Epidemiological Disparities and Risk Factors of Esophageal Cancer in Türkiye: A Systematic Review

EPH214

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Conclusions

- **This comprehensive review marks the first extensive examination of esophageal cancer (EC) epidemiology specific to Türkiye, revealing significant regional disparities in incidence and risk profiles**
- **The analysis revealed that the incidence of EC in Türkiye falls within the range of 0-5 cases per 100,000 for the entire country**
- **There are significant regional differences in Türkiye with the eastern part of the country falling within the "Asian Belt" for EC, having the highest incidence and prevalence rates**
- **These insights are crucial for healthcare providers and policymakers and underscore the need for tailored preventive and treatment strategies in the eastern regions of the country, to respond to unique epidemiological patterns**

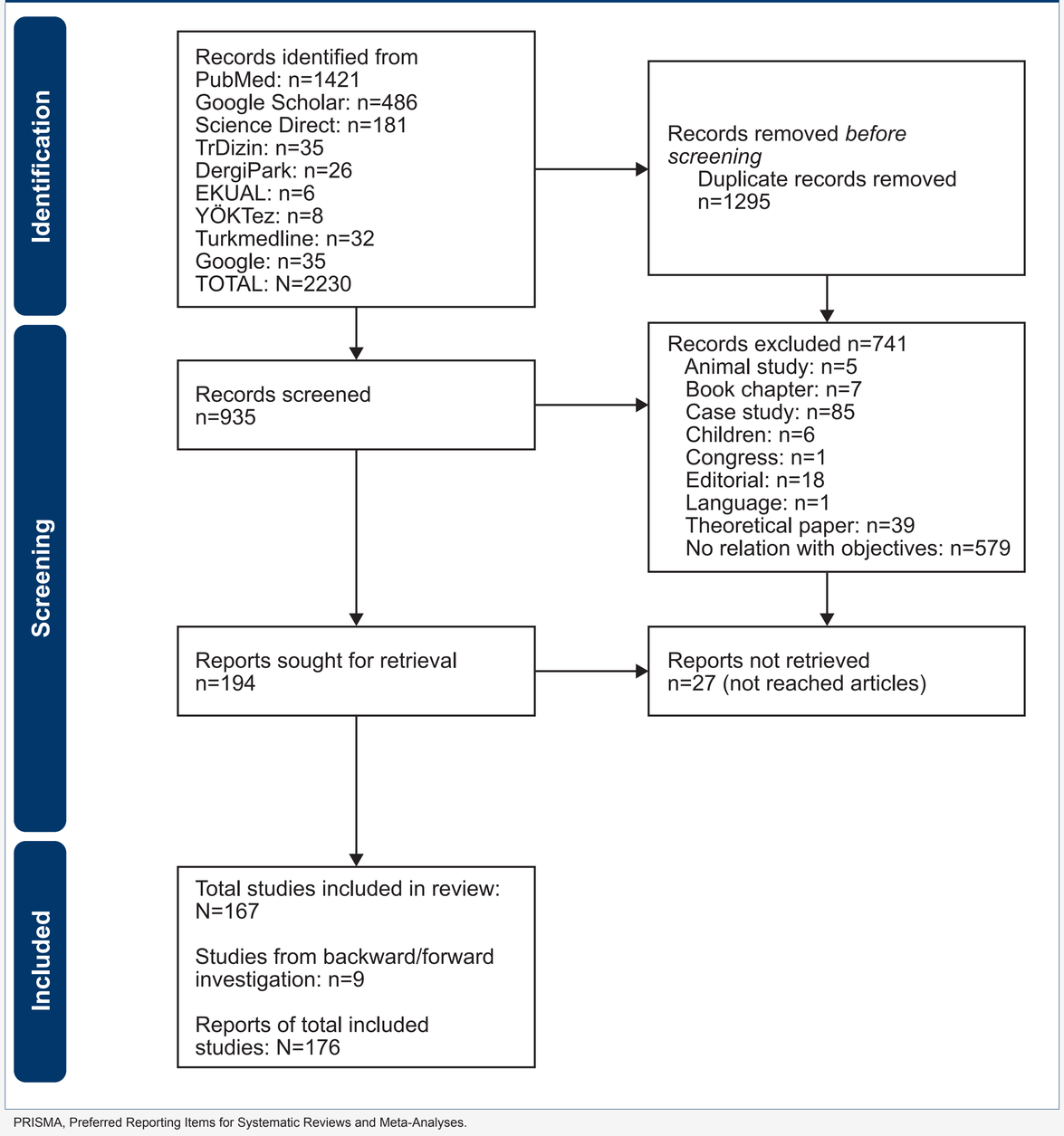
Background

- Esophageal cancer is one of the deadliest cancers worldwide.[1] According to the Global Cancer Observatory (GLOBOCAN) figures, globally, EC ranks eighth in new cancer cases each year, sixth in mortality, and eighteenth in 5-year prevalence[2]
- The age-standardized incidence of EC was 5.9 (5.7-6.1) per 100,000 population and age-standardized mortality was 5.5 (5.3-5.6) per 100,000.[3] Türkiye's eastern region is part of the "Asian Esophageal Cancer Belt," which extends from Eastern Türkiye, through Iran, Iraq, and the southern part of the former Soviet Union to Mongolia and western/northern China. This region, along with South America is considered a high-risk area for EC with an incidence of 100 cases per 100,000 inhabitants[4]
- The objective of this study is to elaborate on the epidemiology and treatment algorithms of EC in Türkiye. The following review questions were posed to address the study:
  - What are the incidence, prevalence, morbidity, and mortality rates for EC in Türkiye and how do they compare with international data?
  - What are the diagnosis and treatment patterns for EC and how do they align with international guidelines?

Methods

- We conducted a systematic literature review adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The review focused on studies published after the year 2000 involving the adult population and were available in both Turkish and English. Electronic databases and websites in both English and Turkish were searched between January 1 and January 23, 2024
- Accessing Turkish websites and materials allowed for the analysis of local data and enriched the study's coverage. Backward and forward research was also conducted to ensure no studies or publications were missed
- Searches were performed using PubMed/MEDLINE, ScienceDirect, Google Scholar, WHO.INT, and Turkish databases such as TrDizin, Ulakbim, DergiPark, EKUAL, TezlerYOK, and Turkmedline. Initially, 2230 publications were identified, from which 1295 duplicates were removed
- A total of 935 records were screened based on title and abstracts, with 741 being excluded due to irrelevance or non-compliance with eligibility criteria. Eventually, 176 studies were included after eliminating 27 inaccessible reports (**Figure 1**). Quality check of the selected studies was conducted using the STROBE tool for relevant content

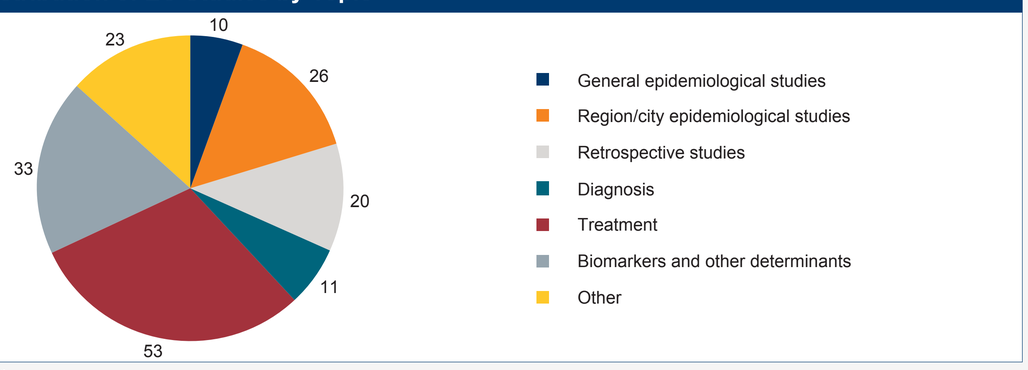
Figure 1. PRISMA Flow Diagram



PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

- The studies were classified by their focus. **Figure 2** presents the distribution of studies. As can be seen, the majority of the studies focused on treatment of EC followed by biomarkers and other determinants

Figure 2. Distribution of EC Studies by Topic



EC, esophageal cancer.

- **Figure 3** presents the distribution of studies by publication year

Figure 3. Distribution of EC Studies by Year

EC, esophageal cancer.

Results

Incidence and Prevalence

- Survival rates of EC in Türkiye align with those of Western countries, ranging from 20% to 30%[5]
  - An analysis of the CONCORD-3 study investigating the global trends in cancer survival reported that survival of EC in Türkiye ranged from 20% to 30%. Five-year age-standardized net survival was 14.8% for 2000-2004, 14.7% for 2005-2009, and 19.0% for 2010-2014.[5] Türkiye was grouped with countries such as the US, Belgium, Netherlands, Switzerland, Israel, and Australia
  - A cancer registry from Karachi, Pakistan, that compared results with the countries in the Asian Belt, including Türkiye, reported the age-standardized rate of incidence per 100,000 as 4.3 for males and 3.0 for females. The highest rate was found in China for males (18.6) and in Karachi for females (10.7)[6]
- The incidence of EC in Türkiye falls within the range of 0-5 cases per 100,000
- The mortality rate for EC in Türkiye is also within the range of 0-5 cases per 100,000
- Analysis of GLOBOCAN data projects an increase in both the incidence and mortality rates of EC in Türkiye by 2040
- Esophageal squamous cell carcinoma is more frequently seen than esophageal adenocarcinoma

Incidence Among Women

- Contrary to global trends, EC is most frequently seen among women in the eastern part of Türkiye, known as the Asian Belt
- The prevalence among women is attributed to preparing oven (tandır) baked bread with dried dung (tezek) along with other risk factors
- In the eastern part of the country, environmental factors, diet, drinking hot tea, consuming herbal cheese (otlu peynir), and tandır baked bread were considered potential risk factors for EC

Diagnostics

- Expression of cyclooxygenase-2 is correlated with metastasis and is a significant factor in determining prognosis in EC
- Interleukin 6 and tumor necrosis factor-α plasma levels, insulin-like growth factor (IGF)1, IGF-binding protein 3 levels, dickkopf-related protein 1 serum levels, serum mac-2-binding protein levels, calcium, C-reactive protein, uric acid levels, nitric oxide levels and arginine activity, *AURKA* and *NEK6* gene markers, mRNA expression of the IGF-binding protein 7 promoter in peripheral blood and plasma homocysteine levels could be used as predictors for diagnosis of EC
- C-reactive protein level, serum mac-2 binding protein level, microvessel density, mast cell density, serum levels of hepatocyte growth factor, and CK18 can be predictors of prognosis and survival
- Magnetic resonance imaging can be used as a diagnostic tool to differentiate between benign lymph nodes and malignant ones while positron emission tomography/computed tomography (PET/CT) is a valuable tool for staging, assessing response to treatment, and monitoring the disease
- CT perfusion visualizes stage 1 tumors more accurately than do contrast-enhanced CT and PET/CT (CT is preferred in the case of lung metastases)

Current Treatment Modalities

- Neoadjuvant therapy is recommended to increase the likelihood of surgical resection, reduce the stage, control the disease, and improve survival rates. Adjuvant chemotherapy can also improve survival rates. This is in line with ESMO guideline[7]
- Combining chemotherapy and radiotherapy can enhance resection chances and survival rates. This is also in line with ESMO guideline[7]
- Stents can be safely used for palliative treatment
- A procedure known as a vessel sealing system can be a safe alternative compared with conventional clamping methods in EC surgery
- The decision on surgical techniques should be based on specific patient characteristics

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Presenter Disclosures

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