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Study of Changes for Total Sialic Acid and Lipid-Bound Sialic Acid Levels in Tuberculosis and Lung cancer

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Abstract

Sialic acid (SA) have been used as one of laboratory markers in diagnosis a variety of pathological conditions, and it have been found to be elevated in a number of different cancers .Many studies have shown that mean values of total sialic acid (TSA) or lipid-bound sialic acid (LSA) were higher in patients with cancer than in normal subjects .The aim of the present study was to determine the serum of total sialic acid (TSA), lipid-bound sialic acid (LSA),total protein (TP) and TSA/TP levels in the(Tuberculosis TB and Lung cancer LC) compared with healthy controls , data analysis indicated a significant increase (P=0.0001) in TSA and LSA levels in (TB,LC) groups in comparison with healthy controls, no difference was observed in TSA concentrations between (TB,LC) groups, no difference LSA levels were observed when (TB) patients compared with healthy controls ,.The concentration of TP was slightly elevated(P=0.042) in (TB,LC) groups comparison with healthy controls ,there was a significant increased (P=0.0001) in TSA/TP levels in (TB,LC) groups in comparison with healthy controls.

المستخلص

يعتبر حمض السياليك أحد الدلائل المختبرية لتشخيص العديد من الحالات المرضية غير السرطانية ووجد أن ارتفاع مستواه في العديد من السرطانات , والكثير من الدراسات تؤكد أن مستويات حمض السياليك الكلي TSA وحمض السياليك المرتبط بالشحوم LSA تزداد بصورة ملحوظة في مصل عدد من المصابين بالحالات السرطانية مقارنة مع الأشخاص السليمين, تتضمن هذه الدراسة تقدير لمستويات TSA, LSA ,TP, TSA/TP في مصل المرضى المصابين بداء السل وسرطان الرئة بالمقارنة مع مستوياتهم في مصل الأشخاص السليمين, حيث أظهرت زيادة معنوية(P=0.0001) في مستوياتLSA, TSA لمصل المرضى المصابين بداء السل وسرطان الرئة بالمقارنة مع مستوياتهم في مصل الأشخاص السليمين, ولكن لم يظهر فرق معنوي في مستوىTSA بحالتي داء السل وسرطان الرئة وعندما قورن مستوى LSA بمصل المرضى المصابين بداء السل مع مستوياته في مصل الأشخاص السليمين لم تظهر زيادة معنوية. كذلك وجدت زيادة بسيطة(P=0.042) في مستوى البروتين الكلي TP بحالتي داء السل وسرطان الرئة عندما قورن بمصل الأشخاص السليمين وللحصول على حساسية وخصوصية عالية في تشخيص حالتي داء السل وسرطان الرئة تم حساب نسبة(حمض السياليك/البروتين TSA/TP) والتي تعتبر ذات أهمية في التفريق بين الحالات السابقة, حيث أظهر زيادة معنوية (P=0.0001) في مستوياته لمصل المرضى المصابين بداء السل وسرطان الرئة بالمقارنة مع مستوياته في مصل الأشخاص السليمين.

Introduction

Sialic acid SA, a family of acylated derivatives of neuraminic acid, usually occurs as a terminal component at the non-reducing end of carbohydrate chains of glycoproteins and glycolipids [1] ,it is generally considered that human serum contains no free and that 90% of the serum sialic acid is bound to the α and β globulins. Moreover, the only member of the sialic family so far identified in human serum is the N acetyl derivative of neuraminic acid [2], which occur widely in nature, as present in variety of tissues and body fluids of higher animals and some bacteria but not plants or lows invertebrates [3].It is found in negatively charged surface polyanions on various cell membranes and plays an important role in the antigenic characterization of cells [4]. Sialic acid is present in high concentrations as components of glycoproteins, glycolipids such as gangliosides, or polysaccharides [5]. Serum sialic acid levels have been used as laboratory markers in a variety of pathological conditions [6, 7] .Studies with normal children showed that serum sialic acid levels were independent of age and sex .In children with various diseases (tubercular meningitis and rickets) the serum sialic acid levels increase [8], and it have been found to be elevated in a number of different cancers, therefore, is a biologic marker for malignant diseases [9]. Sialic acid concentrations have been reported to be related not only to diagnosis ,but also to staging ,prognosis and detection of early recurrence[1].Although considerable individual variation exists ,increases in the serum sialic acid level have been shown to be proportional to the tumor stage and are significantly higher than in normal population, the relationship between sialic acid(N-acetyl neuraminic acid),tumor stage ,and clinical course indicates that serum sialic acid analysis could prove clinically important as a monitor of tumor burden in individual patient [10]. A significant correlation has been demonstrated between TSA levels; activity and tumor stage of breast cancer [11].Marked elevation of serum TSA and lipid-bound sialic acid LSA that correlate with the clinical activity of a disease have been documented in many malignancies [12]. Dnistrian and Schwart were the first, in 1982 [13], to begin determination of plasma lipid-associated sialic aced (LSA) as a sensitive marker in leukemia and malignant lymphoma they have reported raised level of LSA in cancer patient [13].

Plucinsky et.*al*, [14] have studied TSA, LSA and TSA/TP ratios in various cancers (including skin cancer) and indicated that TSA and TSA/TP are elevated in patients with cancer compared with healthy controls [14]. However, elevated TSA levels have been found in many circumstances apart/from malignancy ,such as myocardial infarction and some autoimmune disorders [4].The present study was undertaken in an attempt to explore the severely affected parameters TSA, LSA ,TP, TSA/TP in sear of patients with (Tuberculosis TB and Lung cancer LC) in comparison with normal healthy controls .

Materials and Methods

A total of 38 patients, 20 with Tuberculosis TB (pathologic control) (5 women, 15 men) and 18 with Lung cancer LC (6 women, 12 men) were entered present study .The median age of patients with TB was 61 years (range 44-73) and these with LC was 64 years (range 47-80) .Diabetes mellitus and any heart diseases were excluded from the study. 25 healthy non smoking (11 women,9 men) median age 62 years old (range 45-75) were normal healthy control .A total of blood sample were

collected from patients from hospital of AL-Hussain education ,sinus to period from (Jan. 2006 to the end of Jul. 2006).
Serum TSA and LSA were measured according to the method resorcinol [4,15] . Serum total protein TP was determined by the Biuret method [16].

All the statistical analysis were done through the ANOVA program, data was given as mean ± standard deviation (SD) and student of predictive values for TSA , LSA , TP and TSA/TP levels in (TB and LC) groups with healthy control and P value< 0.05 was considered significant.

Results

Table (1,2,3,4) show Biostatistical calculation for the comparison of TSA, LSA, TP and TSA/TP values respectively from serum sample of patients with (TB, LC) groups and healthy controls.Figure (1,2,3,4)Distribution of TSA, LSA, TP and TSA/TP values from serum sample of patients with (TB, LC) groups and healthy controls .Table and Figure (1),data analysis indicated significant differences in TSA value in (TB, LC) groups with healthy controls (P<0.0001),also there was no significant in TSA value in the TB group with LC group Table and Figure (2), no significant difference was observed in LSA levels between TB group and the healthy control, but there was significant between LC group and the healthy control.Table and Figure (3), shows there was slightly rise in three groups .Table and Figure (4), shows that TSA/TP values astatically significant increase was observed between (TB, LC) groups with healthy controls, no significant difference of TSA/TP values was observed when compared between (TB, LC) groups.
Table (٥,a)The predictive values for the biochemical markers in Tuberculosis (TB) with normal healthy control .Table (٥,b)The predictive values for the biochemical markers in Lung Cancer (LC) with normal healthy control .

Table (1): Biostatistical calculation for TSA values of patients with Tuberculosis (TB) , Lung Cancer (LC) and Normal healthy control ((mean±SD and P value))

Group/Test	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
Healthy control	25	56.40	10.206	2.041	52.19	60.61	40	74
Tuberculosis	20	71.20	11.048	2.470	66.03	76.37	53	90
Lung cancer	18	73.94	11.730	2.765	68.11	79.78	50	95
Total	63	66.11	13.403	1.689	62.74	69.49	40	95

P	.0001	S

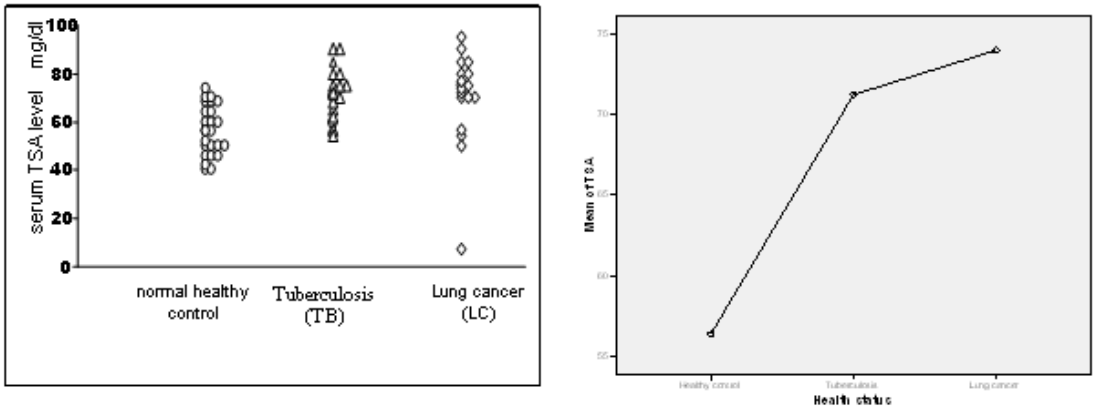


Figure (1) Distribution of TSA values from serum sample of patients with (TB, LC) groups and healthy controls.

Table (2): Biostatistical calculation for LSA values of patients with Tuberculosis (TB) , Lung Cancer (LC) and Normal healthy control ((mean±SD and P value))

Group/Test	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
Healthy control	25	15.32	3.119	.624	14.03	16.61	10	22
Tuberculosis	20	15.00	2.271	.508	13.94	16.06	11	19
Lung cancer	18	19.22	3.541	.835	17.46	20.98	13	25
Total	63	16.33	3.492	.440	15.45	17.21	10	25

P	.0001	S

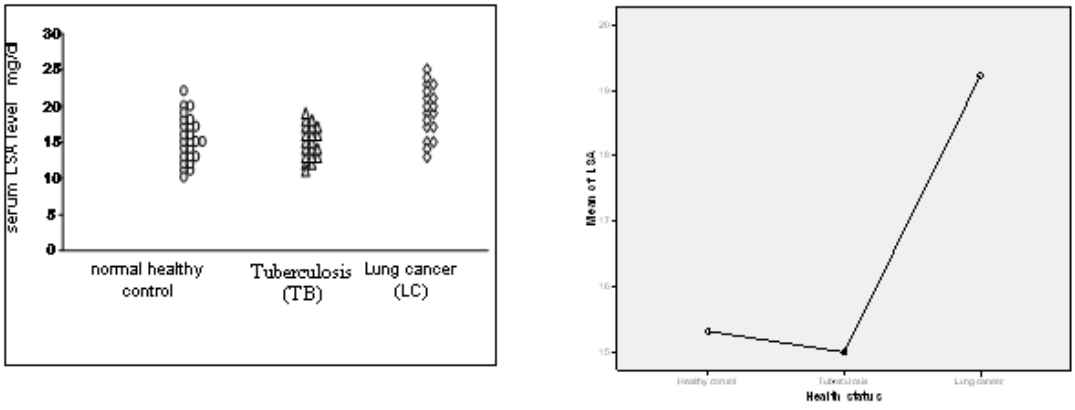
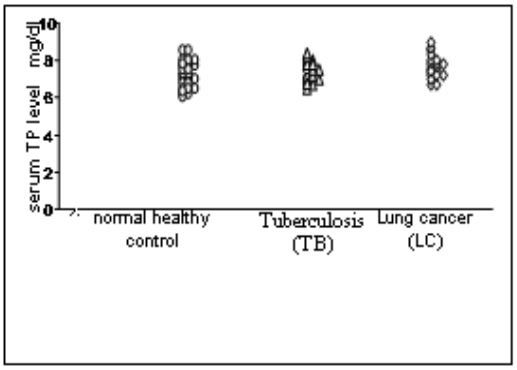


Figure (2) Distribution of LSA values from serum sample of patients with (TB, LC) groups and healthy controls.

Table (3): Biostatistical calculation for TP values of patients with Tuberculosis (TB) , Lung Cancer (LC) and Normal healthy control ((mean±SD and P value))

Group/Test	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
Healthy control	25	7.184	.6719	.1344	6.907	7.461	6.0	8.5
Tuberculosis	20	7.370	.5516	.1234	7.112	7.628	6.5	8.4
Lung cancer	18	7.689	.6570	.1549	7.362	8.016	6.7	9.0
Total	63	7.387	.6554	.0826	7.222	7.552	6.0	9.0

P	.042	S



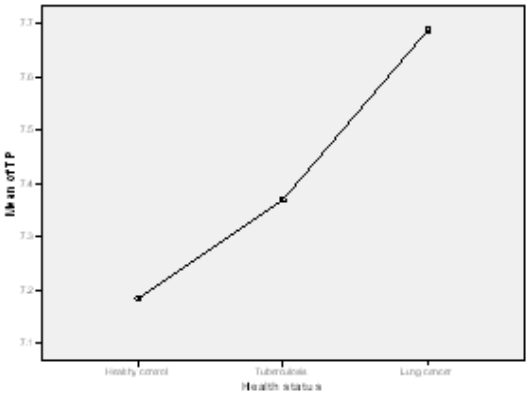


Figure (3) Distribution of TP values from serum sample of patients with (TB, LC) groups and healthy controls.

Table (4): Biostatistical calculation for TSA/TP values of patients with Tuberculosis (TB) , Lung Cancer (LC) and Normal healthy control ((mean±SD and P value))

Group/Test	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
Healthy control	25	7.860	1.5753	.3151	7.210	8.510	5.1	10.9
Tuberculosis	20	9.475	1.1392	.2547	8.942	10.008	7.0	11.5
Lung cancer	18	9.683	1.8037	.4251	8.786	10.580	6.3	13.2
Total	63	8.894	1.7237	.2172	8.460	9.328	5.1	13.2

P	.0001	S

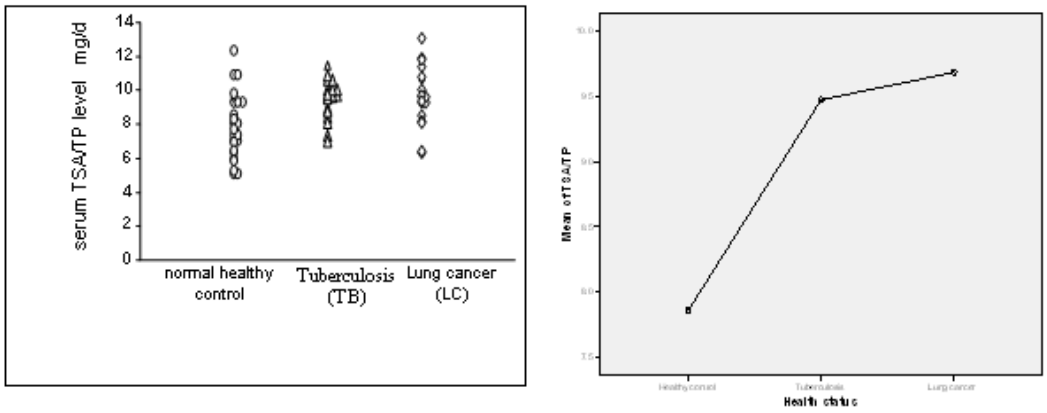


Figure (4) Distribution of TSA/TP values from serum sample of patients with (TB, LC) groups and healthy controls.

Table (5, b): The predictive values for the biochemical markers in Lung Cancer (LC) with normal healthy control.

predictive values/ Test	TSA	LSA	TP	TSA/ TP
Sensitivity	90%	78%	33%	89%
Specificity	56%	56%	52%	60%
Positive Predictability	62%	56%	33%	61.5%
Negative Predictability	87.5%	77%	52%	88%
Efficiency	71%	65%	44%	72%

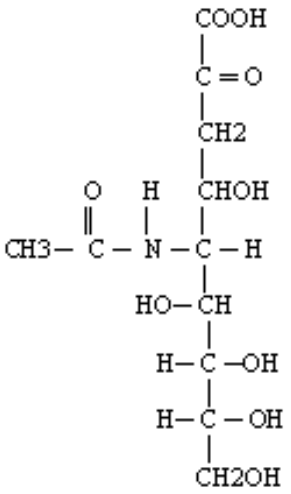
Discussion

In the present study serum TSA levels in the (TB and LC) groups were significantly increase in comparison with healthy controls (P=0.0001) Table (1) and Figure (1), this results indicate that most of the circulation serum glycoproteins (immunoglobulin and acute phase proteins) increase markedly during many conditions involving tissue destruction or inflammation [8, 17]. Changes in serum glycoproteins levels are characteristic of many pathological conditions including malignancy[18,19], therefore, neoplastic cells ,surface glycoproteins and glycolipids have different carbohydrate compositions, the major constituent of glycoproteins and glycolipids is sialic acid [4,20].Malignant diseases are process encompassing the whole body: they disturb the structure and function of many organs and system .one of these is the change in composition of serum proteins, including a decrease in the content of albumin with a concomitant increase of glycoproteins that include ,among other N-acetyloneuraminic acid or sialic acid. The sialic acid in blood serum is derived mainly from liver cells, where it is synthesized from glycolipids and glycoproteins of membranes

of lysed cells ,and showed that the enzymes regarding cell investigation are active in cancer cells [21].Malignant cells have been reported to have more sialic acid in their cell membrance than normal cells [22,23]. As a result of increased turnover, secretion and shedding , these glycoproteins and glycolipids can be released into the sera, therefore, TSA levels have been increased, but there was no difference in TSA values in (LC) group when compared with (TB) group .However, elevated TSA levels have been found in many malignancy, myocardial infarction and some autoimmune disorders[7,24].At the same time it was noted that cancer cells contain almost twice the amount of sialic acid in their cell membrance than normal cells .Many studies have attest to the raised concentration of sialic acid in serum from patients suffering from various neoplastic diseases[4,25].It has been considered a useful neoplastic marker, sensitive but non-specific[25].LSA levels were significantly increase(P=0.0001)when compared between (LC)group and healthy controls as shown in table(2) and Figure (2),but no significance in LSA levels when compared between (TB) group and healthy controls. Moreover, elevated serum levels of TSA and LSA have been observed in many malignancies [26, 27]. Some studies report that LSA is better indicator of malignancy in prostate and breast cancer [10, 13]. LSA as a sensitive marker in Leukemia and malignant Lymphoma, have reported raised level of LSA in cancer patient, that serum total sialic acid (TSA) and lipid associated sialic acid (LSA) levels have drawn considerable interest because of carbohydrate aberrations in malignant cells [28,29].The level of total protein TP was found only a slight rise in occurs in three groups (P=0.042)Table(3)andFigure(3),
concentration of proteins rise significantly during acute inflammation owing to cause such as surgery ,myocardial infarctions ,infections and tumors[30]. Disease often alters amount and proportions of plasma proteins in body fluids in characteristic ways. Most plasma proteins are catabolized in the liver;for some, the signal that marks them for degradation appears to be the loss of part or all their sialic acid content [30].

A statistically significant increase(P=0.0001)was observed in TSA/TP values when compared between (LC and TB) groups with normal healthy controls as shown in Table and Figure (4),the results show that TSA/TP was the most useful of markers tested detecting malignancies. This markers should prove useful for monitoring malignant disease recurrence or progression and evaluating the effectiveness of various therapeutic approaches [29].TSA/TP values follow the same pattern as serum TSA concentrations, the TSA increment is probably related to increased turnover of malignant cells .The results of this investigation indicate that TSA and TSA/TP are sensitive markers for detecting (LC and TB) groups table (°, a, b) .

The study suggests that TSA, LSA and TSA/TP are strong predictor for both (LC and TB) groups compared with healthy controls ,LSA can be used as an indicator of malignancy in (LC) group and TSA and TSA/TP values along with biochemical criteria may be valuable in establishing diagnosis .



Structure of Sialic acid References

References

1- Kemal.M.,James.D.and George.G. ,1985. "Use and limitations of serum total Lipid-Bound sialic acid concentrations as markers for colorectal cancer" *Cancer*,Vol. 55,PP.404-409.

2- Gottschalk, A.(1960) .the chemistry and Biology of sialic acid and related substance .University Press, Cambridge.

3- Reid,P.E,Culling,C.F.A and Dunn,W.l. ,1978. "Ahistochemical method for the identification of 9-O-acytated sialic acid. An investigation of bovine sub maxillary gland and investinal mucins" *J.Histochem.Cytochem*, Vol.26,PP.187-192.

4- Vural,P.,Canbaz,M.and Selçuki,D. ,1999 ."Total and Lipid-Bound sialic acid levels in Actinic Keratosis and Basal cell Carcinoma" *Tr.J.of Medical Sciences*,Vol.29,PP.419-423.

5- Schauer,R. and Gollub,M. ,1997 ."Function and biosynthetic aspects of sialic acid diversity" *Indian J.BiochemBiophys* , Vol.34,PP.131-141.

6- Taniuchi ,K.,Chitu,K.,Hayashi,N. and etal. ,1985 ."Anew enzymatic method for the determin- ation of sialic acid in serum and its application for a marker of acute phase reatants" *Kobe J Med Sci* , Vol.27,PP.91-102.

7- Hakamory,SI.,1981"Glycosphingolipids in cellular interaction, differentiation an oncogene- sis " *Ann Rev Biochem*, Vol.50,PP.733-764.

8- Alfred,G., ,1972. G*lycoproteins.,A.* Gottschalk,London.

9- ANN Carter and N.H.Martin,1962. "serum sialic acid level in health and disease" *J.Clin. Phath*., Vol.15,No.69,PP.69-70.

10- Ujjaini ,Kh.,James ,H. ,1983. " serum sialic acid is a biologic marker for malignant disease"*J .Surgical Oncology* , Vol.23,PP.163-166.

11- Horgan-Ryan A.Fennelly JJ.Jones M *et al*. ,1980 ."serum sialic acid and CEA concentration in human breast cancer"*Br3 Cancer*, Vol.41,PP.587-592.

12- Ryan,AH.and Fennelly,JJ. ,1981. " serum sialic acid concentration in malignant melanoma " *Eur J Cancer Clin Oncol* , Vol.17,PP.843-844.

13- Dnistrian ,AM.,Schwartz,MK.,Katopodis,N. and *et al*,1982. "Serum Lipid-Bound sialic acid as a marker in breast cancer " *Cancer*, Vol.50,PP.1815-1819.

14-Plucinsky,Mc.,Riley,WM.,Prorok,JJ *et al*. ,1986 ."Total and Lipid-associatioed serum sialic acid level in cancer patients with different primary sites and differing

degrees of metastatic involvement" *Cancer*, Vol.58, PP. 2680-2685.

15-Svennerholm,L.,1957."Quantative estimation of sialic acids, colorimetric resorcinol-hydrochloric acid method" *Biochem-Biophys Acta*, Vol.24,PP.604-611.

16- Heny,R.J.,cannon,D.C. and Winkelman,J.W., 1974.*Clinical chemistry, Principle and Tichni- ques*, Harper& Raio,(2nd ed).

17- Katopodis,N.,Hirshaut,Y.,Geller,NL.And *etal*,1982 ."Lipid-Bound sialic acid test for the detection of human cancer " *Cancer Res*, Vol.42,PP.5270-5375.

18-Cunietti, E., Vaiani,G.and Reggiani,A. ,1985 ." Carcinoembryonic antigen, Feritin, Anionic glycoprteins and their sialic acid content in advanced colorectal cancer " *J. Cancer Detec.Prev*, Vol.8,PP.222-*Detec.Prev*, Vo232.

19-Doğan,H.,Pasaoğlu,H. and *et al* ,1992 ."A comparative study of total protein, Total and Lipid- associated serum sialic acid levels in patients with Behcet's disease and control groups " *Acta ophthalmol Copenh*, Vol.70,PP.790-794.

20-Yagci,A.Karcioğlu,ZA.Akkin,C.and et al ,1990 ."serum and aqueous humor sialic acid levels in Behcet's disease" *Ophthalmology*, Vol.97,PP.1153-1155.

21-Shamberger,R.J. ,1984 ." Serum sialic acid in normal and in cancer patients ".J.Cli.Chem.Cli.Biochem,Vol.22,PP.647-651.

22-Lehninger,AL.,Nelson,DL.and Cox,MM., 1993. *Principle of Biochemistry* ,Worth Publishers, New York, ,(2nd ed).

23-Hakamory,SI.,1984 "Tumor-associated carbohydrate antigens" *Annual Review of Immunol*, Vol.2,PP.103-126.

24-Yogeswaran,G. ,1983 "Cell surface glycolipids and glycoproteins in malignant trans-formation" *Adv Cancer Res*, Vol.38,PP.289-350.

25-Xing. RD. Chen, R.M.(1994) *Int J .Biol*. [11].Markers .9(4):239-242 .

26-Snyder,S.and Ashwell,G.,1971 ."Quantitation of specific serum glycoproteins in malign-ancy" *J.Clin.Acta*,Vol.34,PP.449-455.

27- Bradley,W. ,Blasco,A. and Chretien,B. ,1977 ." Correlation amono serum protein-Bound carbohydrates, serum glycoprotein ,Lymphocyte reactivity and tumor burden in cancer patients"*J.Cancer* ,Vol.40,PP.2264-2272.

28-Burger,AM,et al.(1997)*Clin.Cancer.Res*; 3(3):455-463.

29-Mark C.Plucinsky,W.michael Riley, Joseph J.Prorok .,1986"Total and Lipid-associated serum sialic acid levels in cancer patients with different primary sites and differing degrees of metastastatic involvement " *J.Health Care*.

30-Burtis C.A.and Shwood E.R.(1999), Tietz. "Text-book of clinical chemistry " ,(3rd edition),W.B.Saunder Company,Tokyo.