enzyme profile during haematological malignancy. *Int J Hum Genet*. **10(4):** 247-250.

5. **Arnett S. D., Osbourn D. M., Moore K. D., Vandaveer S. S. and Lunte C. E. 2005.** Determination of 8-Oxoguanine and 8-Hydroxy-2'-deoxyguanosine in the rat cerebral cortex using microdialysis sampling and capillary electrophoresis with electrochemical

detection, *J. Chromatogr. B. Analyt. Technol. Biomed. Life Sci*. **827(1):** 16-25.

6. **Sabbatini P. 2000.** The relationship between anemia and quality of life in cancer patients. *The Oncologist*. **5(2):** 19-23.

7. **Tavares-Murta B. M. and Murta E. F. C. 2008.** Systemic leukocyte alterations in cancer and their relation to prognosis. *The Open Cancer Journal.* **2:** 53-58.

8. **Erlinger T. P., Muntner P. and Helzlsouer K. J. 2004.** WBC count and the risk of cancer mortality in a national sample of U.S. adults: results from the second national health and nutrition examination survey mortality study, *Cancer Epidemiology Biomarkers & Prevention*. **13:** 1052.

9. **Yoshizumi A., Satoshi K. and Ping M. K. S. 2010.** DRR1 is expressed in the developing neurons system and down regulated during neuroblastoma carcinogenesis, *Biochemical and Biophysical Research communications.* **394(20):** 829-835.

10. **Jean G., Chantal E., Pierre G. and Genevieve M. 2007.** Comparative proteome analysis of human epithelial ovarian cancer, *Proteome Science*. **5(16):**1477-5956.

11. **Thakur T., Bhide A., Chaudhury A., Thota A., Kasala L. and Hulikal N. 2018.** Effects of tobacco smoking on innate immunity: A study based on neutrophil phagocytic index. *Indian Journal of Physiology and Pharmacology*. **62(2):** 182-186.

12. **Mc Bride J. A., Dacie J. V., Shapley R. 1968.** The effect of splenectomy on leucocyte count. *British Journal of Haematology*. **14(2):** 225-231.

13. **Gulati G., Song J., Dulau F. A. and Gong J. 2013.** Purpose and criteria for blood smear scan, blood smear examination and blood smear review, *Annals of Laboratory Medicine*. **33(1):**1-7.

14. **Singla P. N., Chand S. and Agarwal K. N. 1979.** Cord serum and placental tissue iron status in maternal hypoferreimia. *Amer. J. Clin. Nutr*. **32:**1462-1465.

15. **Harshman L. C., Kuo C. J., Wong B. Y., Vogelzang N. J. and Srinivas S. 2008.** Increased hemoglobin associated with VEGF inhibitors in advanced renal cell carcinoma, *Blood*. **112:** 1185.

16. **Quirt I., Robeson C., Lau C. Y., Kovacs M., Burdette-Radoux S., Dolan S., Tang S. C., Mc Kenzie M. and Couture F. 2001.** Epoetin alfa therapy increases hemoglobin levels and improves quality of life in patients with cancer-related anemia who are not receiving chemotherapy and patients with anemia who are receiving chemotherapy. *Journal of Clinical Oncology.* **19(21):**4126-4134.

17. **Shankar A., Wang J. J., Rochtchina E., Yu M. C., Kefford R., Mitchell P. 2006.** Association between circulating white blood cell count and cancer mortality: a population-based cohort study. *Arch Intern Med*. **66(6):** 681-683.

18. **Mikirova N. A., Klykov A. A., Jackson J. A. and Riordan N. H. 2008.** Granulocyte activity in patients with cancer and healthy subjects, *Cancer Biology & Therapy*. **7(9):** 1362-1367.

19. **Huang Z. S., Chien K. L., Yang C. Y., Wang C. H., Chang T. C. and Chen C. J. 2003.** Peripheral differential leukocyte counts and subsequent mortality from all diseases, cancers, and cardiovascular diseases in Taiwanese. *J. Formos. Med. Assoc*. **102(11):** 775-781.

***