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SUBNORMAL TOTAL ANTIOXIDANT ACTIVITY IN BLOOD SERUM OF NEWLY DIAGNOSED NON-COMMUNICABLE DISEASE SUBJECTS: A PREFATORY STUDY

Public Health

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ABSTRACT

Purpose: The incidences of Non-Communicable Diseases (NCDs) are increasing globally and are major contributors of morbidity and mortality worldwide. Their incidence is considered to be linked to imbalance in intracellular generation of Reactive Oxygen Species (ROS) and adequate level of antioxidants that leads consecutively to development of intracellular Oxidative Stress (OS), pro-inflammatory changes followed by systemic inflammation. In view of this concept the level of antioxidants namely the Total Antioxidant Activity (TAA) was determined in blood serum of newly diagnosed NCD subjects. **Methods:** Serum samples were obtained from OPD of a tertiary care hospital in district Barabanki Uttar Pradesh. Test subjects were categorized to explore gender or age related changes. Central tendencies of sTAA data viz. mean, median, and mode values were calculated. **Results:** Mean sTAA value in NCD subjects was found to be significantly low compared to mean value of sTAA in healthy subjects. Mode value was found to be low in male compared to female subjects; moreover, age wise decrease in mean, median and mode values of sTAA was also noticed. **Conclusion:** Conclusively, sTAA is found to be decreased in newly diagnosed NCD subjects. (word counts 182)

KEYWORDS

Oxidative Stress, Diabetes, Hepatitis, CKD, COPD, CVD, CLD

INTRODUCTION

Non Communicable diseases (NCDs) are one of the major causes of morbidity and mortality worldwide (1). These include a large spectrum of diseases e.g. obesity, anemia, diabetes, cardiovascular disease, hepatobiliary disorder, pulmonary disease, chronic kidney disease, neurological disorder, strokes, and cancer. As per World Health Organization (WHO), NCDs cause seventy one percent of total global deaths. Forty one million people die every year only due to NCD. In south Asia, NCDs in India alone account for nearly five million deaths in a year; and the disease burden and resultant mortality is expected to rise in coming years (2).

The molecular basis of NCDs is not well understood. However as per relevant literature, OS is understood to play a vital role in pathogenesis of a variety of NCDs viz. cancer, cardio-vascular disease, atherosclerosis, hypertension, ischemia/reperfusion injury, diabetes mellitus, neurodegenerative diseases including depression, anxiety disorders, schizophrenia and bipolar disorder due to high oxygen consumption and damage to lipid-rich structure of nerve cells. A prolonged OS (i.e. an imbalance in generation of free radicals and adequate levels of antioxidants) followed by pro-inflammatory changes and systemic chronic inflammation (SCI) is considered a pathogenic event that contributes to development of common types of NCDs (3-5). SCI and loss of antioxidants is considered to be an evil axis that creates risk of developing metabolic syndrome and morbidity during entire life span (4, 6, 7). Mitochondrial dysfunction is also advocated in development of metabolic syndrome *and is considered* a basic change in inflammation related NCDs *(8)*.

In view of the importance of antioxidants in regulation of OS, inflammation, mitochondrial dysfunction and NCD onset, a cross sectional study determining Total Antioxidant Activity in human blood serum (sTAA) of newly diagnosed NCD subjects was carried out. There is a paucity of knowledge in literature on the subject. The sTAA is considered a dynamic equilibrium of antioxidants influenced by interactions of serum constituents; and it is quantifiable in human body fluids. The sTAA reflects a cooperation of antioxidants than any other single antioxidant in human serum to provide an enhanced protection against reactivity of free radicals (9).

METHODS

A descriptive hospital based cross sectional study with consecutive sampling was carried out after due approval of the Institutional Ethics Committee. The discarded and non-hemolyzed blood serum samples of newly diagnosed NCD subjects before initiating treatment were obtained from blood collection center of hospital and were analyzed for sTAA. The demographic details about age, gender, and differential diagnosis were taken from medical record division. Pregnant subjects or the patients diagnosed for NCD and undergoing treatment were excluded.

The sTAA was determined by the method of Koracevic et al (9). In this assay, a standardized solution of Fe–EDTA complex is allowed to react with H_2O_2 leading to formation of hydroxyl radicals (OH) and superoxide anions (O_2^-). These ROS degrade benzoate and release Thiobarbituric Acid Reactive Substances i.e. TBARS. Antioxidants present in the added sample of human serum suppress formation of TBARS, which is measured at 532 nm using spectrophotometer. The inhibition of color development by TBARS is defined as TAA. Uric acid (500–2500μM) causing linear inhibition of TBARS production is used to make a standard curve for sTAA estimation; TAA value in blood serum is expressed as equivalent to mmol UA/L inhibiting TBARS production as per the standard curve.

Statistical parameters namely mean, SD, median, mode, and range values were determined to analyze the central tendency of the obtained data. Median value was considered as the sTAA level value in a particular group, which divided all the observed values into two equal numbers of higher or lower TAA levels. Mode was calculated as per formula: 3*median value minus 2*mean value. Mode revealed frequency of occurrence of sTAA level. The student's *t*-test was used to compare sTAA values of this study with sTAA values of healthy subjects reported in literature.

RESULTS

Demographic details of test subjects are summarized in Table-1. The mean sTAA levels in male and female subjects were found to be considerably lower than the same found in male or female healthy subjects reported in literature (Table-2). The change was statistically significant ('p' <0.001). The decreased sTAA level of newly diagnosed NCD subject is displayed individually in a scatter plot (Figure-1). As evident, the obtained sTAA levels were distinctly scattered around mean value observed in male and female subjects. Difference between sTAA mean values of male & female subjects was statistically insignificant ($p > 0.05$).

Median of sTAA values in newly diagnosed NCD subjects were found to be lower as compared to mean of sTAA values in healthy subjects (Table-2); median of sTAA values in test subjects of both the genders were nearly alike. Mode of sTAA values was found to be distinctly low in both male & female subjects as compared to the mean of sTAA values found in literature for either gender (Table-2). Frequency of low sTAA level (0.52 mmol UA/L) was found to be more in male subjects than sTAA value (0.74 mmol UA/L) seen in female subjects. Range of low sTAA values was relatively similar in both male and female subjects.

Age wise trend of changes in mean, median and mode values of sTAA in NCD subjects was also investigated; result is summarized in Table-3. Analysis of mean values of sTAA level in test subjects of different age groups showed a decreasing trend compared to mean sTAA levels of healthy subjects. The analysis revealed a unique pattern of age dependent decrease in mean values of sTAA. In an intra-group comparison, mean value of sTAA (1.20mmol UA/L) was found to be relatively more in younger (≤ 18y) test subjects compared to sTAA (0.76-0.87 mmol UA/L) in elder (≥19y) test subjects. The mean value

of sTAA level in aged subjects (≥19-60y) was found to be decreased by 30-35%. The age dependent changes in sTAA level were found to be irrespective of the gender of test subjects.

Median value of sTAA level in newly diagnosed NCD subjects of ≤18y age was also found to be decreased by 40% in the elder age (19 to ≥ 61y) groups (Table-3). Low median values of sTAA level were found to persist up to the age of ≥ 61 years.

A change in mode value of sTAA with respect to increase in age but irrespective of gender of test subjects was also found (Table-3). Frequency of relatively greater sTAA level was found in NCD subjects of ≤ 18y of age; however, it was lowest in test subjects of ≥ 61y age. Frequency of low sTAA level i.e. 0.76, 0.58, and 0.42 mmol/L UA of TAA was noticed in age groups of 19-40, 41-60, and ≥ 61 years respectively. A decreasing trend in the range of mode values of sTAA in ≤18y to ≥ 61y old newly diagnosed NCD subjects was remarkable.

DISCUSSION

Results of the present study demonstrate an occurrence of low sTAA level in newly diagnosed NCD subjects and show a trend of decrease with respect to ageing and gender. The sTAA level found in test subjects was found to be in range of its values reported in literature; the sTAA levels of healthy subjects are 2.04±0.20 mM UA ('n' = 120), 1.56±0.08 (n=13), and 1.63±0.20 (n=25) irrespective of gender (9-11).

A subnormal sTAA level reflects progressively waning antioxidant defense system and cellular metabolism favoring uncontrolled generation of ROS and propagation of pro-inflammatory changes. It also indicates a probability of persistent OS and uncontrolled cellular oxidative damage. OS dependent alteration in gene expression profile especially of cell signaling system influence physiology of normal cell and create pro-inflammatory changes leading to SCI and influencing tissue homeostasis (12-13). An uncontrolled occurrence of these events can jointly affect human health and contribute to acquisition or exacerbation of NCDs (14). Trend of sub-normal sTAA level in relation to ageing indicates its association with odds of inflammation mediated NCDs occurring across entire life span (7, 15).

The clinical outcomes of SCI-driven damage include higher rates of metabolic syndrome and risk of NCDs incidence e.g. hypertension, hyperglycemia, dyslipidemia, type-2 diabetes, NAFLD, hypertension, cardiovascular disease, chronic kidney disease, variety of cancer, depression, neurodegenerative and autoimmune diseases, osteoporosis, rheumatoid arthritis, and sarcopenia *(8,* 13, 16, 17). Maintenance of normal level of antioxidants in cells is often hypothesized to prevent or regulate key biochemical changes conducive to OS induction, pro-inflammatory changes and NCDs incidences (18, 21, 22). The observed sub-normal level of sTAA in newly diagnosed NCD subjects can be developed into a therapeutic opportunity to attempt the evidence based supplementation of antioxidants as adjuvant to improve clinical management of OS and SCI mediated NCDs.

Management of NCDs based on sTAA monitoring and use of dietary antioxidants can lessen rate of premature deaths and related secondary complications observed in NCD subjects. Importance of 'healthier' dietary patterns inclusive of antioxidants and scavengers of free radical or peroxide have been pointed out for prevention and management of Sarcopenia (23). Use of dietary antioxidants can lessen NCD incidences and current annual mortality rate of nearly forty million people killed by NCDs each year (equivalent to 74% of all deaths globally). According to WHO, seventeen million people die from NCD between the age of 30 to 70 years; and great majority of all NCD deaths occur in low and middle income countries that indicates role of malnutrition in onset of NCDs. Cardiovascular diseases, cancers, chronic respiratory diseases, chronic kidney diseases and diabetes make approximately 80% of all premature NCD deaths (24).

More of such studies are needed to assess and appraise efficacy of dietary antioxidant based therapeutic intervention of NCD management. More investigations confirming subnormal sTAA may pave the way for including supplementation of antioxidants as adjunct therapy in clinical management of newly diagnosed NCDs.

CONCLUSION

The levels of TAA are sub-normal in blood serum of newly diagnosed NCD subjects irrespective of their age and gender.

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Table-1: Characteristics of newly diagnosed NCD subjects

Parameter	Male	Female
'n' value	10	18
Range of age	1-61 year	18-77 year
NCD present	Diabetes; diseases of lung, liver, kidney, CNS	

Table-2: sTAA levels in newly diagnosed NCD subjects

Parameter	Male	Female	sTAA (mM UA) value of healthy subjects as per literature
Mean (mM UA) ± SD	0.88 ± 0.33*	0.74 ± 0.19*	2.04 ± 0.20 mM UA ('n'=120, healthy subjects irrespective of age)9, 1.56 ± 0.08 mM UA (n=13, male, 29-78y,)10, 1.63 ±0.20 mM UA (n=25, female, 18-39y)11 Mean=1.74 mM UA ('n'=120+13+25)
Median (mM UA)	0.76	0.74	
Mode (mM UA)	0.52	0.74	
Range (mM UA)	0.51-1.65	0.53-1.65	
'n' value	10	18	

*** Statistically significant ('p' <0.001)**

Table-3: Age vise change of serum TAA levels in newly diagnosed NCD subjects

S. No.	sTAA (mM UA)				sTAA (mM UA) value of healthy subjects as per literature
	<18 years	19-40 years	41-60 years	≥61 years	
Mean ± SD	1.2± 0.59	0.76± 0.21	0.83± 0.30	0.87±0. 25	2.04 ± 0.20 mM UA ('n'=120±0.2, healthy subjects irrespective of age)9, 1.56±0.08 mM UA (n=13, male, 29-78y,)10, 1.63 ±0.21 mM UA (n=25, female, 18-39y)11 Mean=1.74±0.16mM UA ('n'=120+ 13+25)
Median	1.27	0.76	0.74	0.72	
Mode	1.41	0.76	0.58	0.42	
Range	0.68-1.65	0.42-1.02	0.51-1.65	0.65-1.12	
'n' value	3	9	12	4	

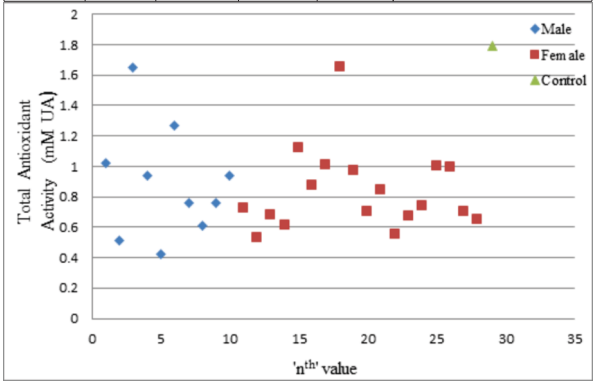

Figure-1: Scatter plot of sTAA level in newly diagnosed NCD subjects

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