Journal of Cancer Research and Therapeutics

Nagraj G. Huilgol
Editor-in-Chief
Chief Radiation Oncologist,
Nanavati Hospital

Rajiv Sarin
Executive Editor
Director,
ACTREC

Consulting Editors
Hassan Awwad, Cairo, Egypt (Africa / Middle East)
Michael Brada, UK (London)
Minesh Mehta, Wisconsin, USA (America)
Yin Weibo, Beijing, China (Asia)
Kailash Narayan, Melbourne, Australia (Australia)
John Yarnold, London, UK (Europe)
SK Shrivastava, Mumbai, India (ICRO)
Vikram Bhadrasain, National Cancer Inst (USA)
R Sankaranarayananan, IARC, Lyon (IARC)
Jens Overgaard, Aarhus, Denmark (ESTRO)

Consulting Editors - Specialities
Taisei Nomura, Osaka, Japan - (Cancer and Radiation Biology)
Rakesh Jalali, Mumbai, India - (Radiation Oncology (Clinical))
V Kannan, Mumbai, India - (Radiation Oncology (Technology))
Tharmar Ganes, Delhi, India - (Radiation Physics)
Purvish Parikh, Mumbai, India - (Medical Oncology)
Rajan Badwe, Mumbai, India - (Surgical Oncology)
Van der Zee Cobi, Rotterdam, The Netherlands - (Hyperthermia)
Mhoira Leng, Scotland, UK - (Palliative Care)

Statistician
R Gurusamy, Mumbai, India

Editorial Board Members

Ahmed Mansoor, Kentucky, USA
A. K. Anand, Delhi, India
Billimagga R, Bangalore, India
Buffalo ER, USA
Bulakova EB, Moscow, Russia
Chul Koo Cho, Seoul, Korea
Datta NR, Lucknow, India
Deshpande DD, Mumbai, India
Dinshaw K, Mumbai, India
Dwarakanath BS, Delhi, India
Dobrowski Werner, UK
Giri GV, Bangalore, India
Gupta T, Mumbai, India
Hurtwitz Mark, Massachusetts, USA
Kampinga HJ, AV Groningen, Netherlands
Kataria Tejinder, Delhi, India
Kaushal Vivek, Haryana, India
Kumarswamy, Bangalore, India
Kumar Shaleen, Lucknow, India
Lim Gerard, Kuala Lumpur, Malaysia
Manjunath N, Roschildale, USA
Marotta F, Milano, Italy
Martinez Alvaro, MI, USA
Mishra KP, Mumbai, India
M. Babaiah, Secunderabad, India
Negi PS, Delhi, India
Ohnishi T, Nara, Japan
Patel F, Chandigarh, India
Pillai RK, Trivandum, India
Prabir Kumar Sur, Kolkata, India
Raina V, Delhi, India
Rajan Bal, Trivandum, India
Rao Koteswara, Manipal, India
Rana P. Singh, USA
Sathiyanarayan VK, Mumbai, India
Koulooulas E Vassilis, Athens, Greece
Sethi VK, Singapore
Sharma SC, Chandigarh, India
Sohartari Gondhowiardjo, Jakarta, Indonesia
Tanaka Y, Tokyo, Japan
Uma Devi, Bhopal, India
Vidyasagar MS, Manipal, India
Ye Xiong Li, Beijing, China
Nagathihalli S. Nagaraj, USA

Official publication of the Association of Radiation Oncologists of India
EDITORIAL
Denying open access to published health-care research: WHO has the password?
Rajiv Sarin ...........................................................................................................................................133

ORIGINAL ARTICLES
Methods of intervention in reducing the psychosocial impact while dealing with cancer as a disease: A clinician’s point of view
S Trivedi, J Petera, S Fillip, Z Hrstka .......................................................................................................135

On the transit dose from motorized wedge treatment in Equinox-80 telecobalt unit
Rajesh A Kinhikar, Sachin Patkar, Chandrashekhar M Tambe, Deepak D Deshpande .....................................140

Salvage abdominal irradiation for refractory non-Hodgkin’s lymphoma
Riad Akoum, Emile Brihi, Michel Saade, Therese Hanna, Georges Chahine ................................................143

Treatment outcome and cost-effectiveness analysis of two chemotherapeutic regimens (BEP vs. VIP) for poor-prognosis metastatic germ cell tumors
Venkata Satya, Suresh Attili, Rama C Chandra, G Anupama, Loknath D, PP Bapsy, Hemant K Dadhich, Govind K Babu .............................................................................................................................................150

CASE REPORT
Synchronous dual malignancy: Successfully treated cases
Rashi Agrawal ...........................................................................................................................................153

REVIEW ARTICLE
Brain metastases from breast cancer: Management approach
Tabassum Wadasadawala, Sudeep Gupta, Vaishali Bagul, Namrata Patil ..............................................................157

BRIEF COMMUNICATIONS
Can pomegranate prevent prostate cancer?
Melisa Pereira ...........................................................................................................................................166

Serum total glutathione-s-transferase levels in oral cancer
Krishnananda Prabhu, Gopalakrishna P Bhat ..............................................................................................167

Transient asymptomatic bradycardia in patients on infusional 5-fluorouracil
K Talapatra, I Rajesh, B Rajesh, B Selvamani, J Subhashini ........................................................................169

Synchronous malignancies of breast and thyroid gland: A case report and review of literature
Dwarka P Agarwal, Tej P Soni, Om P Sharma, Shantanu Sharma ..............................................................172

BOOK REVIEW ..............................................................................................................................................174

SCIENTIFIC ABSTRACTS ...................................................................................................................................175
Serum total glutathione-s-transferase levels in oral cancer

ABSTRACT
We conducted a study wherein serum total glutathione-s-transferase levels were measured in patients (n = 27) with various stages of biopsy proven oral cancer (squamous cell carcinoma) and age and sex matched healthy human volunteers (n=10). In all patients with oral cancer, serum total glutathione-s-transferase was measured before the onset of treatment. There was a significant increase in serum total glutathione-s-transferase levels in patients with stage IV oral cancer as compared to stage II (P = 0.001) and stage III (P = 0.002) oral cancer. This shows that alterations in serum total Glutathione-s-transferase levels may have a role in cancer progression.

KEY WORDS: Glutathione-s-transferase, oral cancer, progression

INTRODUCTION
Oral cancer accounts for about 8% of all malignant growths. Men particularly over 40 years are affected twice as often as women. The exact cause is unclear but smoking, alcohol, tobacco chewing, poor oral hygiene, chronic irritation etc are implicated. Reactive oxygen species (ROS) like superoxide, hydrogen peroxide etc. have been implicated in many diseases including cancer. ROS have been known to play an important role in initiation and progression of multi-step carcinogenesis.[1] Alterations in circulating antioxidants and free radical scavengers like glutathione-s-transferase (GST) have been linked with various epithelial malignancies including oral cancer.[1-9] In this study, we evaluated the levels of serum total GST in oral cancer patients and healthy controls.

MATERIALS
Reduced glutathione C₃H₇O₆S and 1-chloro-2, 4, dinitro benzene (CDNB) were purchased from Sigma Chemical Company. All other reagents used were of Reagent grade. Deionized water was used throughout the study.

Permission for the study was granted by the Institutional Ethics Committee. Informed consent was taken from controls (healthy volunteers, n = 10) and patients (n = 27). The age of the subjects (n =37) was 56.4±1.67 yrs [Table 1]. All the patients were admitted for radiotherapy. In cases blood was withdrawn just before initiation of treatment.

Serum total GST levels were measured in biopsy proven cases of oral cancer (n=27) with biopsy showing moderate to well differentiated squamous cell carcinoma.

METHODS
Serum GST was estimated by CDNB method.[10-12]

REAGENTS
a. Phosphate Buffer: 0.1M, pH-6.5 prepared with deionized water and stored in brown bottle in refrigerator.

b. CDNB: 20 mM in 95% ethanol, stored in brown bottle in fridge.

c. GSH: 20mM in deionized water freshly prepared just before the assay.

d. Serum: Blood was collected without any anticoagulant and allowed to clot for 1h. Clotted sample was centrifuged at 3500 rpm × 30 min at 4°C (in cold centrifuge). Serum was separated and stored at 4°C until use and assayed on the same day.

Assay
GST was estimated in 1ml of incubation mixture containing 850 μl of 0.1 M phosphate buffer pH 6.5 and CDNB reagent (20 mM) 50 μl, preincubated at 37°C for 10 min. Reaction was started by adding 50 μl of 20 mM GSH and 50 μl of serum. Reaction was followed at 1 min interval for 5 min by measuring absorption at 340 nm. Simultaneously, blank was run by substituting deionized water for serum. Then O.D change/min was calculated. GST was estimated by using the molar extinction coefficient [9.6 mM⁻¹ cm⁻¹] of GST.[11]
advancing cancer and has been associated with poor prognosis and development of drug resistance.[14,15] In our study there was an increase in serum total GST in later stages of cancer. This enhanced antioxidant capacity made the tumor tissues less susceptible to oxidative stress conferring specific growth advantage.[16]

REFERENCES


| Table 1: Age wise distribution of subjects (both controls and cases) |
|-------------------|-------------------|-------------------|-------------------|-------------------|
| Stage             | 40-49 yrs         | 50-59 yrs         | 60-69 yrs         | 70-79 yrs         |
| Controls (n=10)   | 6 (35%)           | 10 (27%)          | 8 (22%)           | 6 (16%)           |
| Stage II (n=5)    | 2 (35%)           | 3 (27%)           | 1 (22%)           | 3 (16%)           |
| Stage III (n=8)   | 2 (25%)           | 3 (38%)           | 0 (0%)            | 5 (62%)           |
| Stage IV (n=14)   | 3 (21%)           | 1 (7%)            | 7 (50%)           | 3 (21%)           |
| Total (n=37)      | 13 (35%)          | 10 (27%)          | 8 (22%)           | 6 (16%)           |

| Table 2: Serum total GST values in healthy controls and patients suffering from oral cancer (median and inter quartile range) |
|-------------------|-------------------|-------------------|-------------------|
| Group             | GST IU/Ltr (Median and IQR) | Significance* |
| Control (n = 10)  | 6.7(4.8, 7.5)      | -                 |
| Stage II (n = 5)  | 3.8(2.7, 4.6)*     | 0.049             |
| Stage III (n = 8) | 5(3.4, 6.2)        | 0.099             |
| Stage IV (n = 14) | 6.7(6.2, 12)       | 0.318             |

*Kruskal-Wallis Test as compared to controls at P < 0.0083, *Significant at 0.001 level as compared to Stage IV; **Significant at 0.002 level as compared to Stage IV

Formula

\[
\text{O.D of test - O.D of blank} = 9.6 \times 0.05 \times 1000\text{ IU/Ltr}
\]

Statistical analysis

Kruskal Wallis test was used to analyze the results and it showed a significant difference (P = 0.001). In case of significant difference, pair-wise comparison between control and various stages were done by Mann-Whitney Test adjusting α for the number of pairs to be compared. (significance at the level: 0.05/6 = 0.0083)

RESULTS AND DISCUSSION

Comparison of serum total GST between control and cancer patients using Kruskal Wallis showed a significant difference (P = 0.001). However, the paired comparison between control and various groups by Mann Whitney did not show a significant difference.

ROS are tumorogenic by virtue of their ability to increase cell proliferation, survival, cellular migration and also by inducing DNA damage leading to genetic lesions that initiate tumorigenicity and sustain subsequent tumor progression. As shown by earlier studies, loss of antioxidant capacity of cell in early dysplasias can trigger initiation and progression of cancer.[13] Our results showed a decrease in serum total GST in early cancer than the control [Table 2] which may have triggered the initiation and progression of cancer. Many studies also showed progressive increase of GST with advancing cancer and has been associated with poor prognosis and development of drug resistance.[14,15] In our study there was an increase in serum total GST in later stages of cancer. This enhanced antioxidant capacity made the tumor tissues less susceptible to oxidative stress conferring specific growth advantage.[16]