

## Recent Research on Tumor Markers **Nabaneeta Mahata\***

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### Abstract

**Background and Objectives:** Tumor markers are burgeoning concept in the healthcare industry. It has not been fool proof in that their levels may fluctuate with time, may not rise consistently in all cancers, may be present in considerable amount in non-cancer patients, standardization has not been done. But their ease of assay with ELISA and chemiluminescence immunoassay techniques with just a blood sample collected in the clot activator vacutainer, allowed to clot and the tube centrifuged to separate the serum and cells, and the serum is analysed using Beckman coulter Access 2 auto analyzer. It is convenient, time saving, cost effective, and large number of patient samples can be processed in a short time. It gives valuable information about the screening, diagnoses, prognosis, monitoring, surveillance, and progression of cancer in all stages, about planning treatment and monitoring recurrence. Lately a surrogate marker for tissue biopsy, called the liquid biopsy has come in vogue where the plasma is analysed for circulating tumor cells or circulating tumor DNA. The implications of tumor marker research will gain momentum with advancement of molecular diagnoses.

**Keywords:** Tumor Index Substances; Immunoassay; Liquid Biopsy; Single Nucleotide Polymorphism

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### Introduction

A tumor marker is any substance that can be found in tissue, blood, bone marrow, or in any other body fluid which may indicate the presence of cancer or some benign conditions other than cancer [1]. They are also called tumor index substances as they are used to identify, characterize, diagnose, and follow up of disease. They are useful for detection, monitoring, prognosis and recurrence [2]. Caution should be maintained to rule out other non-malignant causes. When blood levels of tumor markers are raised, it should be confirmed by imaging studies and biopsy. Tumor markers can be proteins, antigens, hormones, enzymes, receptors, oncogenes, tumor suppressor genes, or abnormally high routine chemistry parameters like potassium. A high index of suspicion should be maintained in this regard as the tumor marker assays have not been validated and may be raised in benign conditions or even in normal persons. Although tumor markers are sensitive and specific for the condition they are used to diagnose, some markers which are not specific to that particular disease may show a rise in more than what can be by mere chance. For example, it was observed that thyroid stimulating hormone, free thyroxin levels, FT3 and FT4 levels are

increased in diabetic patients in more than what can be concluded by chance [3]. It was observed that patients with low back pain, spondylolisthesis, spondylitis and some cancers had insufficient or low levels of vitamin D3. These observations need deeper research. These are unrelated findings but significant in terms of therapy and prognosis. A combination of tumor markers like CEA, CA125, CA19-9, and AFP were increased in gall bladder cancer. So were the results with a number of other cancers in which two or more markers were increased while the third remained inconclusive. So in terms of follow up, prognosis, recurrence, monitoring, metastasis, multiple tumor markers may increase the chance of detection and prediction. So even as we try to narrow down our basket of choices to a specific and particular marker identifying a particular disease, in practice, a broad base has to be kept in mind while treating a case. Some tumor markers are also markers of other organ function tests like alkaline phosphatase for obstructive liver diseases and hepatocellular cancer [4]. Serum albumin is low in various chronic liver diseases, malnutrition and cancers. Prostate specific antigen is a marker for both benign prostatic hyperplasia and prostate cancer, but generally more useful for prostate cancer. Free PSA is currently the tumor marker

of choice as total PSA is not so specific for prostate cancer. Beta human chorionic gonadotrophin is a marker of choriocarcinoma. It also increases in normal pregnancy. The levels are of the order of 100000 IU/mL in cancer [5].

## Classification of tumor markers helps to pin point the disease in question

### Oncofetal Proteins

- Alpha – fetoprotein (AFP) in hepatoma, germ cell tumors
- Carcinoembryonic antigen (CEA) in Colorectal, gastrointestinal and lung cancer

### Carbohydrate antigens

CA -125 in ovarian cancer of epithelial origin

### Tissue Antigens

Tissue polypeptide antigen for general cancer load

### Enzymes

- Alkaline Phosphatase (ALP) for bone secondary's
- Placental type ALP (Regan) in lung cancer and seminoma
- Prostatic acid phosphatase (PAP) in prostate cancer
- Prostate specific antigen (PSA) in prostate cancer
- Neuron specific enolase in nervous system tumors

### Hormones and their metabolites

- Beta – Human chorionic gonadotropin (beta HCG) in Choriocarcinoma
- Calcitonin in Medullary thyroid carcinoma
- Big adrenocorticotrophic hormone (ACTH) in lung oat cell cancer
- Vasoactive Intestinal Peptide (VIP) in Apudomas (Amine Precursor and Uptake Decarboxylation omas)
- Vanillyl mandelic acid (VMA) in Pheochromocytoma and neuroblastoma
- Hydroxy Indole Actetic Acid in Carcinoid syndrome

### Tissue Catabolic Product

Hydroxy proline - Bone metastasis

### Serum Proteins

- Immunoglobulin's - Multiple myeloma, macroglobulinemia
- Bence Jones Proteins in urine – Multiple myeloma

### Receptor Tumor Marker

- Estrogen receptor, progesterone receptor positive are associated with good prognosis in breast cancer.
- Her 2 neu receptor in breast cancer is a tumor marker for

familial breast cancer.

### Ion channels-

Recently potassium channels are considered tumor markers as they are elevated in some types of cancers. Potassium levels of the order of 10mmol/L was seen in small cell lung cancer in up to 30% cases Tumor markers are assayed either by routine biochemical methods as for potassium estimation which may be abnormally high in case of lung cancer or they may be assayed by immunoassays such as enzyme linked immunosorbent assays or chemiluminescent immunoassays or electrochemiluminescent immunoassay techniques or latest techniques which are even more developed. Alpha fetoprotein or AFP is also called fetal albumin as it is the predominant protein in fetus [6]. AFP is raised in hepatocellular cancers in the range of thousand ng / litre. Reference range being less than 1.5 ng /ml. AFP is used as a diagnostic marker for abdominal tumors, endometrial cancer, gastrointestinal malignancies, abdominal pain syndromes, uterine cancer. In pathological conditions the AFP is raised in malformation of neural tube in pregnancy, non-malignant liver diseases and hepatic cancer [7]. In combination with other biomarkers like Carcino embryonic antigen CEA, Carbohydrate antigen CA 19-9, CA 125 the diagnostic accuracy is increased for abdominal tumors and gastrointestinal cancers and ovarian cancer. Carcinoembryonic antigen or CEA is increased in colorectal cancers, gastrointestinal cancers breast, gastric ovarian, pancreatic and lung cancers. 5 % healthy persons and heavy smokers may also have raised CEA level. B HCG is increased in Hydatidiform mole, choriocarcinoma and germ cell tumors like testicular tumors. Reference range for  $\beta$  HCG is <20 g/ml. Value > 100000 ng/ml indicates trophoblastic tumor. Beta h CG is assayed by a sandwich ELISA technique of quantitative immunoassay testing CA 125 is raised in ovarian cancers. Normal levels of CA 125 is 0-35 U/ml. Levels correlate with tumor mass Prostate specific Antigen reference range is 1-4 ng/ml. Increased levels indicate pancreatic cancer. CA 19.9 is indicative of pancreatic cancer. Increased levels more than 37 ng/ml is indicative of pancreas, gall bladder, and colon or lung cancer. If malignant conditions are not found, caution must be taken as CA 19.9 can also increase in benign conditions. CA 19.9 can be assayed by sandwich ELISA technique of immunoassay. Some gene rearrangements of tumor markers are ALK gene rearrangements and overexpression. AFP, B cell immunoglobulin gene rearrangement or BCL2 gene rearrangement, B2M or beta 2 macroglobulin gene rearrangement, beta hCG gene rearrangement, BRCA1 and BRCA2 gene rearrangement for familial breast cancer, BTA or bladder tumor antigen gene rearrangement. Tumor markers do not have standardized values and may be non-specifically raised in normal persons as well as benign tumors. That is why care must be taken while interpretation of care in diagnosis of cancer and prognosis. Of course if the measurement is 100-1000 times more than the reference range the suspicion for cancer diagnosis increases manifold towards confirmatory evidence.

### Materials and Method

**Place of study:** Cincial biochemistry laboratory

**Period of study:** 6 months

**Type of study:** Cross sectional descriptive case control study

**Cases/ Diagnoses:** abdominal pain, chocolate cyst, amenorrhea, nulliparity, endometriosis, mass in abdomen, dysmenorrhoea, lung cancer,

**Type of tumor markers assayed:** TSH, T3, T4, FT3, FT4, CA19.9, CA125, CEA, AFP, Beta HCG, Ferritin, Vit B12, Vit D, Folic acid, Prolactin, AMH, LH, and FSH Autoanalyser used- Beckman Coulter orthoclinical diagnostics Access 2

**Type of immunoassay:** Sandwich ELISA, spiked with streptavidin and biotin for signal amplification, chemiluminescence.

Reagents used-Quality control used - company's name

Calibrator used-3 level quality control used-high, normal and low level control

Ferritin has been widely used as a tumor marker in lymphoma, Hodgkin's lymphoma, neuroblastoma, cervical, oral, squamous cell, renal cell, T cell lymphoma, breast cancer were associated with increased tumor grade and shorter survival Cancer prevention- Folic acid along with B6, B12 has been associated with lower risk but studies have even shown conflicting evidence in that they may even increase risk of lung and colorectal cancer.

Liquid biopsy is a test done on a blood sample to look for cancer cells or their DNA which is circulating in the blood from a tumor. It is used for screening, diagnosis, and prognosis and to detect recurrence and plan treatment. Blood sample are convenient method of testing as they do not involve taking a sample from the tumor itself but acts as a surrogate marker of the tumor. It is also useful for research to study the genetic, molecular and metabolic changes that the tumor is undergoing over time. A liquid biopsy provides an alternative sampling for molecular testing processes for diagnoses of tumor. It is not a replacement of tissue biopsy. Application of liquid biopsy includes cell free circulating tumor Deoxyribonucleic acid. A specialist trained to analyze fluid and tissue samples for signs of disease (Pathologist) will look for circulating tumor cells, CTCs or circulating tumor DNA or cDNA in the plasma.

Snp

Methods of assay of cancer markers

Genetics of cancer markers

Apoptosis

Caspases

Vaccines for cancer

## References

- 1 <https://www.cancer.net/navigating-cancer-care/diagnosing-cancer/tests-and-procedures/tumor-marker-tests>
- 2 <https://www.cancer.gov/about-cancer/diagnosis-staging/diagnosis/tumor-markers-list>
- 3 <https://medlineplus.gov/lab-tests/tumor-marker-tests/>
- 4 Nagpal M, Singh S, Singh P, Chauhan P, Zaidi MA (2016) Tumor markers: A diagnostic tool. *Natl J Maxillofac Surg* 7: 17-20.
- 5 Sharma S (2009) Tumor markers in clinical practice: General principles and guidelines. *Indian J Med Paediatr Oncol.* 30: 1-8.
- 6 <https://stanfordhealthcare.org/medical-tests/t/tumor-markers/types.html>
- 7 <https://www.cancercenter.com/diagnosing-cancer/diagnostic-procedures/tumor-markers>