

## RESEARCH ARTICLE

# Esophageal Cancer, Gastric Cancer and the use of Pesticides in the Southwestern of Turkey

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### Abstract

**Background:** Esophageal and gastric cancer generally have a poor prognosis and may share common risk factors. It has been demonstrated that the pesticide usage may contribute to development of many cancer types. In this study, the relation between amount of pesticides used in agriculture and esophageal and gastric cancer incidence was researched. **Materials and Methods:** Findings from the data bank of the Ministry of Health Provincial Health Directorate Cancer Records Center between the years of 1998-2010 were used. All patients who were diagnosed with gastric and esophageal cancer histopathologically were included. Data for annual pesticide usage were obtained from Provincial Agriculture Directorate for the same time period. Statistical analysis was performed using the Spearman test. **Results:** One thousand eight hundred and ninety-six patients were involved in the study, 1,233 males (65%) and 663 females (35%), 230 with esophageal cancer (12.1%) and 1,666 with gastric cancer (87.9%). No statistically significant relation was apparent between pesticide amount used and esophageal cancer ( $p: 0.87$ ). **Conclusions:** In our study, there was no relationship between pesticide usage and esophageal or gastric cancer. However, the time between pesticide usage and cancer development was not known, qualifying the comparison.

**Keywords:** Esophageal cancer - gastric cancer - pesticide usage - Turkey

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### Introduction

Esophageal cancer is the sixth frequent cancer in the world and the fifth frequent reason in cancer related deaths (Jemal et al., 2011). Only 10-20% of the patients are suitable for surgery, which is the only curative treatment in esophageal cancer. Despite the adjuvant or neoadjuvant chemotherapy/chemoradiotherapy, 5-year-long survival is less than 25% (Bancewicz et al., 2002; Ychou et al., 2011).

Gastric cancer is one of the most frequent cancers worldwide and the second most frequent reason for cancer related deaths (Parkin et al., 2005). Its incidence can vary from country to country, even from region to region within a country (Torres et al., 2013). Gastric cancer is a progressive disease. Surgical resection is the only potential curative treatment, however despite the adjuvant or neoadjuvant chemotherapy/chemoradiotherapy administered on patients, the disease recurs in majority of the patients (Cunningham et al., 2006).

Gastric and esophageal cancer has some common risk factors such as smoking, increased body mass index, dietary habits such as low fruit and vegetable consumption,

dietary N-nitroso compounds and endogenous nitrosation (Keszei et al., 2013; Li et al., 2013; Pohl et al., 2013). Determination of primary prevention and risk factors is important for such diseases with bad prognosis and fast progression.

Pesticides are chemical substances used to minimize harmful effects of living organisms such as insects, rodents, weeds, fungi which live on or around humans, animals and plants, and decrease the nutritive value of nutritional sources during storing and consumption. Pesticides have subgroups such as insecticides, fungicides, acaricides, nematocides, rodenticides, herbicides. Insecticides are frequently used as one of pesticide subgroups. Insecticides can have chemical origins like organic phosphor or organochlorine carbamate, or biological origins such as pyrethrins and pyrethroides (Yildirim et al., 2013).

The role of pesticide usage in the etiology of gastrointestinal tract cancers such as esophageal and gastric cancer is researched mostly by population based case control studies. The results of these studies are conflicting. In some studies the relationship was determined and in some it was not. (Blair et al., 2009).

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Antalya is in the southwest of Turkey and is a region where intense agricultural lands are present. In this study, the relation between the esophageal and gastric cancer, and the amount of pesticide used in agricultural activity was examined.

## Materials and Methods

### Study population

In the study, 1998-2010 data from the data bank of T.R. Ministry of Health Provincial Health Directorate Cancer Records Center was used and patients who were diagnosed with gastric and esophageal histopathologically between these years were included. Patients, whose histopathological diagnosis was not validated, were not included in the study. Data was scanned in case of duplications and duplicated data was excluded from evaluation.

Annual pesticide usage data was obtained from Antalya Provincial Agriculture Directorate between 1998 and 2010. Annual population data was obtained from household survey registries of community clinics between 1998 and 2006, and population data between 2007 and 2010 was obtained from vital records data based on address records of Turkey Institution of Statistics. Rough incidence rate was calculated by dividing the number of new cases to total population.

### Statistical analysis

Statistical analysis was made by using SPSS 15.0 software. Population by year, the amount of pesticide used and appropriateness of other variants to normal dispersion were examined by using visual (histogram and possibility graphics) and analytic (Kolmogorov-Smirnov/Shapiro-Wilk tests) methods. For relationship between at least one abnormal or ordinal dispersion correlation coefficients and statistical significances were examined with Spearman test. For statistical significance, Type-1 error level was used as 5%.

## Results

There were total 1,896 patients in the study, 1233 of whom were male (65%) and 663 of whom were female. Mean age of patients was determined as 60.7 (range 5-95). 230 of the patients (12.1%) had esophageal cancer and 1666 of them had (87.9%) gastric cancer. 148 patients with esophageal patients were male (64.3%) and 82 of them were female (35.7%). 1085 of gastric cancer patients were male (65.1%) and 581 of them were female (34.9%). Regarding gender and age, there wasn't any difference determined in esophageal and gastric cancers ( $p$  0.817, 0.30).

Among the tumors of patients with esophageal cancer, 20 of them were (8.7%) cervical esophagus, 74 of them were (32.2%) thoracic esophagus, 12 of them were (5.2%) abdominal esophagus, and in 124 patients the location of tumor was not determined. Among cervical esophagus tumors 17 patients (85%) had squamous cell cancer, 39 patients (52.7%) among thoracic esophagus cancer and 7 patients (58.3%) among abdominal esophagus cancer

had squamous cell cancer. There wasn't any statistically significant relation determined between the amount of pesticide and esophageal cancer incidence ( $p$  0.87).

182 gastric cancer patients (10.9%) had cardia, 38 of them (2.3%) had fundus, 121 of them (7.3%) had corpus, 258 of them (15.5%) had antrum, 24 of them (1.4%) had pylorus, 112 of them (6.7%) had small curvature, 24 of them had (1.4%) had large curvature lying tumors. 1052 of gastric cancer patients (63%) had adenocarcinoma and this was followed by lymphomas with 101 patients (6%) based on frequency. The relationship between the amount of pesticide used and gastric cancer incidence was examined with Spearman correlation analysis and again, statistical significance was not obtained,  $p$  value was found as 0.88.

## Discussion

Pesticide usage and cancer development have been researched in many studies. Pesticides can show their carcinogenic effects with mechanisms such as genotoxicity, hormonal effects and immunotoxicity. Genotoxic effects of some pesticide types on hemopoietic cells were demonstrated. Even though there are studies which demonstrate the increase of esophageal and gastric cancer in agricultural workers who were exposed to pesticides, there are also studies which demonstrated that they are unrelated. In our study, there wasn't any relationship determined between esophageal and gastric cancer, and pesticides used in agriculture.

There are many risk factors such as age, male gender, ethnic origin, gastro esophageal reflux, low level of fruit and vegetable consumption, hiatal hernia determined in the development of esophageal adenocarcinoma (El-Serag, 2002). In the development of squamous esophageal cancer, factors such as alcohol usage, smoking, chronic irritation and human papilloma virus are accounted for (Holmes et al., 2007; Stoner et al., 2013).

Meyer et al. (2011) demonstrated that death risk related to esophageal cancer among workers who were exposed to high level of pesticide in the case-control study they conducted on Brazilian agricultural workers (Meyer et al., 2011). On the contrary, Jansson et al. (2006) did not determine any significant relation between exposure to pesticides and esophageal cancer development, similar to the result of our study (Jansson et al., 2006).

Even though the exact etiology of gastric cancer is not known, previously present situations such as unhealthy diet, *Helicobacter Pylori*, genetic factors, pernicious anemia, and atrophic gastritis are thought to be risk factors (Chen et al., 2013).

It has been demonstrated that exposure to methyl bromide, a pesticide, increases the risk of gastric cancer (Barry et al., 2012). Santibanez et al. (2012) examined the relation between histological types of gastric cancer and exposure to pesticides, and claimed that there was a relationship between exposures to pesticides and diffuse type gastric cancer (Santibanez et al., 2012).

Leeuwen et al. (1999) found that nitrate level was negatively correlated with gastric cancer incidence in their study in which they were examining the relationship

between drinking water contamination with atrazine and nitrate, which are pesticides, and gastric cancer; and they demonstrated that atrazine levels were positively correlated with gastric cancer incidence (Leeuwen et al., 1999).

Mills and Yang demonstrated that gastric cancer risk increased in agricultural workers who were exposed to pesticides in the study they conducted on Hispanic farm workers in California (Mills et al., 2007). Just like it was in our study, the fact that these studies were based on population-based cancer registry and other potential confounding variables were not evaluated, was one of the important limitations (Jowa et al., 2011).

Chrisman et al. (2009) examined the relation between pesticide sales and male cancer mortality in Brazil (Chrisman et al., 2009). In that study there was a significant relation determined between pesticides and esophageal cancer but no significant relationship was demonstrated between pesticides and gastric cancer.

Lee et al. (2004) could not demonstrate the relation between exposure to pesticides and development of esophageal and gastric cancers in the population based case-control study they conducted in Nebraska, USA (Lee et al., 2004). In that study, exposure to pesticides was determined via phone calls. In our study, the relation between pesticide amount used and esophageal cancer incidence was examined. In a study where the job-related exposure to pesticides was examined for Barrett's esophagus, the precursor of esophageal adenocarcinoma, there wasn't any relation determined between exposure to pesticides and Barrett's esophagus (Qureshi et al., 2013).

The relationship between the medicines used in our study and esophageal and gastric cancer incidence was examined, and no relationship between pesticide usage and esophageal and gastric cancer was demonstrated. Despite this, we believe that new studies that include pesticide level measurements should be performed because of the limitations of our study.

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