Lipids and Glucose in Cerebrospinal Fluid of Children with Acute Lymphoblastic Leukemia and Hydrocephalus Disease

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***Abstract*—This study estimated the levels of lipids and glucose in cerebrospinal fluid (CSF) from children with acute lymphoblastic leukemia (ALL) and hydrocephalus disease. The study was conducted on 458 CSF, of which 176 of them have ALL, 140 have hydrocephalus, and 142 were healthy as control group from both the sexes. The age of children ranged from 1 to 15 years was divided into three subgroups according to age and sex, whereas the age of infants with hydrocephalus ranged from 1 to 14 months for both the sexes. The results showed that there was a significant decrease in cholesterol and glucose levels but increased in triglyceride and very low-density lipoprotein levels for all subgroups in both the sexes for ALL and hydrocephalus patients.**

***Index Terms*—Acute lymphoblastic leukemia, Cerebrospinal fluid, Glucose, Hydrocephalus, Lipids.**

I. Introduction

Leukemia is a group of disorders characterized by the accumulation of malignant white cells in the bone marrow and blood. These abnormal cells cause symptoms because of bone marrow failure and infiltration of organs [1]. Clinically and pathologically, leukemia is subdivided into a variety of large groups. The first division is between its acute and chronic forms [2].

Cerebrospinal fluid (CSF) is considered a part of the transcellular fluids. It is contained in the ventricles and the subarachnoid space and bathes the brain and spinal cord. The CSF is contained within the meninges and acts as a cushion to protect the brain from injury with position or movement. CSF is a clear, colorless, body fluid found in the brain, and spine produced from the choroid plexuses of the ventricles of the brain and serves several purposes as buoyancy, protection, chemical stability, prevention of brain ischemia, and clearing waste. The CSF also serves a vital function in cerebral autoregulation of cerebral blood flow [3].

Hydrocephalus was characterized by disordered secretion, circulation, and/or absorption of CSF [4]. It is generally defined as abnormal accumulation of CSF within the ventricles and subarachnoid spaces and is often associated with dilatation of the ventricular system and increased intracranial pressure [5]. It can be classified into congenital and acquired hydrocephalus. Both of the main forms of hydrocephalus come in two categories: Communicating and non-communicating depending on whether it was reabsorption problem or a blockage somewhere within the ventricular [6].

II. Materials and Methods

The study was done on 140 subjects for CSF who had acute lymphoblastic leukemia (ALL), 95 of them were male, 45 were females, and 73 were healthy children as control group take 39 male and 34 female. The age of children with ALL is between 1 and 15 years for both the sexes.

The hydrocephalus patients were 176 samples for CSF (110 male and 66 female) and 67 were healthy children as control group take 39 male and 28 female. The age of children with hydrocephalus and control group was between 1 and 14 months for both the sexes. The samples of CSF were collected by specialized doctors, and the method lumbar puncture for ALL patients was during the shunt operation for hydrocephalus patients. Different questions were asked the patients and control groups that included: Medical history, duration of disease, acute illness, weight, height, and drugs usage. The biochemical tests included each of cholesterol, triglyceride, very low-density lipoprotein (VLDL), and glucose were measured using the standard kits from Biolabo.

A. Statistical Analysis

A statistical analysis includes mean ± standard deviation and significant differences (*P* value) between groups

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that examined by an available statistical SPSS 17.0, and significant differences were estimated as the $P \leq 0.05$ [7].

III. Results and Discussion

B. Acute Lymphoblastic Leukemia

Cholesterol level in CSF

The results in Tables I and II showed that there was a significant decrease ($P \leq 0.0001$) for cholesterol levels in the CSF of children with ALL for both the sexes and in all age groups. The lowest level of cholesterol was recorded in the age group of 11–15 years for male, and this result is in agreement with previous reports [8,9]. Low plasma cholesterol levels were found to be associated with increased risk of mortality in hematopoietic cancer patient's. On the contrary, there are few studies that report no association between total serum cholesterol levels and the risk of leukemia [10]. It has been reported that the conversion of cholesterol to bile acids is suppressed in the leukemia patients, a phenomenon that may also result in a decreased intestinal absorption of cholesterol and subsequent hypocholesterolemia [11]. Dyslipidemia in cancer patients is reported to be linked with cancer risk and progression of the disease. Previous research findings showed that low levels of serum cholesterol and elevated levels of serum triglycerides are associated with the risk of overall cancers [10].

The results in Tables I and II also showed that the levels of cholesterol decreased with age and in male less than female; this result is in agreement with the report of Russo, *et al.* [12], and this may be due to severity and progression of the disease [13].

Triglyceride level in CSF

The results in Tables I and II showed that there was a high significant increase $P \leq 0.0001$ for triglyceride levels in the CSF of children with ALL for both the sexes, and in all age groups, the highest level of triglyceride was recorded in age group of 11–15 years for male; our result is in agreement with the previous report [10]. The results showed that the level of triglyceride was less in male than female, and this was in agreement with the findings of Marhoum, *et al*. [14]. However, several studies have clearly associated the risk of developing leukemia with atypical serum lipoprotein levels. Hence, a causative role of aberrant lipoprotein levels is also suggested by previous studies, at least for the malignancies of non-hematopoietic origins. Some researchers have suggested that peroxidation of plasma lipoproteins may also play a key role in cancer development [10].

Lipoproteins are susceptible to peroxidation triggered by reactive oxygen species and reactive nitrogen species. It has been proposed that lipid peroxidation product malondialdehyde that forms adducts with adenosine and cytosine may contribute to mutagenicity and carcinogenicity in mammalian cells [15].

TABLE I
Levels of Some Lipids and Glucose in CSF of Female with All

Lipids levels and glucose in CSF	Age group (mean ± SD)					
	(1–5) years		(6–10) years		(11–15) years	
	Control	Patient	Control	Patient	Control	Patient
	−10	−14	−12	−16	−11	−15
Cholesterol Mg/100 ml *10²	51.3±9.07	19±0.4**	47.3±7.02	18.2±1.9**	45.6±9.07	17.1±1.0**
Triglycerides Mg/100 ml *10²	4.3±0.65	42±2.6**	4.6±1.21	48.3±7.6**	4.7±0.87	51.0±2.6**
VLDL Mg/100 ml *10²	0.86±0.13	8.4±0.5*	0.92±0.24	9.66±1.5*	0.94±0.29	10.2±0.53*
Glucose Mg/100 ml	69.4±8.22	51.8±6.9*	67.4±5.3	50±4.6*	65.6±4.8	49.8±2.4*

CSF: Cerebrospinal fluid, ALL: Acute lymphoblastic leukemia, SD: Standard deviation, VLDL: Very low-density lipoprotein

TABLE II
Levels of Some Lipids and Glucose in CSF of Male with All

Lipids level and Glucose in CSF	Age group (mean ± SD)					
	(1–5) years		(6–10) years		(11–15) years	
	Control	Patient	Control	Patient	Control	Patient
	−12	−30	−13	−32	−14	−33
Cholesterol Mg/100 ml *10²	44.2±8.08	17.26±1.55**	43.3±13.01	17±1.0**	42.33±8.6	15±0.2**
Triglycerides Mg/100 ml *10²	4.13±1.1	39.0±3.0**	4.43±1.91	43.6±5.7**	4.66±0.85	56±12**
VLDL Mg/100 ml *10²	0.83±0.22	7.8±0.6*	0.89±0.38	8.73±1.14*	0.93±0.17	11.2±2.4*
Glucose Mg/100 ml	68.4±6.2	53.6±4.98*	66.4±6.4	52±4.6*	65.6±2.8	45.8±4.4*

CSF: Cerebrospinal fluid, ALL: Acute lymphoblastic leukemia, SD: Standard deviation, VLDL: Very low-density lipoprotein

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VLDL level in CSF

The results in Tables I and II showed that there was a significant increase ($P \leq 0.05$) for triglyceride levels in the CSF of children with ALL for both the sexes, and in all age groups, the levels of VLDL was increased with age, the highest level of triglyceride was recorded in age group of 11–15 years for male, and our result was in agreement with previous studies [16,17]. The high levels of VLDL may be due to low activity of lipoprotein lipase in leukemia patients [18].

Glucose level in CSF

The results in Tables I and II showed that there was a significant decrease ($P \leq 0.05$) for glucose levels in the CSF of children with ALL for both the sexes and in all age groups. Abnormal results include higher and lower glucose levels. Abnormal results may be due to bacterial or fungal inflammations of the central nervous system (CNS) tumor [19].

C. Hydrocephalus

Cholesterol level in CSF

The results in Table III showed that there was a high significant decrease $P \leq 0.0001$ for cholesterol levels in the CSF of children with hydrocephalus, and this result was in agreement with previous studies of Orth and Bellosta [20], who noticed a significant decrease in cholesterol level in patients' serum with Smith–Lemli–Opitz syndrome and in patients with Huntington disease [21]. Cholesterol is tightly regulated between the major brain cells neurons and glia and is essential for normal brain development. Cholesterol is required for synapse and dendrite formation [22], and depletion leads to synaptic and dendritic spine degeneration, failed neurotransmission, and decreased synaptic plasticity [23]. Cholesterol is a pivotal constituent of cell membranes, steroid hormones, and for the function of the hedgehog protein [24]. Besides of, defects in cholesterol metabolism lead to structural and functional CNS diseases such as Smith-Lemli-Opitz syndrome [25], Niemann-pick type C disease [26], and Huntington's disease [21].

Triglycerides level in CSF

The results in Table III showed that there was a significant increase ($P \leq 0.0001$) for triglycerides levels in the CSF of children with hydrocephalus and its levels in male higher than female this may be due to severity of disease in male than female, and this was in agreement with previous studies of Marhoum, *et al*., Pramanik and Harley [14,27] who found that high levels of triglycerides in CSF of children with tuberculosis meningitis may be due to the defect in blood brain barrier (BBB) [27]. This defect in the BBB maybe due to the high oxidative stress combined children with hydrocephalus [28].

VLDL level in CSF

The results in Table III showed that there was a significant increase ($P \leq 0.05$) for VLDL levels in the CSF of children with hydrocephalus, and this result was in agreement with the previous reports [27]. The lossing of BBB function by effect of oxidative stress and high level of rective oxygen species ROS which lead to defective permeability [29], and hence, the lipoproteins cross from serum to CSF.

Glucose level in CSF

The results in Table III showed that there was a significant decrease ($P \leq 0.0001$) for glucose levels in the CSF of children with hydrocephalus and for both the sexes. The low levels of glucose in CSF may be due to inflammation in the CNS or due to high consuming of glucose by white blood cells during its fight against infection and inflammation [19]. The glucose entir the brain by glucose transports any abnormality in these transporters can lead to CNS disease [30].

IV. Conclusion

The BBB losses its function in maintaining brain homoeostasis because of the oxidative stress. The age group of 11–15 years of male with ALL was the most affected subgroup with disease and the male with hydrocephalus was suffered more than female from the disease.

V. Recommendations

Conducting genetic studies to identify why male is more severly affected than female. In addition to estimate more biochemical parameter in CSF and study its relation with the disease.

TABLE III
Levels of Some Lipids and Glucose in CSF of Children with Hydrocephalus

Lipids level and glucose in CSF	Age group (mean±SD)			
	Male (1–14) months		Female (1–14) months	
	Control (39)	Patients (110)	Control (28)	Patients (66)
Cholesterol Mg/100 ml *10^2	42.6±11.07	4.34±0.51**	43.2±10.96	5.51±1.17**
Triglycerides Mg/100 ml *10^2	0.87±4.16	13.57±2.68*	3.8±0.43	11.3±3.43*
VLDL Mg/100 ml *10^2	0.83±0.17	2.17±0.64*	0.76±0.19	2.26±0.79*
Glucose Mg/100 ml	69.8±8.7	28.75±9.2**	71.2±12.3	34.9±10.1**

CSF: Cerebrospinal fluid, SD: Standard deviation

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