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Study on some enzymatic, hematologic and oxidative stress markers of leukemic variants

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Abstract

The requirements of additional insight on the knowledge of Leukemia were a driving impetus for this study. The expression of a myriad of circulating markers elucidates the pathological state in various types of Leukemia. Elevated oxidative stress with concomitant reduction in antioxidant factors are key indices having a nexus with Leukemic abnormalities. In this research we examined these markers in 100 participants in which 75 were Leukemic patients and 25 were normal subjects. The Leukemic subjects were further differentiated based on some parameters evaluated using spectrophotometric and microscopic methods. Results show a significant elevation of MDA in disease variants (all - b = 9.3 $\pm$ 1.25; all - t = 9.88 $\pm$ 0.87; aml = 9.2 $\pm$ 1.57 nM/ml) as compared to the controls that gave (2.12 $\pm$ 0.02 nM/ml); $P < 0.05$). While there was a reduction in platelets and Vitamin E levels, there was marked increase in ESR and leucocyte count. These results are indicative of a stressed state in Leukemia. Knowledge of these biomarkers could enhance management efforts at confronting this disease condition.

Keywords: Enzymatic; Hematological; Oxidative stress; Leukemic; Variant

1. Introduction

Leukemia is a disease common in both children and adults differentiated through classification into four main variants. It is cancerous with a common adult erythropoetic malignancy especially in Western countries. Prevalence among blacks is a little less than whites [1, 2]. A notable feature of Leukemia is the fact that treatment outcomes are divergent even in this era of personalized medicine where medication is being made specific utilizing target agents [3, 4]. The variant forms of Leukemia are Acute Lymphoblastic Leukemia (ALL), Chronic Lymphoblastic Leukemia (CLL), Acute Myeloid Leukemia (AML) and Chronic Myeloid Leukemia (CML) [5].

Acute Lymphoblastic Leukemia is a malignant tumour having haemopoetic precursor cells arising from Lymphoid lineage. Its predisposing factors includes viruses, chemical pollutants, ionizing radiation and close residency to power lines [6].

Chronic Lymphocytic Leukemia is the commonest adult Leukemia and present diverse disease courses. Findings of white blood cell count of greater than 5 - 10 x 10^9/L in a minimum duration of 3 months is strongly suggestive. Leukemic cells usually found in blood smear are uniquely small, and immature with observable dense nuclear with couple of chromatin bodies. It is now known that Chronic Lymphoblastic Leukemia cells expresses the B–cell antigen CD_{19}, CD_{20} and CD_{23} [7, 8]. Novel drugs are now available especially for patients that have developed active and symptomatic disease. In such cases inhibitors of B-cell receptors signaling pathway and those of the anti-apoptotic protein BCL-2 are more effective in comparison to the well known chemoimmunotherapy drugs [9, 10].

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Acute Myeloid Leukemia is a haemopoetic cell line of non-Lymphoid lineage. This is the commonest acute Leukemia among adults 3 per 100,000 yearly with a predominant high frequency with age among children < 15 years, 68% are greater than 60 years of age [11]. The etiology is not quite clear but there is usually pre-existing Myelodysplasia precedent to cytotoxic chemotherapy, ionizing radiation, constitutional chromosomal abnormalities and benzene exposure are some of the aetiologic factors. The degree of differentiation and the pathway in its development determines the classification.

2. Materials and Method

Whole blood was collected from subjects and put into EDTA bottles and plain bottles. The sample in EDTA was used for estimation of hemoglobin, packed cell volume, white blood cell count, erythrocyte sedimentation rate and platelets. The sample in plain container was spurn to obtain serum which was used for biochemical and enzymatic studies.

Vitamin C and E were evaluated with the Human Diagnostic Kit using spinlab - spin react clinical analyzer.

Sodium Dismutase and Catalase activities were determined by the methods of [12] and [14] respectively.

Glutathione perioxidase and reductase were evaluated with the methods of Achi and Bermeyer (1983) and Moron, et al (1979) respectively.

Nitric oxide and malondialdehyde were measured by the method of Moshage, et al (1995) and Okhawa, et al (1979) respectively.

The Transaminases (ALT and AST), ALP, Creatinine, urea and uric acid were estimated using Randox Kit (A product of Randox Laboratories Ltd, UK).

Potassium was determined with flame photometry using Corning Instrument. Calcium and magnesium were determined with spectroscopy (AAS).

Hb was determined by spectroscopy and PCV by Hematocrit.

We used the Westergreen method for the determination of ESR and coulter counter Naubear chamber for WBC and platelets counts.

2.1. Analysis of Data

Results obtained from data were analyzed statistically using SPSS software version 23. Expressions were by means and standard deviation. Correlation between different variants were determined at a p value set at 0.05.

3. Results

Results obtained from the various analysis are shown in tables 1, 2, 3 and 4.

Table 1 Levels of enzymatic variables in the 3 variants compared with control

Parameter	Control	all - b	all - t	aml
	(n=25)	(n=25)	(n=25)	(n=25)
ALT (iu/L)	13.3 ± 0.4	63.2 ± 12.2	68.2 ± 13.4	65.7 ± 12.1
AST (iu/L)	15.7 ± 0.8	44.1 ± 8.4	47.5 ± 10.2	42.3 ± 10.4
ALP (iu/L)	18.8 ± 12.3	260 ± 15.1	204.3 ± 13.1	184.2 ± 9.3
LDH (u/L)	168 ± 9.4	240.4 ± 22.7	219.7 ± 18.2	175.7 ± 12.0
CRP (mg/L)	10.3 ± 0.5	12.4 ± 0.7	14.3 ± 0.2	15.6 ± 0.9

Legend: All, Acute Lymphoblastic Leukemia - b; all - t acute lymphoblastic Leukemia - t; aml, Acute Myeloid Leukemia.; The values are mean ± SEM of triplicate determination

Table 2 Level of Antioxidants variables in the 3 variants compared with control

Parameter	Control	all - b	all - t	Aml
	(n=25)	(n=25)	(n=25)	(n=25)
MDA (nM/ml)	128.3 ± 0.10	140.5 ± 0.7	163.2 ± 18.4	153.2 ± 14.1
SOD (ng/ml)	0.7 ± 0.01	0.04 ± 0.01	0.03 ± 0.01	0.04 ± 0.02
GSH (mg/dl)	11.7 ± 0.4	10.2 ± 0.3	8.4 ± 0.2	9.7 ± 0.3
GP_X (μmol/ml)	0.9 ± 0.1	0.7 ± 0.1	0.8 ± 0.2	0.7 ± 0.02
Catalase (μ/mol)	6.8 ± 0.4	5.3 ± 0.3	4.8 ± 0.4	5.2 ± 0.1
Vit E (μg/ml)	0.7 ± 0.06	0.42 ± 0.1	0.38 ± 0.3	0.37 ± 0.2
Vit C (μg/ml)	0.54 ± 0.22	0.99 ± 0.7	1.3 ± 0.05	1.5 ± 0.3

Table 3 Levels of Urea, Creatinine and Electrolytes in the 3 variants compared with control

Parameter	Control	all - b	all – t	Aml
	(n=25)	(n=25)	(n=25)	(n=25)
Creatinine (μmol/L)	85.5 ± 5	122.3 ± 7.8	100.5 ± 4.2	98.5 ± 7.2
Urea (mmol/L)	6.4 ± 0.8	10.5 ± 2.2	9.6 ± 0.8	12.6 ± 1.4
Na+ (mmol/L)	137 ± 3.2	140 ± 2.1	145 ± 3.0	139 ± 0.9
K^+ (mmol/L)	3.7 ± 0.1	9.5 ± 0.7	8.7 ±	11.4 ± 0.7
Mg^+ (mg/dl)	2.3 ± 0.4	24 ± 0.3	2.8 ± 0.5	1.9 ± 0.3
Ca^{++} (mmol/L)	12.3 ± 0.7	2.4 ± 0.1	3.3 ± 0.02	2.4 ± 0.02

Table 4 Levels of Hematological indices in 3 variants compared with control

Parameter	Control	all - b	all – t	Aml
	(n=25)	(n=25)	(n=25)	(n=25)
Hb (g/dl)	12.24 ± 1.3	11.8 ± 1.2	13.3 ± 1.2	11.2 ± 1.3
PCV (vol %)	36.7 ± 1.2	34.1 ± 1.0	33.4 ± 0.9	30.4 ± 0.6
WBC ($x10^9$/L)	5.3 ± 0.5	10.8 ± 5.3	14.7 ± 3.3	16.3 ± 9.0
Platelets (cells)	200 ± 16.5	153.5 ± 20.2	185.4 ± 15.2	196.6 ± 14.7
Ferritin (ug/L)	42.4 ± 3.3	77.4 ± 16.2	83.4 ± 14.2	58.2 ± 12.1
ESR (mm/hr)	15 ± 3	44 ± 12	40 ± 5	65 ± 12

4. Discussion

It is now known that Leukemia is common as exemplified by analytical outcomes from blood samples of subjects. Here we have used some biomarkers in an attempt to consolidate this fact. We used hematological, antioxidant and some biochemical parameters based on the variants identified. These results as shown in tables 1, 2, 3 and 4 focused on enzymes, antioxidants, electrolytes and hematological factors respectively. We observed elevation of the transaminases which confirms the work earlier done by [14].

The fall in levels of antioxidants reflects the fact that Reactive oxygen species (ROS) accumulates. Moreover, decreased level of glutathione elucidates the fact that there is over production of ROS [15]. As shown on Table 4 we observed a significant increase in the concentration of ferritin. Explanation to this could be offered by the fact that cell damage results in release of iron into the blood system. This result was identical to the findings of [16, 17].

Oxidative stress is mediated and enhanced imbalance in antioxidant activity. The major role of antioxidants is to protect the body against the debilitating role of Reactive oxygen species. The degradation of Hydrogen Peroxide (H_20_2) by SOD, Catalase, and glutathione improves the defense system against ROS generation [18, 19].

Our result shows that the production of MDA was enhanced. This has been supported by some previous findings [20]. The role of MDA in lipid peroxidation has earlier been reported [21]. They are known to play the role as important biomarkers of Leukemia. We observed marked increase in MDA concentration when compared with the control. In particular the production of hydrogen peroxide and its neutralization has been made possible by the combined actions of MDA and catalase. These antioxidant enzymes and vital micronutrient coexist at low concentration in Leukemia as a primary level of defense [22]. It has been scientifically proven that GSH deficiency accounts for the failure of immune system to act when sensitized by stimulator cells [23, 24]. Furthermore, GSH plays a role in the synthesis of DNA and repair and in Leukemia its reduction is a reflection of the decrease in the non-enzymatic antioxidant enzyme excess. Marked increase in erythrocyte sedimentation rate in all cases of Leukemia is supportive of infection, autoimmune disturbances or Rheumatoid arthritis.

The findings in this work highlight the potential of these parameters in Leukemic disease and necessitate the need to include them in our investigative panel.

5. Conclusion

Leukemia is a disease affecting all age groups. The elucidated stress state observed in this work acts in synergy to complicate blood chemistry prompting a cascade of reactions that worsens the patient's health state. Inclusion of these parameters and evaluation would enhance management decision making disease diagnosis more differential and specific.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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