

Alterations in Total Sialic Acid (TSA), Total Proteins (TP) and TSA/TP ratio in cancer patients.

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Abstract

Total serum sialic acid (TSA), total proteins (TP) and TSA/TP ratio (as tumor markers) have been estimated in 108 cancer patients, 30 pathological controls and 50 normal healthy controls. Data analysis indicated a significant increase ($p < 0.001$) in the TSA and TSA/TP ratio in cancer patients (98.41 ± 13.5 mg/dl and 15.31 ± 2.57 mg/gm) as compared to pathological controls (77.57 ± 21.09 mg/dl and 11.94 ± 3.43 mg/gm) and normal control (64.77 ± 7.98 mg/dl and 8.9 ± 1.15 mg/gm) respectively. A significant decrease ($p < 0.001$) in serum levels of total proteins were found in all cases of cancer compared to the normal (6.46 ± 0.48 mg/dl and 7.29 ± 0.55 gm/dl) and pathological controls (6.53 ± 0.36 gm/dl). Further analysis of the data in patient subgroups of malignancy based on tissue involved indicated that the lack of specificity of the markers but the sensitivity of TSA and TSA/TP increased as the malignancy become more severe. The results show that TSA/TP was the most useful marker for detecting malignancies.

Key words: Sialic acid, Serum protein, Cancer.

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Introduction

Tumor markers are the substances specific for certain tumor or cancer cells and thus could be of appreciable diagnostic value in cancer patients [1]. The cell surface membrane is chiefly composed of glycoproteins and glycolipids. Any intracellular micro environmental change may lead to alteration in the surface membrane constituents, releasing certain molecules in the blood of such patients. Since a sialic acid is one of the major components of cell membranes, its expected alteration in sera of cancer patient has been reported by a few workers [2, 3]. The utility of lipid-associated sialic acid has been emphasized [4, 5]. In a parallel study, changes in total serum proteins (TP), total serum sialic acid (TSA) and TSA/TP have been documented [6]. A comprehensive study to find out the best suitable marker is of immense value to the knowledge of oncology.

Present study was undertaken to evaluate the relative utility of serum levels of TSA, TP and TSA/TP for detecting and /or monitoring the progression of cancer in a variety of patients and their reliability as cancer markers.

Materials and Methods

Institutional ethical committee approval was taken. In the present study 108 cancer patients, 30 pathological controls and 50 normal healthy controls were included. Whole blood samples were collected from normal controls (donors at a hospital blood bank with no apparent disease), pathological controls (nonmalignant) and cancer patients (with different sites and degrees of biopsy-proved cancer). Blood samples were allowed to clot at room temperature and then centrifuged at 3000 rpm for 15 minutes and the resulting sera were placed into test tubes for analysis. In this study the serum levels of TSA, TP and TSA/TP ratio were estimated. TSA was estimated by the method of Plucinsky et al [7]. TP was estimated by Biuret method [8].

Statistical analysis

Statistical analysis was performed using SPSS-16.0 software. ANOVA test was used to determine if the mean values for TSA, TP and TSA/TP ratio were significantly different in the cancer, pathological control and control groups. P value < 0.01 was considered significant.

Results

Table I represents the comparisons of mean TSA, TP and TSA/TP ratio from the sera of cancer patients, pathological controls and normal controls. The TSA from the cancer patients and pathological controls was significantly increased ($P < 0.001$). When compared to normal controls. TP was significantly decreased ($p < 0.001$) in the cancer patients and pathological controls compared to the normal

controls. Total sialic acid values normalized to total protein (TSA/TP) showed significant increase ($p < 0.001$) for the cancer patients and the pathological controls when compared to normal controls. Also significant difference were noted when the TSA, TSA/TP values for the cancer patients were compared to those of the pathologic controls but alone TP values difference were no significant ($P > 0.5$)

Table 1. Comparison of TSA, TP and TSA/TP, for normal controls, pathological controls and cancer patients.

Group	Total TSA (mg/dl)	Total protein (gm/dl)	TSA/TP (mg/gm)
Normal Controls (50)	64.77 ± 7.98	7.29 ± 0.55	8.90 ± 1.15
Cancer patients (108)	98.41 ± 13.5*	6.5 ± 0.48**	15.35 ± 2.54*
Pathological controls (30)	77.57 ± 21.09*	6.53 ± 0.36**	11.95 ± 3.43*

* $P < 0.001$ Significant, ** $P < 0.5$ Non significant

Table 2. Comparison of TSA & TP values for normal control and subgroups of cancer patients.

NORMAL Control & Subgroups of cancer patients	TSA (mg/dl)	TP (gm/dl)	TSA/TP ratio (mg/gm/dl)
Normal control(50)	64.77±7.98	7.29±0.55	8.92±1.2
Breast cancer(29)	101.4±11.65	6.45±0.34	15.76±2.45*
Maxilla(22)	99.8±13.85	6.58±0.47	15.30±2.45*
Lung(11)	96.31±14.8	6.20±0.49	15.48±2.98*
Cervix (10)	100.30±16.5	6.42±0.62	15.81±3.42*
Chick(8)	98.46±16.4	6.3±0.48	15.67±2.95*
Rectum(8)	98.22±13.03	6.5±0.65	15.20±2.56*
Stomach(8)	93.82±17.10	6.6±0.57	14.30±3.56*
Thyroid(7)	91.08±9.42	6.25±0.27	14.62±1.76*
Tongue(5)	94.4±10.7	6.5±0.54	14.58±1.99*

* $P < 0.005$ significance level

Table 2 represents comparisons of TSA, TP and TSA/TP values of the subgroups of cancer patients and normal controls. Compared to normal controls, a significant increase ($p < 0.001$) in TSA was recorded in the cancer patients subgroups. However, serum TP values were found to be significantly reduced ($p < 0.001$) for all cancer patient subgroups when compared with the normal controls. Significant increases ($p < 0.001$) in TSA/TP values were

also recorded in all cancer patient subgroups when compared to the normal controls.

Discussion

In the present investigation, levels of TSA, TP and TSA/TP ratio were determined and compared in patients with malignant or nonmalignant diseases. In malignant

cells the membrane glycoproteins and glycolipids have altered carbohydrate metabolism which could be responsible for all the abnormal behavior i.e. abnormal cell recognition, cell adherence, antigenicity and invasiveness [8]. The glycoproteins and glycolipids can be released into the blood through increased turnover, secretion and/or shedding. Several studies have shown a positive association of glycoproteins with malignancies [9]: Since sialic acid is one of the major components of the cell membranes, its expected alteration in sera of cancer patients, has been reported [10].

Although several researchers [11,12] have studied TSA, TP and TSA/TP ratio levels for the purpose of diagnosis and management of cancer, but rarely analyzed all the three parameters simultaneously [13].

Our results showed a significant rise in TSA levels in all cancer patients, the rise being directly proportional to the degree of metastasis. Rise in TSA levels could be attributed to malignant potential and changes in immunogenicity due to nonspecific changes. It has been suggested that sialic acid may be closely related to tumor associated antigen [14]. It may also reflect an increased amount of cellular destruction due to rapid tumor growth.

TSA, TP and TSA/TP ratio were determined in our patients with malignant diseases, patients with non malignant diseases (pathologic controls), and normal controls to determine that which of these markers might be most useful for detecting and monitoring the progression of malignant disease. TSA and TSA/TP ratio were significantly increased and TP were significantly decreased in both the cancer patients and pathologic controls when compared to normal controls.

Results of this investigation indicate that TSA/TP ratio seems to be the best tested markers. Although this marker is quite sensitive, it however, lacks specificity of the markers may be due to very small subgroup sample size in cancer and pathological control. However, these results do indicate that there is a significant increase in TSA and TSA/TP as malignant diseases progress, suggesting that these markers may be useful in monitoring or therapeutic interventions and disease progression.

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