



Research Article

Clinical Chemistry Studies in Children with lymphadenopathy at Tanta University Hospital

Ahmed Samy El-Shafey^{1,*} , Saida Mohamed Amer¹ ,
Nanis Gamal El-Din Alam¹ , Mohamed Ramadan El-Shanshory² ,
Fatma Abdel Hamid Ibrahim³

¹Faculty of Science, Tanta University, Tanta, Egypt

²Faculty of Medicine, Tanta University, Tanta, Egypt

³Biochemistry Department, National Research Center, Cairo, Egypt

Abstract

Lymphadenopathy refers to the enlargement of lymph nodes that can be due to autoimmune disease, and malignancy or microbial infections. The lymph nodes, often referred to as lymph glands, are essential for the body's ability to combat infections. They function as filters, capturing viruses, bacteria, and other pathogens before they have the chance to infect other regions of the body. Frequently, swollen lymph nodes can be found in the neck, beneath the chin, in the armpits, and in the groin. Lactate dehydrogenase (LDH), β 2 Microglobulin, Total bilirubin, direct bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), Albumin, Creatinine and urea were measured in serum of children with lymphadenopathy to help for diagnosis and monitoring of lymphadenopathy. The results Showed that, there was significant increase in serum LDH level and β 2 Microglobulin, ALT, AST in children with lymphadenopathy compared to healthy control children (P value = 0.005), (P value = 0.006), (P value = 0.026), (P value = 0.004) respectively. there was no significant differences in serum level of total. bilirubin, direct bilirubin, Albumin, Creatinine and urea in children with lymphadenopathy compared to healthy control children (P value = 0.322), (P value = 0.098), (P value = 0.694), (P value = 0.837), (P value = 0.850) respectively.

Keywords

Lymphadenopathy, Lactate Dehydrogenase, β 2 Microglobulin, Alanine Aminotransferase, Aspartate Aminotransferase (AST), Albumin, Creatinine, Urea

1. Introduction

Lymphadenopathy denotes the swelling of lymph nodes, which is frequently observed in routine clinical practice. While the occurrence of neoplasms in individuals with lymphadenopathy in a primary care environment is relatively low, ranging from 1% to 2%. The causes of lymphadenopathy,

aside from neoplasms, encompass several categories: infections, autoimmune disorders, and idiopathic conditions [9].

Evaluating lymphadenopathy in pediatric patients poses a diagnostic challenge due to the wide range of differential di-

*Correspondence: Ahmed Samy El-shafey (ahmedsamymmd@gmail.com)



agnoses, which encompass both reactive and malignant conditions. Understanding the etiological patterns of lymphadenopathy specific to a geographical area is crucial for achieving an accurate diagnosis or for raising suspicion of a particular disease. [8].

An increased level of LD is a recognized observation in cases of non-Hodgkin lymphoma or leukemia. Nevertheless, it can also occur in a range of other medical conditions, as LD is produced by multiple tissues, including muscle, liver, kidney, and hematopoietic cells. Numerous studies have identified an elevated LD level in necrotizing lymphadenitis, making it one of the most commonly noted laboratory findings [5, 16].

Beta 2-Microglobulin is a low molecular weight protein that shares sequence homology with immunoglobulins. As a component of the HLA complex, this protein serves as a significant cell-surface structure. Under typical circumstances, beta 2-microglobulin is produced and released by various cells, especially lymphocytes, and can be found in the bloodstream of healthy individuals. Due to its small molecular size, it is usually filtered efficiently at the glomerulus and is broken down by the proximal tubular cells in the kidney. Both impaired kidney function and excessive production of beta 2-microglobulin are linked to elevated serum levels. A role for beta 2-microglobulin as a modulator of lymphocyte surfaces and a possible regulator of the immune system has been suggested. [3].

Aminotransferase comprises AST and ALT. These enzymes serve as indicators of hepatocellular damage. They are involved in gluconeogenesis by facilitating the transfer of amino groups from aspartic acid or alanine to ketoglutaric acid, resulting in the formation of oxaloacetic acid and pyruvic acid, respectively. AST exists in both cytosolic and mitochondrial isoenzymes and is located in the liver, cardiac muscle, skeletal muscle, kidneys, brain, pancreas, lungs, leukocytes, and red blood cells. It is less sensitive and specific for liver conditions compared to ALT, and elevations in AST levels may also occur due to nonhepatic factors. In neonates and infants, AST activity is roughly double that of adults, but this level decreases to that of adults by around six months. [14].

Bilirubin is the final product of heme breakdown, with 80% originating from hemoglobin. Unconjugated bilirubin is carried to the liver while loosely attached to albumin. Being water-insoluble, bilirubin cannot be eliminated through urine. In contrast, conjugated bilirubin is water-soluble and can be found in urine. It undergoes conjugation in the liver to form bilirubin glucuronide, which is then secreted into bile and subsequently into the gut. [6].

Albumin is produced by the hepatic parenchymal cells at a rate influenced by colloidal osmotic pressure and dietary protein consumption. The synthesis rate of albumin is also regulated by feedback mechanisms that depend on the concentration of plasma albumin. It is possible to maintain plasma albumin levels with merely 10% of the normal hepatocyte mass. The half-life of albumin is approximately

21 days. Traces of albumin are present in nearly all extracellular body fluids. Minimal amounts are lost from the body through excretion. Albumin is catabolized in various tissues, and its uptake by cells occurs via pinocytosis. The amino acids that make up albumin are released through intracellular proteolysis and returned to the body's amino acid pool. In cases of liver disease, there is a decrease in serum albumin, indicating reduced synthesis. If liver function is normal but serum albumin levels are low, this may indicate inadequate protein intake (malnutrition) or protein loss due to conditions such as nephrotic syndrome, malabsorption, or protein-losing enteropathy. [4].

The assessment of serum creatinine and serum urea nitrogen concentrations is highly significant in evaluating renal function within a clinical context. It is most effective to consider these two serum measurements together, taking into account both their absolute values and their interrelationship. The serum creatinine concentration is less affected by factors outside the kidneys compared to the serum urea nitrogen concentration, making it the more reliable test [12].

2. Material and Methods

2.1. Sampling

Blood samples were taken from children with lymphadenopathy and healthy children at Tanta university hospital. This study was done according to guidelines of Ethics Committee of Scientific Research for medical research at Tanta University with code # 32017/02/18

This study included

First group: Children with lymphadenopathy (35 children; 22 males and 13 females) (their age ranged from 2 to 13 years old)

Second group: The control group will contain healthy children (20 children; 11 males and 9 females) (their age ranged from 2 to 13 years old).

2.2. Determination of Serum Lactate Dehydrogenase (LDH)

Lactate dehydrogenase (LDH) test is in vitro test for the quantitative determination of lactate dehydrogenase in human serum on Roche/Hitachi cobas c systems. This occurs according to [17].

2.3. Determination of Serum Beta2-Microglobulin (β2M)

Beta2-Microglobulin (β2M) test is in vitro diagnostic test for the quantitative determination of beta 2-microglobulin in samples of human origin by immunoturbidimetry on photometric systems. This occurs according to [2].

2.4. Determination of Alanine Aminotransferase (ALT/GPT)

Alanine aminotransferase (ALT or GPT) facilitates the transfer of the amino group from alanine to 2-oxoglutarate, resulting in the formation of pyruvate and glutamate. The catalytic concentration is ascertained from the rate of decrease of NADH, which is measured at 340 nm, through an LDH coupled reaction as referenced in [7].

2.5. Determination of Aspartate Aminotransferase (AST/GOT)

Aspartate aminotransferase (AST) facilitates the transfer of the amino group from aspartate to 2-oxoglutarate, resulting in the formation of oxaloacetate and glutamate. The catalytic concentration is ascertained from the rate of decline of NADH, which is measured at 340 nm, through the malate dehydrogenase (MDH) coupled reaction as outlined in [7].

2.6. Determination of Bilirubin

Bilirubin is transformed into the colored compound azobilirubin through the action of diazotized sulfanilic acid and is subsequently measured using photometric methods. Among the two forms present in serum, namely bilirubin-glucuronide and free bilirubin that is loosely associated with albumin, only the former reacts directly in an aqueous solution (referred to as direct bilirubin), whereas free bilirubin necessitates solubilization with caffeine in order to react (known as indirect bilirubin). In this determination, the results reflect the total bilirubin level. The intensity of the color formed is proportional to the bilirubin concentration in the sample according to [19].

2.7. Determination of Serum Creatinine

Spectrum Diagnostics creatinine reagent is intended for the in-vitro quantitative, diagnostic determination of creatinine in human serum according to [18].

2.8. Determination of Serum Urea

Spectrum colorimetric urea reagent is intended for the in-vitro quantitative, diagnostic determination of urea in human serum according to [1].

3. Results

3.1. Determination of Serum Lactate Dehydrogenase (LDH)

Serum samples were collected from children with lymphadenopathy and healthy children to determine the level of serum lactate dehydrogenase (LDH). The results in Table 1 showed that, there was significant increase in serum LDH level in children with lymphadenopathy compared to healthy control children (P value = 0.005).

Table 1. Comparison between children with lymphadenopathy and healthy control children as regards serum lactate dehydrogenase (LDH) level.

Groups	Serum lactate dehydrogenase (LDH)		T test	
	Range by (mg/dl)	Mean $\pm$ SD	T-test	P-value
Children with lymphadenopathy	224 - 1589	534.97 $\pm$ 279.35	4.018	0.005*
Healthy control children	123 - 517	275.80 $\pm$ 89.83		

3.2. Determination of Serum Beta2-Microglobulin (β 2M)

Serum samples were collected from children with lymphadenopathy and healthy children to determine the level of serum level Beta2-microglobulin (β 2M). The results in Table 2 showed that, there was significant increase in serum level of Beta2-microglobulin (β 2M) in children with lymphadenopathy compared to healthy control children (P value = 0.006).

Table 2. Comparison between children with lymphadenopathy and healthy control children as regards serum level of Beta 2-microglobulin.

Groups	Serum level of Beta2-microglobulin		T test	
	Range by (mg/dl)	Mean $\pm$ SD	T-test	P-value
Children with lymphadenopathy	1.1 - 5.76	2.028 $\pm$ 1.04	4.605	0.006*
Healthy control children	0.7 - 1.95	1.17 $\pm$ 0.376		

3.3. Determination of Serum Alanine Aminotransferase (ALT/GPT)

Serum samples were collected from children with lymphadenopathy and healthy children to determine the level of serum alanine aminotransferase (ALT/GPT). The results in Table 3 showed that, there was significant increase in serum ALT level in children with lymphadenopathy compared to healthy control children (P value = 0.026).

Table 3. Comparison between children with lymphadenopathy and healthy control children as regards serum alanine aminotransferase (ALT/GPT) level.

Groups	Serum alanine aminotransferase (ALT/GPT)		T test	
	Range by (mg/dl)	Mean $\pm$ SD	T-test	P-value
Children with lymphadenopathy	10 - 106	33.21 $\pm$ 21.81	2.442	0.026*
Healthy control children	10 - 32	18.20 $\pm$ 7.24		

3.4. Determination of Aspartate Aminotransferase (AST/GOT)

Serum samples were collected from children with lymphadenopathy and healthy children to determine the level of serum aspartate aminotransferase (AST/GOT). The results in Table 4 showed that, there was significant increase in serum AST level in children with lymphadenopathy compared to healthy control children (P value = 0.004).

Table 4. Comparison between children with lymphadenopathy and healthy control children as regards aspartate aminotransferase (AST/GOT) level.

Groups	Aspartate aminotransferase (AST/GOT).		T test	
	Range by (mg/dl)	Mean $\pm$ SD	T-test	P-value
Children with lymphadenopathy	12 - 69	34.57 $\pm$ 13.94	3.168	0.004*
Healthy control children	11 - 34	21 $\pm$ 7.90		

3.5. Determination of Serum Total Bilirubin in Children with Lymphadenopathy Compared to Healthy Control Children

Serum samples were collected from children with lymphadenopathy and healthy children to determine the level of serum total bilirubin. The results in Table 5 showed that, there was no significant difference in serum total bilirubin level in children with lymphadenopathy compared to healthy control children (P value = 0.322).

Table 5. Comparison between children with lymphadenopathy and healthy control children as regards serum total bilirubin level.

Groups	Serum total bilirubin		T test	
	Range by (mg/dl)	Mean $\pm$ SD	T-test	P-value
Children with lymphadenopathy	0.4 - 1.1	0.714 $\pm$ 0.195	1.008	0.322
Healthy control children	0.5 - 1	0.785 $\pm$ 0.179		

3.6. Determination of Serum Direct Bilirubin in Children with Lymphadenopathy Compared to Healthy Control Children

Serum samples were collected from children with lymphadenopathy and healthy children to determine the level of serum direct bilirubin. The results in Table 6 showed that, there was no significant difference in serum direct bilirubin level in children with lymphadenopathy compared to healthy control children (P value = 0.098).

Table 6. Comparison between children with lymphadenopathy and healthy control children as regards serum direct bilirubin level.

Groups	Serum direct bilirubin		T test	
	Range by (mg/dl)	Mean $\pm$ SD	T-test	P-value
Children with lymphadenopathy	0.1 - 0.5	0.221 $\pm$ 0.112	1.743	0.098
Healthy control children	0.1 - 0.2	0.164 $\pm$ 0.049		

3.7. Determination of Serum Albumin in Children with Lymphadenopathy Compared to Healthy Control Children

Serum samples were collected from children with lymphadenopathy and healthy children to determine the level of serum albumin. The results in Table 7 showed that, there was no significant difference in serum albumin level in children with lymphadenopathy compared to healthy control children (P value = 0.694).

Table 7. Comparison between children with lymphadenopathy and healthy control children as regards serum albumin level.

Groups	Serum albumin		T test	
	Range by (mg/dl)	Mean $\pm$ SD	T-test	P-value
Children with lymphadenopathy	3.4 - 4.5	3.985 $\pm$ 0.348	0.398	0.694
Healthy control children	3.7 - 4.4	4.028 $\pm$ 0.201		

3.8. Determination of Serum Creatinine in Children with Lymphadenopathy Compared to Healthy Control Children

Serum samples were collected from children with lymphadenopathy and healthy children to determine the level of serum creatinine. The results in Table 8 showed that, there was no significant difference in serum creatinine level in children with lymphadenopathy compared to healthy control children (P value = 0.837).

Table 8. Comparison between children with lymphadenopathy and healthy control children as regards serum creatinine level.

Groups	Serum creatinine		T test	
	Range by (mg/dl)	Mean $\pm$ SD	T-test	P-value
Children with lymphadenopathy	0.4 - 0.68	0.519 $\pm$ 0.085	0.207	0.837
Healthy control children	0.3 - 0.8	0.528 $\pm$ 0.143		

3.9. Determination of Serum Urea in Children with Lymphadenopathy Compared to Healthy Control Children

Serum samples were collected from children with lymphadenopathy and healthy children to determine the level of serum urea. The results in Table 9 showed that, there was no significant difference in serum urea level in children with lymphadenopathy compared to healthy control children (P value = 0.850).

Table 9. Comparison between children with lymphadenopathy and healthy control children as regards serum urea level.

Groups	Serum urea		T test	
	Range by (mg/dl)	Mean $\pm$ SD	T-test	P-value
Children with lymphadenopathy	16 - 36	25.35 $\pm$ 5.017	0.190	0.850
Healthy control children	15 - 34	25.7 $\pm$ 5.31		

4. Discussion

Lymphadenopathy refers to an abnormality in the size and texture of lymph nodes, a condition that is relatively prevalent during childhood. When the swelling of lymph nodes results from inflammatory and infectious processes, it is termed lymphadenitis [15].

In the present work, the obtained results indicated that there was significant increase in the levels of serum lactate dehydrogenase enzyme in children with lymphadenopathy compared to their levels in healthy control children. Usefulness of lactate dehydrogenase in differentiating abnormal cervical lymphadenopathy could be explained by [10] who studied relationship between lactate dehydrogenase and lymphadenopathy they reported that An increased level of LDH serves as a valuable indicator for cervical lymphadenopathy, necessitating additional clinical monitoring or intervention in cases such as necrotizing lymphadenitis, hematologic neoplasms, metastatic lymphadenopathy, tuberculous lymphadenitis, bacterial infectious diseases, infectious mononucleosis, autoimmune disorders, and various other abnormal conditions. On the same context, [11] studied Serum lactic dehydrogenase (LDH) levels in acute leukemia and examined LDH levels in 42 patients diagnosed with acute leukemia, 9 patients with chronic myeloid leukemia, 6 of whom were in blastic crisis, and 53 patients

suffering from lymphoma and other lymphoproliferative disorders. The findings indicated that the differences in serum LDH levels between acute lymphocytic leukemia (ALL) and acute non-lymphocytic leukemia (ANLL) were statistically significant ($p < 0.001$). It seems that significantly elevated serum LDH levels in cases of acute leukemia are indicative of ALL, and in individual patients, the LDH levels correlated with the number of blasts observed during both remission and relapse. These findings align with those of [8], who investigated lymphadenopathy in Egyptian pediatric patients. They reported the presence of certain abnormal complete blood count findings, including blast cells in blood films and elevated lactate dehydrogenase levels.

In the present work, the obtained results indicated that there was significant increase in serum level of Beta2-microglobulin ($\beta 2M$) in children with lymphadenopathy compared to their levels in healthy control children. The findings align with those of [13], who investigated blood biomarkers in patients with lymphadenopathy, highlighting their diagnostic importance in identifying malignancy. Their study assessed serum levels of beta2-microglobulin and concluded that elevated beta2-microglobulin ($\beta 2M$) ($P = 0.012$) was linked to malignant conditions. A cut-off value of 3699.5 $\mu\text{g/L}$ was established to distinguish malignancies from benign conditions, providing a sensitivity of 63.4% and specificity of 87.0%.

Abbreviations

LDH /LD	Lactate dehydrogenase
β2 M	β2 Microglobulin
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
HLA	Human Leukocyte Antigen

Author Contributions

Ahmed Samy El-Shafey: Data curation, Formal Analysis, Funding acquisition, Methodology, Writing, Investigation Conceptualization

Saïda Mohamed Amer: Supervision, Project administration

Nanis Gamal El-Din Alam: Supervision, Validation

Mohamed Ramadan El-Shanshory: Supervision, Visualization

Fatma Abdel Hamid Ibrahim: Supervision, Software

Conflicts of Interest

The authors declare no conflicts of interest.

References

- [1] Batton, C. J & crouch, S. R (1977): Anal. Chem. 49: 464-469.
- [2] Carl AB, Edward RA and David EB (2006): Tietz Textbook of Clinical chemistry and molecular Diagnostics, fourth edition. pp: 138: 140.
- [3] Bernier GM. (1980): beta 2-Microglobulin: structure, function and significance. Vox Sang. 38(6): 323-7.
<https://doi.org/10.1111/j.1423-0410.1980.tb04500.x>
- [4] Chen CB, Hammo B, Barry J, Radhakrishnan K.(2021): Overview of Albumin Physiology and its Role in Pediatric Diseases. Curr Gastroenterol Rep. 23(8): 11.
- [5] Erez A, Shental O, Tchebiner JZ, Wasserman A, Sella T, Guzner-Gur H (2014): Diagnostic and prognostic value of very high serum lactate dehydrogenase in admitted medical patients. Israel Med Assoc J. 2014; 16(7): 439-43.
- [6] Fevery J.(2008): Bilirubin in clinical practice: a review. Liver Int. 28(5): 592-605.
- [7] Gella, F. J.; Olivella, T.; Cruz, Pastor. M.; Arenas J.; Moreno, R.; Durban, R. and Gómez, J. A.(1985) A simple procedure for routine determination of aspartate aminotransferase and alanine aminotransferase with pyridoxal phosphate. Clin Chim Acta, USA; 153: 241-247.
- [8] Gwili NM, Hadi MA, Eldin AN, Hassab HM, Eldin YS, Fadel SH, Mashali NA.(2014): Lymphadenopathy in a series of Egyptian pediatric patients and the role of pathology in the diagnostic workup. Pediatr Dev Pathol. 17(5): 344-59.
<https://doi.org/10.2350/14-03-1480-OA.1>
- [9] Habermann TM, Steensma DP. (2000): Lymphadenopathy. Mayo Clin Proc. 2000; 75(7): 723-32.
- [10] Kamiya N, Ishikawa Y, Takeshima T, Sagara Y, Yamamoto S, Naka Mieno M, Kotani K and Matsumura M. (2020): Usefulness of lactate dehydrogenase in differentiating abnormal cervical lymphadenopathy. J Gen Fam Med. 22(2): 75-80.
- [11] Kornberg A and Polliack A. (1980): Serum lactic dehydrogenase (LDH) levels in acute leukemia: marked elevations in lymphoblastic leukemia. Blood. 56(3): 351-5.
- [12] Lyman JL.(1986): Blood urea nitrogen and creatinine. Emerg Med Clin North Am. 4(2): 223-33.
- [13] Ma S, Guo J, Lu D, Zhu L, Zhou M, Zhou D, Li L, Zhu J, Yang X, Zheng Y, Ye X, Xie W. (2017): Blood biomarkers in adults with lymph node enlargement contribute to diagnostic significance of malignancy. Oncotarget. 2017 Oct 23; 8(58): 98533-98541. <https://doi.org/10.18632/oncotarget.21963>
- [14] Oh RC, Hustead TR, Ali SM, Pantsari MW.(2017): Mildly Elevated Liver Transaminase Levels: Causes and Evaluation. Am Fam Physician.; 96(11): 709-715.
- [15] Pecora F, Abate L, Scavone S, Petrucci I, Costa F, Caminiti C, Argentiero A and Esposito S. (2021): Management of Infectious Lymphadenitis in Children. Children (Basel). 8(10): 860.
- [16] Shihadeh F, Reed V, Faderl S, Medeiros LJ, Mazloom A, Hadziahmetovic M. (2012): Cytogenetic profile of patients with acute myeloid leukemia and central nervous system disease. Cancer. 2012; 118(1): 112-7.
- [17] Thomas L, (1992): ed. Labor und Diagnose [Laboratory and diagnosis]. 4th ed. Marburg: Die Medizinische Verlagsgesellschaft [The Medical Publishing Company]. pp 120.
- [18] Tietz NW: (1986): Textbook of clinical chemistry. WB Saunders, Philadelphia, 1986.
- [19] Tietz, N. W. (1995): Clinical Guide to Laboratory Tests, 3rd ed. AACC. USA.