# Comparison of Plasma Taurine Levels between Patients with Esophageal Cancer and Healthy Controls

**Mahsa Taherizadeh (MSc)**
Golestan University of Medical Sciences, Gorgan, Iran

**Masoud Khoshnia (PhD)**
Golestan Research Center of Gastroenterology and Hepatology, Golestan University of Medical Sciences, Gorgan, Iran

**Sedighe Shams (MD)**
Children Medical Center, Tehran University of Medical Sciences, Tehran, Iran

**Hamidreza Joshaghani (PhD)**
Golestan Research Center of Gastroenterology and Hepatology, Golestan University of Medical Sciences, Gorgan, Iran

**Corresponding author:** Hamidreza Joshaghani

**Tel:** +98(17)32423093

**Email:** taherizadeh.mahsa@yahoo.com

**Address:** Golestan University of Medical Sciences, Gorgan, Iran

**Received :** 28 Sep 2015
**Revised:** 01 Feb 2016
**Accepted:** 12 Feb 2016

## ABSTRACT

**Background and Objectives:** The incidence rate of esophageal cancer (EC) is high in north and northeast of Iran. Taurine is a sulfur-containing amino acid with a wide range of vital biological functions. The aim of this study was to compare plasma levels of taurine between patients with EC and healthy controls.

**Methods**: Plasma samples from 36 recently diagnosed cases of EC and 36 healthy adults were analyzed by high-pressure liquid chromatography. Data analysis was done using SPSS (version 16). The t-test was used to evaluate significant differences in the level of taurine between the two groups. P-values less than 0.05 were considered statistically significant.

**Results**: Patients with EC had significantly higher levels of plasma taurine compared with the controls ($P<0.05$).

**Conclusion:** Patients with EC have significantly higher levels of plasma taurine compared with healthy individuals. This finding suggests that the measurement of plasma taurine in patients with EC could be useful for the early diagnosis of the disease.

**Keywords:** Esophageal Cancer, Taurine, HPLC.



This paper should be cited as: Taherizadeh M, Khoshnia M, Shams S, Joshaghani HR[Comparison of Plasma Taurine Levels between Patients with Esophageal Cancer and Healthy Controls] . mljgoums. 2017; 11(2): 1-4

## INTRODUCTION

The incidence rate of esophageal cancer (EC) is high in the north and northeast of Iran (1, 2). Golestan Province is one of the high-risk areas in northeastern Iran, followed by Mazandaran and Khorasan Provinces (2). According to an early survey by the Cancer Institute of Iran, esophageal carcinoma accounts for 9% of all cancers and 27% of gastrointestinal cancers, with a male to female ratio of 1.7:1 (3).

Taurine is a sulfur containing amino acid with antioxidant and free radical scavenging properties that has a wide range of vital biological functions ranging from neuromodulation to cell membrane stabilization (4, 5). Decreased plasma taurine level has been observed in certain states of metabolic stress such as sepsis, trauma and surgery (6). Evidence suggests that regulation of pro-inflammatory cytokines and stimulation of inflammatory cytokines could facilitate the resolution of inflammatory response in patients with EC, preventing the onset of complications and improving survival. These benefits could be related to the actions of taurine (7, 8). Limited number of studies have investigated the plasma level of taurine in patients with cancer, especially EC (8, 9). In the last decade, taurine has been widely used in the field of oncology as a chemoprotective agent against hepatocarcinogenesis (10, 11) and colon carcinogenesis (12, 13). Moreover, taurolidine (an anti-endotoxin) was found to reduce tumor necrosis factor toxicity (14, 15) and induce suppression of vascular endothelial growth factor production on the protein and mRNA level, indicating an apoptotic and antiangiogenic effect for taurine (16). Thus, the aim of the present study was to compare plasma taurine levels between patients with esophageal cancer and healthy controls.

## MATERIAL AND METHODS

Blood samples (5 ml) were obtained from healthy controls and patients with esophageal squamous cell carcinoma (ESCC) prior to any medical treatment. The samples were collected from forearm vein in tubes containing ethylene diamine tetra acetic acid after overnight fasting. Plasma was prepared by centrifugation at 1000× g for 10 min, and then stored at -280 $^{o}$C until analysis.

Plasma taurine levels were analyzed by reverse phase chromatography (RP-HPLC) using HPLC instrument (KNAUER model, Germany), operated at gradient and flow rate of 1 ml/min and pH=7.02 (17). First, 200 µl of each sample were mixed with 50 µl of homoserine standard and 800 µl of methanol. After incubation for 5 min at 4 °C, the mixture was centrifuged at 4000 RPM for 5 minutes. Then, 250 µl of the supernatant was mixed with 100 µl of borate buffer (to adjust PH) and vortexed for 5 seconds. Later, 50 µl of OPA derivatives was incubated at room temperature for 2 min. After vortexing for 5 seconds, 25 µl of HCL 75% normal was added to the mixture. Then, 50 µl of the mixture was mixed with 200 µl of solution A. After vortexing for 5 min, 20 µl of the mixture was taken and injected to the device using Hamilton syringe. The HPLC instrument measured level of plasma taurine in 60 min.

Statistical analysis of data was done using SPSS (version 16). Mean taurine concentrations and standard deviations (SDs) were determined for both EC patients and controls. P-values less than 0.05 were considered statistically significant. The t-test was used to evaluate significant differences in the taurine concentrations between the two groups.

## RESULTS

Univariate analysis was done to compare taurine levels in the controls and ESCC patients. As shown in table 1, taurine levels differed significantly between the ESCC patients and controls. The plasma concentrations of taurine were significantly higher in ESCC patients compared with the controls ($P < 0.05$).

**Figure 1- Mean plasma concentration of taurine (nmol/mL) in the patients and healthy controls**

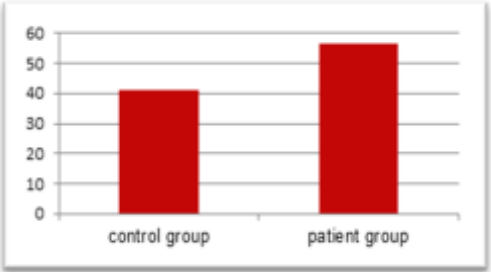

**Table1- Comparison of mean concentrations of taurine in the ESCC patients and controls**

| Amino acid | Healthy controls (N=37) | | | ESCC patients (N=37) | | | Comparison of the amino acid parameters (t-test) | | |
|---|---|---|---|---|---|---|---|---|---|
| Taurine (nmol/mL) | Median | SD | Mean concentrations of taurine | Median | SD | Mean concentrations of taurine | P-value | P-value | |
| | | | | | | | | Equal variances assumed | Equal variances not assumed |
| | 38 | 21.59 | 41.11 | 49 | 32.2 | 56.74 | 0.112 | 0.017 | 0.017 |



## DISCUSSION

EC is the seventh most common cancer in Iran and among the leading causes of cancer death worldwide (18). This poor prognosis disease has median survival of 15-18 months after esophagectomy for patients with localized tumor and 5-year survival rate of 20-25%. At the time of diagnosis, most patients report ingestion of small amounts of liquid or pasty food or else no food due to rapid progressive dysphagia (19). In the last decade, several studies have investigated the possible correlation of antioxidants with the pathogenesis of cancer (20, 21). Taurine was used successfully as a chemotherapeutic agent against diethyl nitrosamine (DENA)-induced hepatocellular carcinoma in rats (5). Moreover, it has been successfully used for treatment of colorectal cancer induced by azoxymethane and hydrophobic bile acid (12, 13). Three main processes have been implicated in tumor growth; increased cell proliferation, inhibition of tumor cell apoptosis and enhanced angiogenesis (22). Tauromustine is an effective treatment for disseminated malignant melanoma (23) and colorectal cancer (24). It was also used to potentiate the antitumor effect of 5-flurouracil and hydralazine in the treatment of colorectal adenocarcinoma (25), and nitrosourea in the treatment of hepatoma and lung cancer (26).

In previous studies, changes in the level of taurine in patients with cancer have been contradictory. In our study, plasma concentration of taurine in patients with ESCC was significantly increased. Lamonica et al. (27) evaluated plasma levels of taurine,cysteine and homocysteine by the HPLC method and found that plasma levels of taurine and homocysteine have increased significantly. The liver is a major site of taurine biosynthesis and release into the plasma. Hepatocyte hydration is thought tochange within minutes in response to hormones, amino acids, bile acids, and metabolites of oxidative stress. Oxidative stress and various inflammatory mediators might cause hepatocellular shrinkage by opening $K^+$ channels in the plasma membrane, resulting in a hepatocellular $K^+$ efflux and release of antioxidants such as taurine. The elevation of taurine in plasma could also be due to renal failure, since kidneys are the organs responsible for regulating sulfur balance. However, a study reported that assessment of renal function was satisfactory in all patients with EC. Moreover, the accumulation of taurine in plasma could be due to its decreased disposal as taurocholate, which has not been investigated in the present study.

## CONCLUSION

The present study shows that EC patients have significantly higher plasma levels of taurine compared with healthy controls, which could be useful for the early diagnosis of the disease. However, further studies should be conducted in this regard to verify the results of our study.

## ACKNOWLEDGEMENTS

We would like to thank the laboratory of Golestan University of Medical Sciences and all the personnel who cooperated in conducting this study. Firoozgar Hospital in Tehran and Research Center of Gastroenterology and Hepatology in the Golestan Province are kindly acknowledged for cooperation in sample collection.

## CONFLICT OF INTEREST

The authors declare that they have no competing interest.

**REFERENCES**:


1. Islami F KF, Nasrollahzadeh D, Aghcheli K,Sotoudeh M, Abedi-Ardekani B, et al. *Socio-economic status and oesophageal cancer: results from a populationbased case-control study in a high-risk area.* Int J Epidemiol. 2009; 38(23): 978-88. doi: 10.1093/ije/dyp195.

2. Kamangar F MR, Dawsey SM, Saidi F. Esophageal cancer in northeastern Iran: a review. Arch Iran Med. 2007; 10(4): 70-82.

3. Ghavamzadeh A MA, Jahani M, Rastegarpanah M, Iravani M. *Esophageal cancer in Iran.* Semin Oncol. 2001; 28(2): 153-7.

4. Huxitable R. *Physiological action of taurine.* Physiol Rev. 1992; 72(1): 101-63.

5. El-Agousa I E-nD, Eissa S, Sharoud M. *Possible ameliorative effect of antioxidant (Taurine) in pregnant toxemic female Rats.* Open Hypertention J. 2009; 2: 1-15.

6.Schuller-Levis GB PE. *Taurine: new implications for an old amino acid.* FEMS Microbiol Lett. 2003; 226: 195-202.

7. Abe M TM, Takeuchi K, Fukuda M. *Studies on the significance of taurine in radiation injury*. Radiat Res. 1968; 33: 563-73.

8. Gray GE LA, Meguid MM. *Taurine-supplemented total parenteral nutrition and taurine status of malnourished cancer patients.* Nutrition. 1994; 10(1): 11-5.

9. Vinton NE LS, Ament ME, Kopple JD. *Taurine concentrations in plasma and blood cells of patients undergoing long-term parenteral nutrition*. Am J Clin Nutr. 1986; 44: 398-404.

10. Warskulat U, Borsch E, Reinehr R, Heller-Stilb B, Mönnighoff I, Buchczyk D, et al. *Chronic liver disease is triggered by taurine transporter knockout in the mouse.* FASEB J. 2006; 20(3): 574-6.

11. Reddy BS, Rao CV, Rivenson A, Kelloff G. *Chemoprevention of colon carcinogenesis by organosulfur compoubds.* Cancer Res. 1993; 53(15): 3493-8.

12. Cheng K, Xie G, Raufman JP. *Matrix metalloproteinase-7-catalyzed release of HB-EGF mediates deoxycholyltaurine-induced proliferation of a human colon cancer cell line.* Biochem Pharmacol. 2007; 73(7): 1001-12.

13. Monoson J RP, Donohue J. *Taurolidine inhibits tumor necrosis factor (TNF) toxicity - New evidence of TNF and endotoxin synergy*. Eur J Surg Oncol. 1993; 19(3): 226-31.

14. Jacobi C MC, Braumann C. *Taurolidine-a new drug with anti-tumor and anti-angiogenic effects.* Anticancer Drugs. 2005; 16(9): 917-21.

15. Rodak R KH, Ishihara H. *Induction of reactive oxygen intermediates-dependent programmed cell death in human malignant ex vivo glioma cells and inhibition of the vascular endothelial growth factor production by taurolidine.* J Neurosurg. 2005; 102(6): 1055-68.

16. Turnell D, Cooper J. *Rapid assay for amino acids in serum or urine by pre-column derivatization and reversed-phase liquid chromatography.* Clinical Chemistry. 1982; 28(3): 527-31.

17. Aledavood A1 AK, Sabouri G1. *Esophageal Cancer in Northeast of Iran.* Iran J Cancer Prev. 2011; 4(3): 125-9.

18. Zacarias-Castillo RR H-RA, Zajarias-Rabchinskey A, González-Bárcenad D. *Hiperhomocisteinemia. Um nuevo factor de riesgo coronariano.* Gac Med Mex. 2001; 137(4): 335-45.

19. Ishigami T FT, Simbula G. *Regulatory effects of senescence marker protein 30 on the proliferation of hepatocytes.* Pathol Int. 2001; 51(7): 491-7.

20. El-Idrissi D MK, Belgacem S. *Constraints and obstacles to social health protection in the Maghreb: the cases of Algeria and Morocco.* Bull World Health Organ. 2008; 86: 902-4.

21. Folkman J KR. *Tumor Angiogenesis.* In Kufe DW, Bast RC, Hart WN, et al. (Holland-Feri. Cancer Medicin) 6th Ed by BC Decker Inc Hamolton, London. 2003:161-94.

22. Folkman J KR. Tumor Angiogenesis. In Kufe DW, Bast RC, Hart WN, et al. (Holland-Feri. Cancer Medicin). On line 7th Ed by BC Decker Inc Hamolton, London. 2006:161-94.

23. Gjedde SB, Mouridsen HT, L-Madsen E, Jensen NV, Blomquist E, Bergh J, et al. *Phase I study of tauromustine administered in a weekly schedule*. Eur J Cancer. 1993; 29(13): 1901-2.

24. Singh G GH, Milsom JW, Chaudry IH. *Tauromustine is more effective than conventional chemotherapy in the treatment of colonic tumors.* Dis Colon Rectum. 1993; 36(4): 394-9.

25. Bibby M LP, Al-Ghabban A, Double J. *Influence of hydralazine on the pharmacokinetics of taurmustine in mice-.* Br J Cancer Biochem Biophys. 1992; 65(3): 347-50.

26. Tabassum H PS, Rehman H, Dev Banerjee B, Siemen D, Raisuddin S. *Nephrotoxicity and its prevention by taurine in tamoxifen induced oxidative stress in mice.* Hum Exp Toxicol. 2007; 26(6): 509-18.

27. Lamonica-garcia V MF LM MF, Henry M, Burini R. *Plasma taurine levels in patients with esophagus cancer.* Arq Gastroenterol. 2008; 45(3): 199-203.