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DETERMINATION OF ALPHA-1-ACID GLYCOPROTEIN LEVEL,
TOTAL PROTEINS, AND PROTEIN ELECTROPHORESIS IN
SERUM OF CHILDREN WITH ACUTE
LYMPHOBLASTIC LEUKEMIA

A THESIS

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BY

ADEL MOHAMED ABDALLA ABOUZEID
[M.B., B.Ch.]

618.72994
A.M

SUPERVISORS

PROF. DR. FOUAD EL BADRAWY
Professor Of Pediatrics
Faculty Of Medicine
AIN SHAM UNIVERSITY

25398

Prof. Dr. ALI KHALIFA ALI
Professor Of Biochemistry
Faculty Of Medicine
AIN SHAMS UNIVERSITY

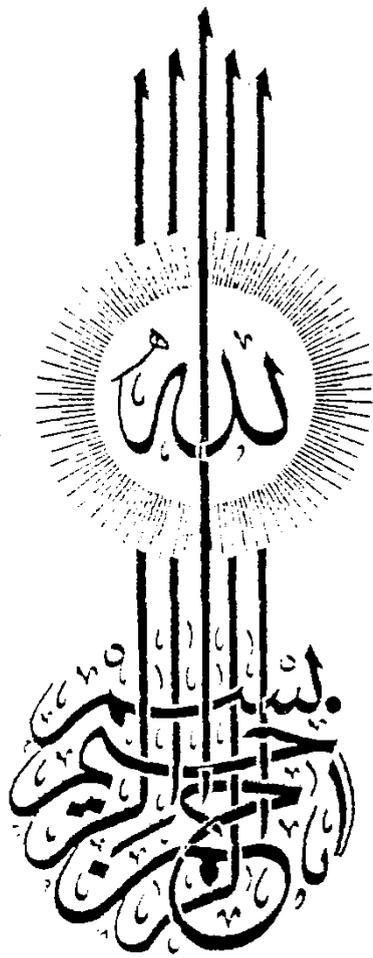
Prof. Dr. MOHAMED REDA HANZA
Professor Of Medical Oncology
National Cancer Institute
CAIRO - UNIVERSITY

FACULTY OF MEDICINE
AIN SHAM UNIVERSITY

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ABREVIATIONS

Alb : Albumin

ALL : Acute lymphoblastic leukemia.

B.M biopsy : Bone marrow biopsy.

Fig. : Figure.

No. : Number

% : Percent

Y : Year

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INTRODU

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INTRODUCTION

LITRATURE REVIEW



PLASMA PROTEINS

The proteins of the plasma are actually a very complex mixture of components which differ in properties and functions. They include not only simple proteins but also mixed or conjugated proteins such as glycoproteins and various types of lipoproteins [Mortin ,1985].

ORIGIN OF PLASMA PROTEINS

The liver is the sole source of fibrinogen, prothrombin and albumin. Most of the alpha and beta globulins are also of hepatic origin , but the gamma globulins originate from plasma cells and lymphoid tissue. Indeed , gamma globulins are the only proteins secreted by isolated lymph node cells . Sever hypoproteinaemia develops when the products of digestion are deviated from the liver by anastomosis of the hepatic vein with the inferior vena cava [Eck's Fistula] which results in progressive impairment of liver functions. [Harper,1985].

Dietary proteins serves as a precursor of plasma proteins. All dietary proteins are not equally effective in supplying materials for the regeneration of plasma proteins. High quality proteins such as beef , egg , albumin and liver are extremely effective in maintaining plasma protein levels, while those poor in quality such as wheat

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gluten and gelatin are poor in this respect. [Whipple,1948].

NORMAL PLASMA PROTEIN COMPONENTS

Plasma contains many different proteins, each with a specific function or a set of functions which differ in their chemical constitution. This difference in chemical constitution will be reflected on their physical properties as the specific gravity, solubility, electric charge and immunological identity.[Turner and Hulne,1971].

Normal value of total serum protein, in healthy children is 6.0 g/100 ml when recumbent, it is higher when ambulatory [6.5 - 8.5] . This effect of posture varies with the individual and the difference may be as much as 1.2 gm/100 ml [Grant and Kachmar,1976].

Normal values obtained by Kohn and Feinberg [1976] using the small scale cellulose acetate electrophoresis, with ponceau-s staining and evaluation by scanning without correction using transmitted light are :

- Albumin 3.5 - 5.2 gm/100 ml [57-68%].
- Alpha-1-globulin 0.1-0.4 gm/100 ml [1.0-5.7%]
- Alpha-2-globulin 0.4-0.8 gm/100 ml [4.9-11.2%].
- Beta globulin 0.5-1.0 gm/100 ml [7-13%].
- Gamma globulin 0.6-1.3 gm/100 ml [9.8-18.2%].

Table I summarizes normal components of plasma proteins.

The following are the essential fractions of normal proteins in the serum :

1. ALBUMIN

This fraction of the serum proteins, the most abundant of the proteins in the serum is synthesized in the liver. It has a molecular weight of approximately 69,000 . The primary structure of serum albumin consists of 610 amino acids arranged in a single peptide chain . The secondary structure of albumin appears to be one in which the chain is folded back upon itself to form layers which can infolded by lowering the pH and refolded by raising the pH again [Mortin, 1985].

Normal values of protein fractions depend on the analytical methods used. In one series the normal mean serum albumin by electrophoresis was 4.2 gm/100 ml whereas simultaneous analysis using the salting out procedure gave values of 4.9 gm/100 ml [Sherlock,1975].

Similar observations were reported by Simmons and Goller [1964] who found that the auto analytical procedures tend to give lower serum albumin values.

From Grant and Kachmar, [1976]

Table [I] Normal components of plasma proteins

Electrophoretic Bands	Normal Range (depth of staining of electrophoretic fractions) (g/100ml)	Main Constituents and Their Molecular Masses	Average values and Approximate Normal Ranges of Individual Proteins g/100 ml	Biological Function
Albumin	3.5-5.0	Albumin (Alb)	4.4 (3.5-5.0)	Transport of fatty acids; regulation of plasma volume, colloid osmotic pressure. Vides main protein reserve
α ₁	0.17-0.31	α ₁ -antitrypsin(α ₁ ATF). Cause of band on protein staining.	0.25 (0.2-0.4)	Proteinase inhibitor.
		α ₁ -lipoprotein (α ₁ Lp) (Apoprotein A) Cause of band on fat staining.	0.36 (0.23-0.77)	Transport of lipids, fat soluble vitamins, and hormones. Not established.
α ₂	0.42-0.90	Orosomucoid (α ₂ AGP) (α ₂ -acid-glycoprotein, seromucoid) stains only faintly with protein stain.	0.04 (0.05-0.14)	
		α ₂ -macroglobulin(α ₂ M)	0.20-0.25	Plasmin inhibitor
		Haptoglobin(Hpt)	From 85,000 up to more than 1,000,000 in higher polymers. Very large	Binds hemoglobin, preventing loss of iron. Transport lipids, especially triglycerides.
β ₁	0.52-1.07	Pre-β ₁ -lipoprotein(VLDL) (Apoprotein A, B, and C) Seen only on fat staining.		
		Transferrin (Tr) (siderophilin)	80,000-90,000	Iron transport. Dense binding.
		Hemopexin	80,000	
β ₂	0.50-0.14 (only present in fresh serum)	-β ₂ ipoprotein (Ip) (Apoprotein B) Requires fat stain.	about 3,000,000	Lipid transport, especially cholesterol, fat-soluble vitamins, and hormones.
		IC	0.11 (0.08-0.14)	Complement Factor C3. On standing converted to IA.
γ	0.71-1.65	Immunoglobulin G (IGG, G)	150,000	Antibodies
		Immunoglobulin A (IGA, A)	1.16 (1.25 IU/ml) (0.8-1.4)	Antibodies, especially

Normal individuals make about 10 gm albumin daily [Tavil et al.,1968].

The normal half life of serum albumin is 20 - 26 days [Wilkinson and Menden - Hall,1963].

2. ALPHA-1-GLOBULIN

Alpha-1-globulin is second to albumin in its anodal migration and the smallest of the five components routinely fractionated. The normal adult level ranges from 2.5 to 5% of the total plasma proteins level [0.1-0.4 g/dl]. Forfar and Arniel [1984] gave a level of 0.3 gm/100 ml for the newborn , 0.2-0.4 gm/100 ml at one year of age and over.

3. ALPH-2-GLOBULINS

Alpha-2-globulin is the third in its anodal migration . The normal adult range was found to be 7-13 % of total plasma proteins [0.4 - 1.2 g/dl] [Harper,1985].

Forfar and Arniel [1984] gave a level of 0.4 - 0.6 gm/100 ml for the newborn, 0.4 - 1.0 gm/100 ml at one year and over.

4. BETA GLOBULINS

This is the fourth in the relative anodal migration.

The normal adult value is 8-14% of total plasma proteins [0.5 - 1.1 gm/dl] [Harper , 1985].

Forfar and Arniel [1984] gave a level 0.8-1.1 gm/100 ml for the newborn, 0.5 - 1.0 gm/100 ml at one year and 0.6 - 1.1 gm/100ml at four years and over.

5. LIPOPROTEINS

About 3 % of the plasma protein consists of lipid and protein migrating with the alpha globulins and about 5 % of similar mixtures migrating with the beta-globulins [Harper, 1985].

Lipoproteins are classified according to their sedimentation rate into :

- Very low density lipoproteins. [VLDL]
- Low density lipoproteins [LDL]
- and - High density lipoproteins [HDL]

Immunologic properties of lipoproteins have been investigated by using isoimmuno antibodies, usually produced in humans who were immunized in the course at numerous transfusions and by using heteroimmune antibodies produced experimentally in rabbits or other animals by repeated injection of [LDL] isolated from single individuals.

Anti-B-lipoproteins [anti-LDL] sera precipitate LDL and VLDL , but not HDL. Anti- α - lipoproteins [Anti-HDL] sera precipitate native and lipid-free HDL , but not LDL or VLDL. According to the most current model of lipoprotein metabolism, chylomicrons are synthesized in the intestine, released into the lymphatics and eventually reach the systemic circulation at which time they acquire additional protein. This represents the major means of transport of exogenous triglycerides.

VLDL are synthesized in the liver in response to excess dietary carbohydrate or in response to fatty acids mobilized from adipose tissue. This is the main form of transport of endogenous triglycerides and cholesterol. Lipoprotein lipase activity in the serum which may be due to a single enzyme or isoenzyme from various sources, Catalyzes the removal of triglycerides from chylomicrons and VLDL [Henry et al.,1974].

The lipoproteins probable function as major carriers of the lipids of the plasma since most of the plasma that is associated with them . Such combinations of lipid with protein provide a vehicle for the transport of fat in a predominantly aqueous medium such as plasma [Hrper,1985].