

A Comparative Study of Total Antioxidant Status between Pre-Treated Breast Cancer Patients and Healthy Controls of The Same Age Group

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ABSTRACT

Introduction: Breast cancer is the leading cause of cancer deaths in females after cancer of uterine cervix. Cellular damage arising from oxidative stress has been implicated in the initiation and progression of cancer. Total antioxidant status of plasma fall in many types of cancer possibly due to consumption of antioxidants by excessive free radicals generated or reflecting diminished dietary intake of exogenous antioxidants.

Materials & Methods: The study was conducted in the Department of Biochemistry on 50 premenopausal women newly diagnosed with breast cancer and 50 premenopausal controls in collaboration with Department of Surgery and Radiotherapy, G.G.S. Medical College, Faridkot and total antioxidant status was evaluated for all the patients and controls. The 50 premenopausal patients were further sub-grouped into Node-negative/Node-positive (15/35), With/Without Metastasis (21/29) and Early staged/Advanced staged (19/31) premenopausal breast cancer patients.

Results: TAS was found to be lower in premenopausal breast cancer patients as compared to controls ($p < 0.05$), also significantly lower in patients with metastasis ($p < 0.05$) as compared to patients with non-metastatic breast cancer. It was also found to be lower in node positive and advance staged

breast cancer as compared to node negative and early staged breast cancer patients but it was not significant with ($p = 0.09$) and ($p = 0.07$) respectively.

Conclusion: The whole study indicates the overall decrease in TAS with disease involvement and further decrease with disease progression involving metastasis, nodal involvement and advanced staging.


Key words: Breast Cancer, TAS (Total Antioxidant Status).

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INTRODUCTION

The word cancer is derived from French word "chancre" originally meaning "crab". Written descriptions of it can be found on Egyptian papyrus dating back to roughly 1600 BC. Breast cancer is the leading cause of death from cancer among women after cancer of cervix uteri. Cancer constitutes an enormous burden on society in more and less economically developed countries alike. The occurrence of cancer is increasing because of the growth and increasing prevalence of established risk factors such as smoking, overweight, physical inactivity and changing reproductive patterns associated with urbanization and economic development.¹

Risk factors for developing breast cancer include female sex, obesity, lack of physical exercise, drinking alcohol, hormone replacement therapy during menopause, ionizing radiation, early age at first menstruation, having children late or not at all, older age, family history and BRCA 1 and BRCA 2 genetic factors. About 5–10% BRCA 1 and BRCA 2 genetic factors thought to contribute to poor outcome due to genes inherited from a person's parents.²

But there are several other risk factors that exist like family history, race and ethnicity, gender, ageing, genetic factors, dense breast

tissue and oxidative stress. Simply being a woman is not the main risk factor for developing breast cancer. Men also develop breast cancer, but this disease is about 100 times more common among women than men.³

In recent years, measurement of total antioxidant capacity (TAC) of tissues and plasma has been widely used in several human diseases including cancers. Low total antioxidant capacity could be indicative of Oxidative stress or increased susceptibility to oxidative damage. The TAC measurement does not represent the sum of activities. However it could be used for clinical diagnosis, as it is easy and less time consuming process.⁴

Oxidative stress is considered to be involved in the pathophysiology of all cancers and it occurs due to an imbalance between oxidant and anti-oxidant levels. The Reactive Oxygen species (ROS) are highly reactive and may modify or inactivate protein, lipid, DNA, RNA and induce cellular dysfunctions. To prevent free radical induced cellular damage, the body has developed a defense mechanism which is also called anti-oxidative system. This system includes anti-oxidant enzymes which plays a key role in maintaining the physiological balance between pro-oxidant and antioxidant. Plasma proteins can inhibit ROS generation and lipid peroxidation by chelating free transition metals.⁵

When produced in excess ROS can cause tissue injury. However tissue injury can itself cause ROS generation e.g. by causing activation of phagocytes or releasing transition metal ions from damaged cells further contributing to worsening of injury and studies also indicated that anticancer drugs themselves can induce oxidative stress.⁶

MATERIALS & METHODS

The present study was conducted in the Department of Biochemistry in collaboration with the Department of Surgery and Radiotherapy, G.G.S. Medical College, Faridkot, Punjab. A total of 100 subjects were enrolled in the study and they were further sub-grouped into 50 premenopausal breast cancer patients who were newly diagnosed with breast cancer had had not undergone any form of treatment like Surgery, Radiation, Chemotherapy or any type of Hormone therapy or targeted therapy. They were further sub-grouped into Node-negative/ Node-positive (15/35), with and without metastasis (21/29) and with Early staged /Advanced staged (19/31). The diagnosis was confirmed by FNAC and mammography of breast. Similarly 50 premenopausal controls were also included without having any history of disease or on medications that can affect the concerned parameters. Proper informed consent was taken from all the participants included in this study and those willing to participate were only included.

The TAS (Total Anti-oxidant Status) was run for all the samples and statistical evaluation of the results was done by SPSS software.

TAS (Total Antioxidant Levels (in mmol/l) (Principle): It is based on the principle to determine the reaction of antioxidants in the sample with a defined amount of exogenously provided hydrogen peroxide. The antioxidants eliminate a certain amount of the provided hydrogen peroxide. The residual hydrogen peroxide is determined colorimetrically by an enzymatic reaction which involves the conversion of 3, 5, dichloro-2-hydroxy benzene sulphonate to a coloured product.⁷ All samples were run on Fully Automated Chemistry Analyser Beckman Coulter AU 480.

Table 1: TAS levels in Premenopausal Patients and Controls

TAS VALUES	PATIENTS	CONTROLS	P value
MEAN	1.13	1.65	p<0.05
SD	0.32	0.09	Significant
Mean Rank	28.22	72.78	Man Whitney U=2364.00

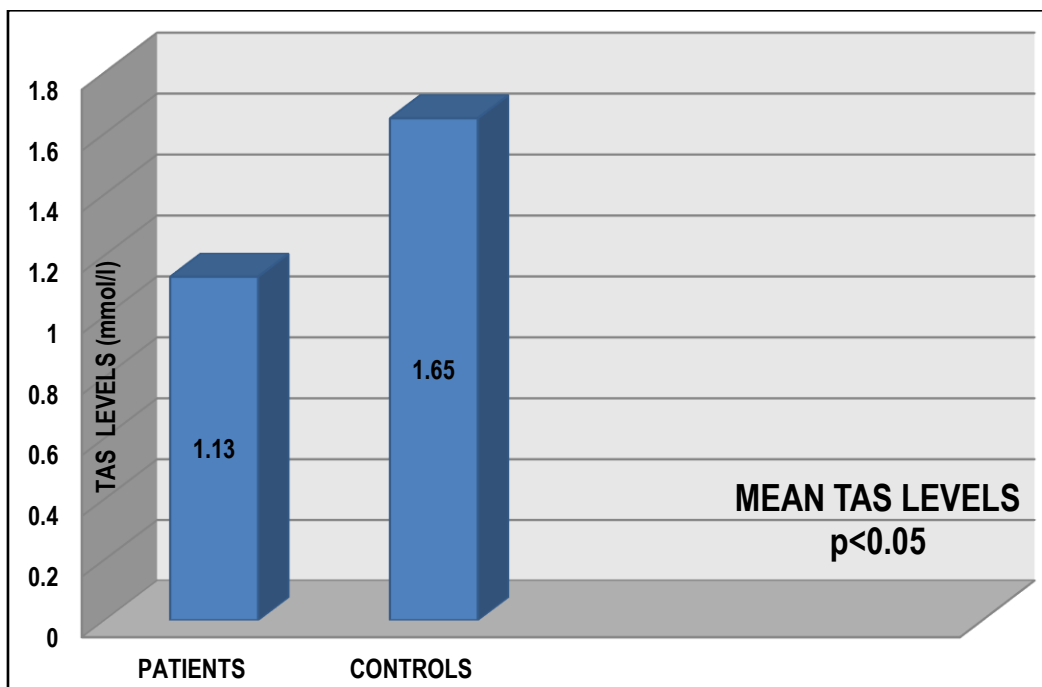


Table 2: TAS comparison in Node negative and Node positive premenopausal patients

TAS VALUES	PRE PAT NODE NEGATIVE	PRE PAT NODE POSTIVE	p value
MEAN	1.24	1.08	p=0.09
SD	0.27	0.32	Non-Significant
Mean Rank	30.83	23.21	Man Whitney U=182.50

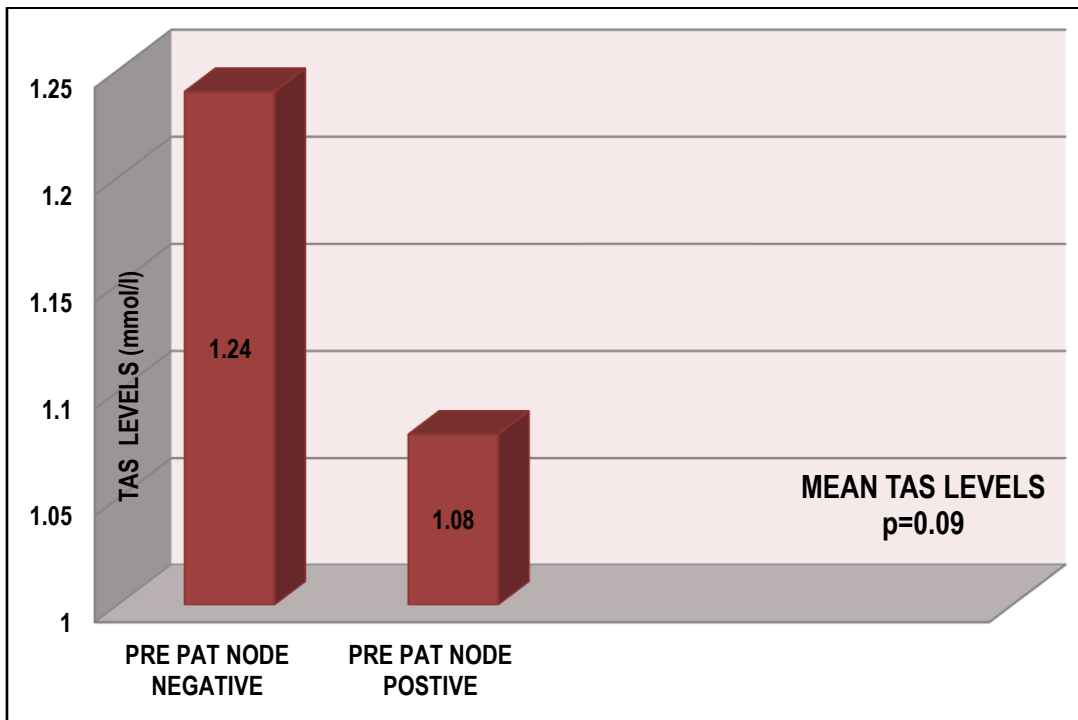


Table 3: TAS Comparison in Premenopausal patients With Metastasis and Without metastasis.

TAS VALUES	PRE PAT WITH METASTASIS	PRE PAT WITHOUT METASTASIS	p value
MEAN	0.96	1.25	p<0.05
SD	0.33	0.25	Significant
Mean Rank	18.40	30.64	Man Whitney U=453.50

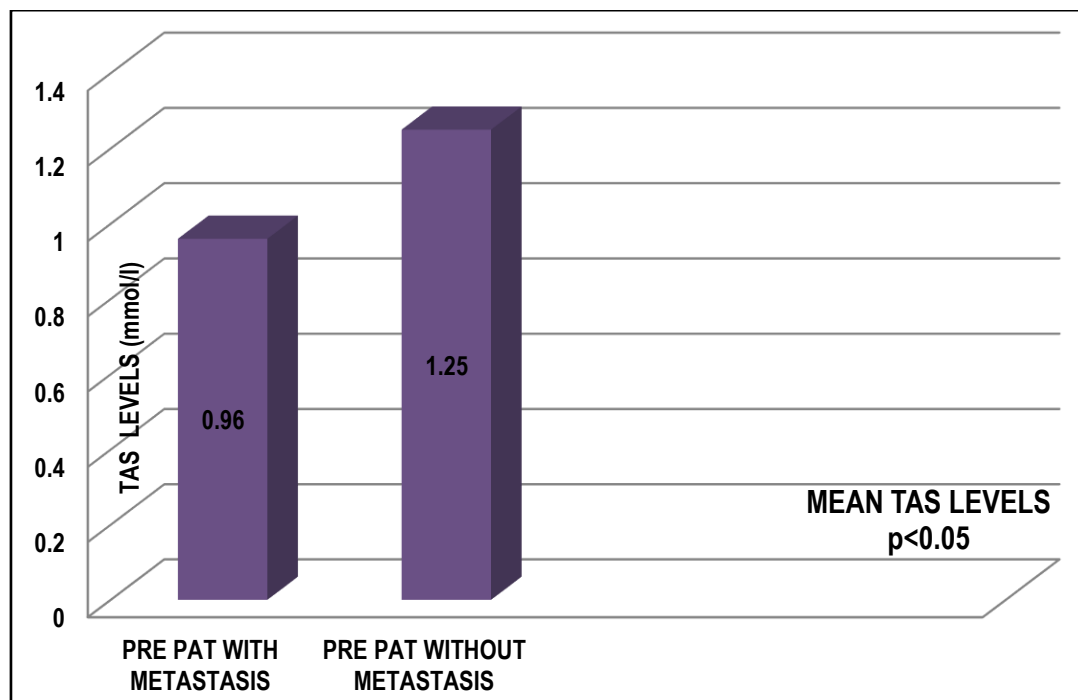
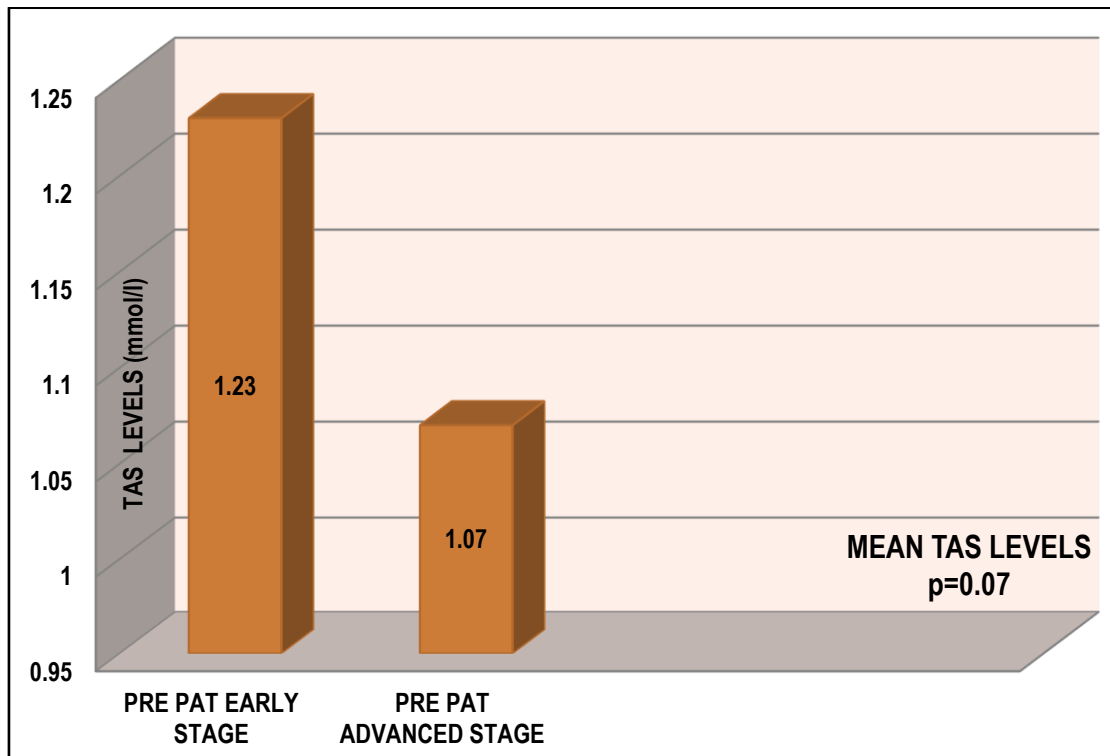


Table 4: TAS Levels In Premenopausal Early & Advance Stage Patients.

TAS VALUES	PRE PAT EARLY STAGE	PRE PAT ADVANCED STAGE	P value
MEAN	1.23	1.07	p=0.07
SD	0.25	0.34	Non-Significant
Mean Rank	30.21	22.61	Man Whitney U=205.00



RESULTS

The TAS levels were compared between premenopausal patients & premenopausal controls. In this study the TAS levels were found to be significantly lower in breast cancer patients as compared to controls with Mean± SD=1.13±0.32 and Mean Rank=28.22 as compared to controls with Mean ± SD 1.65±0.09 and Mean rank =72.78 with Man Whitney U=2364.00 and p value was found to be significant. (p<0.05)

The TAS levels were compared between premenopausal patients with node negative & premenopausal patients with node positive breast cancer. In this study the TAS levels were found to be significantly higher in premenopausal patients with node negative breast cancer as compared to premenopausal patients with node positive breast cancer with Mean ± SD= 1.24 ± 0.27 and Mean rank=30.83 as compared to premenopausal patients with node positive breast cancer with Mean ± SD =1.08± 0.32 and Mean rank=23.21 with Man Whitney U =182.50 and p value was found to be non-significant. (p=0.09).

The TAS levels were compared between premenopausal patients with metastasis & premenopausal patients without metastasis. In this study the TAS levels were found to be significantly lower in premenopausal patients with metastasis as compared to premenopausal patients without metastasis with Mean ± SD= 0.96 ± 0.33 and Mean rank =18.40 as compared to premenopausal patients without metastasis with Mean ± SD =1.25± 0.25 and Mean rank=30.64 with Man Whitney U =453.50 and p value was found to be significant (p<0.05).

The TAS levels were compared between premenopausal patients with early staged & premenopausal patients with advanced stage breast cancer. In this study the TAS levels were found to be higher in premenopausal patients early stage as compared to premenopausal patients advanced stage with Mean ± SD= 1.23 ± 0.25 and Mean rank =30.21 as compared to premenopausal patients advanced stage with Mean ± SD =1.07± 0.34 and Mean Rank=22.61 with Man Whitney U =205.00 and p value was found to be non-significant (p=0.07).

DISCUSSION

The TAS levels were compared between premenopausal patients with breast cancer & premenopausal controls. In this study the TAS levels were found to be significantly lower in breast cancer patients as compared to controls with Mean± SD=1.13±0.32 and Mean Rank=28.22 as compared to controls with Mean ± SD 1.65±0.09 and Mean rank =72.78 with Man Whitney U=2364.00 and p value was found to be significant. (p<0.05)

TAS levels were compared between the patients of breast cancer and controls and TAS was found to be significantly lower with Mean± SD=2.01± 0.01 mmol/l in carcinoma breast cancer patients as compared controls with Mean ±SD = 2.07± 0.03 mmol/l with (p<0.05).⁸

In this study the TAS levels were also compared between premenopausal patients with node-negative & premenopausal patients node-positive breast cancer. The TAS levels were found to be significantly higher in premenopausal patients node negative

as compared to premenopausal patients node positive with Mean \pm SD= 1.24 \pm 0.27 and Mean rank =30.83 as compared to premenopausal patients node positive with Mean \pm SD =1.08 \pm 0.32 and Mean rank=23.21 with Man Whitney U =182.50 and p value was found to be non- significant (p=0.09).

The TAS levels were compared between patients of breast cancer with Lymph node involvement and without lymph node involvement. The TAS was found to be lower in patients with lymph node involvement as compared to patients without involvement with Mean \pm SD=0.2 \pm 0.0 as compared to patients with involvement having Mean \pm SD=0.1 \pm 0.0 and p value=0.010.⁷

The TAS levels were also compared between premenopausal patients with metastasis & premenopausal patients without metastasis. In this study the TAS levels were found to be significantly lower in premenopausal patients with metastasis as compared to premenopausal patients without metastasis with Mean \pm SD= 0.96 \pm 0.33 and Mean rank =18.40 as compared to premenopausal patients without metastasis with Mean \pm SD =1.25 \pm 0.25 and Mean rank=30.64 with Man Whitney U =453.50 and p value was found to be significant (p<0.05).

TAS was found to be lower in breast cancer patients with metastasis as compared to patients without metastasis with Mean \pm SD=0.92 \pm 0.01 as compared to patients without metastasis with Mean \pm SD=0.99 \pm 0.02 and p value<0.05.⁹

The TAS levels were compared between premenopausal patients with early staged & premenopausal patients with advanced stage breast cancer. In this study the TAS levels were found to be higher in premenopausal patients early stage as compared to premenopausal patients advanced stage with Mean \pm SD= 1.23 \pm 0.25 and Mean rank =30.21 as compared to premenopausal patients advanced stage with Mean \pm SD=1.07 \pm 0.34 and Mean rank=22.61 with Man Whitney U =205.00 and p value was found to be non- significant (p=0.07).

The TAS levels were also compared between the premenopausal patients with early and advance stage and TAS was found to be lower in breast cancer patients with advance stage with Mean \pm SD=0.2 \pm 0.0 as compared to early staged with Mean \pm SD=0.1 \pm 0.0 and p value<0.001.⁷

CONCLUSION

With progression of the disease including lymph node involvement, metastasis and advance stages, the TAS levels indicate more and significant decrease indicating the decreased anti-oxidant defense in breast cancer patients with advancement of disease and disease progression.

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