



ORIGINAL ARTICLE

Heat Shock Proteins 27 and 60 Serum Levels in Patients with Gastrointestinal Cancer and Acute Myocardial Infarction in Birjand, Iran

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ABSTRACT

Introduction: Cancer and myocardial infarction are lethal diseases. Their prevalence is increasing worldwide. In both diseases, the level of oxidative stress rises because of tissue damage. The aim of this study was to evaluate the serum levels of heat shock protein 27 and heat shock protein 60 in patients with cancer and myocardial infarction, and then compare them with healthy individuals. **Materials and Methods:** After blood samples were collected from the participants, plasma and serum were separated from these samples for further examination. The serum levels of heat shock protein 27 and heat shock protein 60 were measured with related kits in 30 patients with cancer and 30 patients with acute myocardial infarction, followed by 30 healthy individuals. The collected data were then analyzed in the Statistical Package for the Social Sciences software (version 22). **Results:** The mean serum levels of heat shock protein 27 in cancer patients (25.21 ± 5.57 ng/mL) and in patients with myocardial infarction (45.23 ± 7.43) were significantly higher than those in healthy individuals (10.61 ± 3.11 ; $P < 0.05$). In addition, the mean serum levels of heat shock protein 60 in patients with cancer (19.23 ± 3.41 ng/mL) and patients with myocardial infarction (22.23 ± 2.25 ng/mL) were significantly higher than those in healthy individuals (8.38 ± 2.53 ; $P < 0.05$). **Conclusion:** An increase in the serum levels of heat shock proteins 27 and 60 was observed in patients with cancer and myocardial infarction. Therefore, we can suggest that these biomarkers should help surgeons or physicians to diagnose the diseases.

INTRODUCTION

Despite several efforts, the prevalence of noncommunicable diseases is rising. Among them, heart diseases and cancers are the leading causes of mortality all over the world (1). Cancer is one of the oldest diseases of humankind, and despite several attempts for its therapy, its incidence is on the rise (2). The prevalence of cancer is high in developing countries such as Iran; of all cancers, gastrointestinal cancer is of particular importance (3). In addition, cardiovascular diseases are the leading cause of death and disability. They cause about 50% of all deaths; about 7 million people die annually because of cardiovascular diseases (4).

Shock proteins are produced by cells in response to exposure to stressful conditions such as thermal shock, as well as physical, chemical, and biological stresses (5). Heat shock proteins (HSPs) are regulatory proteins that are divided into

subfamilies based on their weight. So far, 4 large protein families have been detected, including HSP90, HSP70, HSP60, and HSP27. The role of these proteins is to prevent protein aggregation and removal of badly twisted proteins (6). When HSPs bind to the P53 gene, the mutations of this gene increase. This action causes a delay in the death and invasion of cancer cells (7, 8). Moreover, the expression of these proteins in ischemic diseases induces the expression of adhesion molecules, causing the migration of inflammatory cells to the site of lesion, thereby exacerbating inflammation (7).

HSP60 and HSP27 are continuously secreted by cancer cells, which in turn paves the way for tumor progression (8, 9). A higher than normal level of HSP27 expression was detected in various cancers, for example, in breast, prostate, bladder, gastric, ovarian, and oral squamous carcinoma cancers, as well as in Hodgkin disease (5). In isch-

emic diseases, HSP60 is overexpressed by the damaged cells (7, 10). Because acute myocardial infarction (AMI) and gastrointestinal cancers are metabolic diseases, we expect a higher expression of these proteins in both diseases. The aim of this study was to compare the serum levels of these proteins, specifically in patients and healthy people in our population.

MATERIALS AND METHODS

A total of 30 patients with gastrointestinal cancer confirmed by a pathologist and 30 individuals with AMI were recruited for this study. In addition, 30 healthy individuals were selected when matched with demographic factors of other participants. A written consent was obtained from all participants, and the questionnaire was completed for all patients. This study was approved by the Research Council and Ethics Committee of Birjand University of Medical Sciences Birjand, South Khorasan Province, Iran. Blood samples were taken from all individuals, and serum was separated from them; serum was stored at 80°C until used. Biomarkers (HSP27 and HSP60) were measured using ELISA kits (HSP27: Boster Biological Technology Co., Ltd; HSP60: Hangzhou Eastbiopharm Co., Ltd). Statistical analyses were performed using the Statistical Package for the Social Sciences software, version 22 (SPSS, Chicago, IL, USA). $P < .05$ was considered statistically significant.

RESULTS

The patients with AMI and gastrointestinal cancer were compared with 30 healthy subjects in terms of the HSP27 and HSP60 levels. Immunological findings showed that there was a significant increase in the HSP27 levels in the serum of patients with AMI and gastrointestinal cancers and healthy subjects ($P < 0.05$; Table 1).

DISCUSSION

Gastrointestinal cancer and AMI are two of the most important diseases of the 21st century with inflammatory and oxidative stress conditions. Both diseases cause huge fatality in both developed countries and developing countries (1, 11). During inflammation, certain types of cytokines such as tissue necrosis factor-alpha (TNF- α)

and interleukin 1 (IL-1) are secreted, which can induce the production of HSPs (12). The aim of this study was to determine the serum levels of HSP27 and HSP60 in patients with cancer and patients with AMI and to compare the levels with those in healthy people.

This study showed that the levels of HSP27 and HSP60 were significantly higher in patient groups compared with healthy subjects. The rate of HSP27 in patients with cancer and AMI increased 2.5 and 4.5 times, respectively, and the rate of HSP60 in patients with cancer and AMI increased 2.3 and 2.7 times, respectively. Consistent with our study, Zhang et al showed increased levels of HSP60 in the case of stroke, which may be caused by myocardial necrosis and vascular endothelial dysfunction. In line with Zhang et al, several studies have shown that the level of HSP60 increases the production of proinflammatory factors, such as TNF- α , IL-1, IL-6, and IL-12, and sticky molecules such as selectins and integrins; therefore, HSP60 plays a major role in the development of atherosclerosis and predisposes cells to AMI (13). Also, de Haan et al showed that HSP27 and HSP70 serum levels significantly increased inflammation caused by cardiomyopathy ischemia (14). A study by Abharzanjani et al showed that the levels of HSP27 are significantly increased after AMI caused by oxidative stress (11).

HSP60 is actively secreted from tumor cells as well (15). This inflammatory biomarker has a significant relationship with the invasive form of cancers, and it is significantly involved in tissue cancer and lymph node (15). The results of Xiao-Shan et al study showed that the prognosis of gastrointestinal cancer patients with a high level of HSP60 protein is poor (16). In addition, the results of the studies conducted by Faried et al and Cappello et al showed that this biomarker plays a major role in the development of cancers such as the esophageal and intestinal cancers (17, 18). Furthermore, various articles have reported a higher amount of HSP60 protein in inflammatory bowel disease such as the Crohn disease (15).

Ce'line Hamelin's results showed that the expression level of HSP27 protein increased significantly during liver cancer. However, this increase was not significantly correlated with tumor variations (19). The excessive presence of this protein (HSP27) can cause epithelial and mesenchymal changes. Besides, HSP27 expression can cause drug resistance in cancers such as pancreatic cancer (20).

CONCLUSION

The results of the present study showed that the levels of HSP27 and HSP60 were significantly increased in patients with gastrointestinal cancers and AMI compared with those in healthy individuals. It seems that these two HSPs can be used as a prognostic factor for diagnosing AMI and gastrointestinal cancer.

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Table 1. Levels of HSP27 and HSP60 in serum of patients with AMI and gastrointestinal cancers and normal groups

Biochemical Markers	HSP27 (ng/mL)	HSP60 (ng/mL)
Population Studied		
Normal people	10/61 \pm 3/11	8/38 \pm 2/53
Cancer patients	25/21 \pm 5/57 ^a	19/23 \pm 3/41 ^a
AMI patients	45/23 \pm 7/43 ^a	22/23 \pm 2/25 ^a

(Abbreviations: a. HSP: heat shock protein, b. AMI: acute myocardial infarction)

^a $P < 0.05$ (case group compared with the normal group).

AUTHER CONTRIBUTIONS

All authors contributed equally to this study.

CONFLICT OF INTEREST

None declared.

ETHICAL STANDARDS

This study was approved by the Research Council and Ethics Committee of Birjand University of Medical Sciences Birjand, South Khorasan Province, Iran.

REFERENCES

- Almasi A, Shamsi M, BabakEshrati RF, Alimoradi K, Rahmati L. The epidemiology of gastrointestinal cancers (Stomach, esophageal, colorectal) In Markazi province during 2005-2010. *Journal of Neyshabur University Medical Sciences*. 2014;2(2):22-7.
- Siegel RL, Miller KD, Fedewa SA, Ahnen DJ, Meester RG, Barzi A, et al. Colorectal cancer statistics, 2017. *CA: a cancer journal for clinicians*. 2017;67(3):177-93.
- Rafiemanesh H, Rajaei-Behbahani N, Khani Y, Hosseini S. Incidence trend and epidemiology of common cancers in the center of Iran. *Global journal of health science*. 2016;8(3):146.
- Foadoddini M, Amir-Abadi Zadeh M, Ghiravani Z. Cardioprotective effects of ranitidine against ischemia-reperfusion injury in mice. *Journal of Birjand University of Medical Sciences*. 2014;20(4):346-56.
- Okuno M, Yasuda I, Adachi S, Nakashima M, Kawaguchi J, Doi S, et al. The significance of phosphorylated heat shock protein 27 on the prognosis of pancreatic cancer. *Oncotarget*. 2016;7(12):14291.
- Giaginis C, Daskalopoulou SS, Vgenopoulou S, Sfiniadakis I, Kouraklis G, Theocharis SE. Heat Shock Protein-27,-60 and-90 expression in gastric cancer: association with clinicopathological variables and patient survival. *BMC gastroenterology*. 2009;9(1):14.
- Pockley AG, Wu R, Lemne C, Kiessling R, de Faire U, Frostegård J. Circulating heat shock protein 60 is associated with early cardiovascular disease. *Hypertension*. 2000;36(2):303-7.
- Ciocca DR, Calderwood SK. Heat shock proteins in cancer: diagnostic, prognostic, predictive, and treatment implications. *Cell stress & chaperones*. 2005;10(2):86-103.
- King KL, Li AFY, Chau GY, Chi CW, Wu CW, Huang CL, et al. Prognostic significance of heat shock protein-27 expression in hepatocellular carcinoma and its relation to histologic grading and survival. *Cancer*. 2000;88(11):2464-70.
- Madriral-Matute J, Martin-Ventura JL, Blanco-Colio LM, Egido J, Michel J-B, Meilhac O. Heat-shock proteins in cardiovascular disease. *Advances in clinical chemistry*. 2011;54:3.
- Abharzanjani F, Kazemi T, Bijari B, Hemmati M. Comparison of serum level of heat shock protein 27 (HSP 27) and the amount of DNA damage in acute myocardial infarction patients. *Iranian Journal of Endocrinology and Metabolism*. 2016;18(4):243-50.
- Gharibdoost F, Samadi F, Taghipoor R, Akbarian M, Shahram F, Nadji A, et al. Heat shock protein 70 level of synovial fluid in rheumatoid arthritis versus osteoarthritis: a comparative study. *Tehran University Medical Journal TUMS Publications*. 2007;65(7):28-31.
- Zhang X, He Ma, Cheng L, Chen Y, Zhou L, Zeng H, et al. Elevated heat shock protein 60 levels are associated with higher risk of coronary heart disease in Chinese. *Circulation*. 2008;118(25):2687-93.
- De Haan J, Smeets M, Pasterkamp G, Arslan F. Danger signals in the initiation of the inflammatory response after myocardial infarction. *Mediators of Inflammation*. 2013;2013.
- Hamelin C, Cornut E, Poirier F, Pons S, Beaulieu C, Charrier JP, et al. Identification and verification of heat shock protein 60 as a potential serum marker for colorectal cancer. *The FEBS journal*. 2011;278(24):4845-59.
- Li X-s, Xu Q, Fu X-y, Luo W-s. Heat shock protein 60 overexpression is associated with the progression and prognosis in gastric cancer. *PloS one*. 2014;9(9):e107507.
- Faried A, Sohda M, Nakajima M, Miyazaki T, Kato H, Kuwano H. Expression of heat-shock protein Hsp60 correlated with the apoptotic index and patient prognosis in human oesophageal squamous cell carcinoma. *European journal of cancer*. 2004;40(18):2804-11.
- Cappello F, Di Stefano A, D'Anna SE, Donner CF, Zummo G. Immunopositivity of heat shock protein 60 as a biomarker of bronchial carcinogenesis. *The lancet oncology*. 2005;6(10):816.
- Eto D, Hisaka T, Horiuchi H, Uchida S, Ishikawa H, Kawashima Y, et al. Expression of HSP27 in Hepatocellular Carcinoma. *Anticancer research*. 2016;36(7):3775-9.
- Kuramitsu Y, Wang Y, Taba K, Suenaga S, Ryozaawa S, Kaino S, et al. Heat-shock protein 27 plays the key role in gemcitabine-resistance of pancreatic cancer cells. *Anticancer research*. 2012;32(6):2295-9.