Partnership between the GFFCC and WHO at the start of the 1st Palliative Training Course in the Gulf Region
The Gulf Journal of Oncology

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Mohamed Al-Jarallah ....... Kuwait
Mohamed Al-Shahri .......... Saudi Arabia
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Sami Al-Badawy .......... Egypt
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Tim Whelan ................... Canada
Yasser Bahader .......... Saudi Arabia
Yousri Gouda .............. Egypt
Zaidan Al Mazidi .......... Kuwait
# TABLE OF CONTENTS

## Original Articles / Studies

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosimetric consideration of transient volume enlargement induced by edema in prostate brachytherapy seed implants</td>
<td>6</td>
</tr>
<tr>
<td>I. Ali, O. Algan, S. Thompson, P. Sindhwani, S. Ahmad</td>
<td></td>
</tr>
<tr>
<td>Assessment of an existing and modified model for predicting non sentinel lymph node metastasis in breast cancer patients with positive sentinel node biopsy</td>
<td>15</td>
</tr>
<tr>
<td>M. Al-Masri, G. Darwazeh, M. El-Ghanem, B. Hamdan, M. Sughayer</td>
<td></td>
</tr>
<tr>
<td>Docetaxel in advanced or metastatic endometrial cancer: Clinical Outcome</td>
<td>23</td>
</tr>
<tr>
<td>R.H. Hamed, S.A. Elkalk, S. Roshdy</td>
<td></td>
</tr>
<tr>
<td>Dosimetric comparison between bone marrow sparing intensity-modulated radiation therapy and conventional techniques in the treatment of cervical cancer: a retrospective study</td>
<td>30</td>
</tr>
<tr>
<td>T. Sundaram, V. Nagarajan, M. Nagarajan, S. Jayakumar, K.N. Govindarajan, SS Supe, M. Balasubramaniyan, P. Joshi, T.P. Chellappan</td>
<td></td>
</tr>
<tr>
<td>Trends in oesophagus and Stomach cancer incidence in Bangalore, India</td>
<td>42</td>
</tr>
<tr>
<td>BR Gopala Krishnappa, CR Vijay, C Ramesh, PP Bapsy, MU Kumar, M Vijayakumar, SS Supe</td>
<td></td>
</tr>
<tr>
<td>Clinical significance of telomerase genes (hTERC and hTERT) amplification in patients with acute myeloid leukemia</td>
<td>51</td>
</tr>
<tr>
<td>M.M. Eid, N.A. Helmy, I.M. Omar, A.A. Mohamed, D. El Sewefy, I.M. Fadel, R.A. Helal</td>
<td></td>
</tr>
</tbody>
</table>

## Review Articles

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Management of metastatic breast cancer (MBC)</td>
<td>61</td>
</tr>
<tr>
<td>A. AL-Amri</td>
<td></td>
</tr>
<tr>
<td>Extensive review in the diagnosis of the malignant transformation of pleomorphic adenoma</td>
<td>67</td>
</tr>
<tr>
<td>Tarakji, K. Baroudi, S. Hanouneh, M.Y. Kharma, M.Z. Nassani</td>
<td></td>
</tr>
</tbody>
</table>

## Case Reports

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary adenoid cystic carcinoma of the breast: Case report and review of the literature</td>
<td>83</td>
</tr>
<tr>
<td>M.A. Naseer, S.S. Mohammed, R. Alyusuf, R. Al Marzoq, S.K. Das Majumdar, A. Al Hammadi</td>
<td></td>
</tr>
<tr>
<td>Approaches to management of Adenocarcinoma following Colocystoplasty</td>
<td>87</td>
</tr>
<tr>
<td>R. Ramamurthy, S.Susikar</td>
<td></td>
</tr>
<tr>
<td>Primary Non-Hodgkin Lymphoma of Frontal Sinus diagnosed by Fine needle aspiration cytology</td>
<td>92</td>
</tr>
<tr>
<td>J.K.S.S. Philip, A. Al- Jassar, I.S. Naqib, S. Usmani, M. El- Kabani, S.M. Refaat</td>
<td></td>
</tr>
</tbody>
</table>

## Conference Highlights /Scientific Contribution

- Conference Highlights – The Regional Training of the Trainers Palliative Care Workshop | 96   |
- News Notes                                                                           | 101  |
- Advertisements                                                                        | 103  |
- Scientific events in the GCC and the Arab World for the 1st Semester of 2013         | 104  |
Trends In Oesophagus And Stomach Cancer Incidence In Bangalore, India

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Abstract

Background

During recent decades, an increase in the incidence of certain oesophago-gastric cancer has been reported in some countries and in India. This study sought to analyze oesophageal and gastric cancer incidence trends in Bangalore by sex and morphology for the period 1982–2007.

Patients and methods

Oesophageal and gastric cancer cases were drawn from Bangalore population-based cancer registry located at Kidwai Memorial Institute of Oncology starting in 1982 under the national cancer Registry Programme funded by Indian Council of Medical Research. Time trends in sex- and age-standardized cancer incidence rates were analyzed by site and histology over the study period using relative change.

Results

Age-standardized oesophageal cancer incidence rates increased in males; in females it failed to register a significant trend over the study period. Overall, gastric cancer decreased from 9.81 and 5.48 rates per 100 000 person-years from 1982–86 to 9.45 and 5.25 from 2002–2007 among men and women, respectively. Whereas oesophageal adenocarcinomas increased sharply in both sex; among men, oesophageal squamous cell cancer rates increased steadily from the mid-1980s onwards and a small decline was observed towards 1997. The same trend was observed in females. Gastric cancer decreased over the study period. There was a marked decrease in the incidence of oesophago-gastric cancer presenting with unknown and unspecified morphology reported.

Key words

adenocarcinoma, oesophageal and stomach, incidence, age specific rate, age adjusted rate, population-based registry, trends.

Introduction

Oesophageal and gastric malignant tumors are still among the leading cancer types in Bangalore, India. In Bangalore population based cancer registry, stomach and oesophagus cancer ranked second and fourth respectively in terms of cancer incidence in men. In women oesophageus cancer occupies fifth and stomach cancer in sixth position. Owing to their high lethality, overall 5-year survival for oesophageal and gastric cancer is only 12.3% and 24.2% respectively. Over the last few decades, oesophageal cancer incidence and mortality rates have remained stable in most Western countries. In contrast, gastric cancer rates have been steadily declining for the last 50–60 years. Several reports have however, highlighted the fact that the general time trends for cancers arising from these two
organs are actually concealing divergent trends in terms of anatomical location and morphology. Upper and middle third oesophageal cancers, which more often tend to be squamous cell carcinomas, display a relatively stable or even decreasing trend in most countries (6,7) in line with the time trends observed for other tobacco related cancers. On the other hand, the incidence of adenocarcinomas of the lower third of the oesophagus and gastric cardia, which share epidemiological features and risk factors, has increased during recent decades in some areas of Europe (8) and in the USA (6). Lastly, non-cardia gastric cancer, more closely related to Helicobacter pylori infection has maintained a downward trend. (8) Consequently, some authors make the point that there may be at least three, if not four, different cancer entities arising from these organs. (9)

This study examined the most recent data on oesophageal and gastric cancer incidence drawn from population-based Bangalore cancer registry in order to investigate time trends in this registry by morphology. A well-known problem when studying oesophago-gastric cancer is the difficulty of identifying the primary organ in adenocarcinomas of oesophagus and the stomach. As proposed by some authors (10, 11), we also combined adenocarcinomas of the oesophagus and tumors of gastric cancer to better identify real trends in the incidence of these cancers.

Materials and methods

We studied all primary malignant tumors of the oesophagus and stomach (excluding lymphomas) diagnosed over the period 1982–2007 in population-based cancer registry and AAR compared with 25 registries which are located all over India by using published reports by the National Cancer Registry Programme. Registry covered 191.2 km2 of the total 6.8 million Bangalore populations and has collected data by active follow-up method. Oesophageal and gastric cancer cases were identified according to the International Classification of Diseases of Oncology version 3, codes C15 and C16. Estimates of the mid-year populations covered by these registries were obtained from the National Cancer Registry Programme, population estimated by using different distribution method (12).

Oesophago-gastric cancer cases were classified according to age group (5-year age groups to 75+ years), sex, and date of diagnosis and histology. For oesophageal cancers, we defined the following histology into categories: (i) adenocarcinoma (M814–857); (ii) squamous cell carcinoma (M805–808); (iii) Carcinoma (801-8045) (iv) other morphology, including morphology other than adenocarcinoma or squamous cell carcinoma (M809–813, M858–994) and unspecified morphology (M800–804). In the case of gastric cancer cases, the histological groupings were as follows: (i) gastric adenocarcinoma (M814–857); (ii) other morphology, including morphology other than AC (M805–813, M858–994), unspecified or without microscopic confirmation (M800–804).

Age-adjusted incidence rates were calculated using mid-period population figures for each registry, sex and cancer subgroup annually and using the direct method with the world standard population for each 5-year time period. Changes in age- and registry-adjusted incidence rates over the study period were evaluated separately by sex using log-linear Poisson models. (13) First, to describe the observed time trend without assuming any particular functional form; Second, to know the pattern of time trend using the moving average (14); Third, attempt to detect and estimate changes in incidence rates over the study period using the relative percentage change. (15)

Results

From 1982 to 2007, there was a total of 91,740 cases registered. Of this total, 5,974 cases of oesophageal cancer (males 3,223 and females 2,751) were registered and 5,929 cases of gastric cancer (males 3892 and females 2,037) were also registered. (Table 1) lists the number of cases and proportion of particular cancer expressed in percentage, crude rate and age adjusted rates of oesophageal and gastric cancer incidence rates and morphology for both sexes by 5-year period. (Figure 1) depicts the leading sites of cancer
Legends

Table 1.1: Age-adjusted incidence rates of oesophageal cancer by sex and 5-year period in Bangalore PBCR: 1982–2007 (world standard population taken as reference)

<table>
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<td>6652</td>
<td>7341</td>
<td>8575</td>
<td>14734</td>
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<td>7541</td>
<td>8410</td>
<td>9996</td>
<td>17995</td>
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<td>559</td>
<td>634</td>
<td>678</td>
<td>988</td>
<td>353</td>
<td>489</td>
<td>488</td>
<td>546</td>
<td>875</td>
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<tr>
<td>% of Oesophagus</td>
<td>7.4</td>
<td>8.4</td>
<td>8.6</td>
<td>7.9</td>
<td>6.7</td>
<td>6.3</td>
<td>6.5</td>
<td>5.8</td>
<td>5.5</td>
<td>4.9</td>
</tr>
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<td>CR</td>
<td>3.96</td>
<td>5.33</td>
<td>5.20</td>
<td>4.76</td>
<td>4.85</td>
<td>4.27</td>
<td>5.17</td>
<td>4.43</td>
<td>4.23</td>
<td>4.73</td>
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<td>AAR</td>
<td>6.79</td>
<td>9.23</td>
<td>8.60</td>
<td>7.53</td>
<td>7.58</td>
<td>7.67</td>
<td>8.97</td>
<td>7.31</td>
<td>6.54</td>
<td>6.96</td>
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</tbody>
</table>

Morphology

| Adeno carcinoma | 0.11 | 0.63 | 0.50 | 0.53 | 0.40 | 0.15 | 0.11 | 0.28 | 0.13 | 0.22 |
| Squamous cell carcinoma | 3.61 | 5.05 | 5.54 | 5.08 | 4.75 | 4.72 | 5.40 | 5.09 | 4.97 | 4.44 |
| Other Carcinoma's | 1.06 | 0.43 | 0.65 | 0.55 | 1.27 | 0.97 | 0.44 | 0.48 | 0.45 | 1.38 |
| Unknown          | 2.01 | 3.12 | 1.91 | 1.37 | 1.16 | 1.83 | 3.02 | 1.47 | 0.99 | 0.92 |

Table 1.2: Age-adjusted incidence rates of stomach cancer by sex and 5-year period in Bangalore PBCR: 1982–2007 (world standard population taken as reference)

<table>
<thead>
<tr>
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<tr>
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<td>532</td>
<td>605</td>
<td>679</td>
<td>793</td>
<td>1283</td>
<td>266</td>
<td>299</td>
<td>324</td>
<td>434</td>
<td>714</td>
</tr>
<tr>
<td>% of Stomach</td>
<td>10.9</td>
<td>9.1</td>
<td>9.2</td>
<td>9.2</td>
<td>8.7</td>
<td>4.8</td>
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<td>5.76</td>
<td>5.57</td>
<td>5.57</td>
<td>6.30</td>
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<td>3.16</td>
<td>2.94</td>
<td>3.36</td>
<td>3.86</td>
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<td>AAR</td>
<td>9.81</td>
<td>9.78</td>
<td>8.93</td>
<td>8.54</td>
<td>9.45</td>
<td>5.48</td>
<td>5.16</td>
<td>4.54</td>
<td>4.83</td>
<td>5.25</td>
</tr>
</tbody>
</table>

Morphology

| Adeno carcinoma | 4.35 | 4.86 | 5.65 | 5.52 | 5.80 | 2.16            | 2.51    | 2.71 | 2.87 | 3.01 |
| Other Carcinoma's | 2.11 | 0.70 | 0.53 | 0.86 | 1.85 | 1.37            | 0.41    | 0.41 | 0.61 | 1.17 |
| Unknown          | 3.34 | 4.24 | 2.75 | 2.08 | 1.80 | 1.83            | 2.24    | 1.42 | 1.35 | 1.07 |

expressed in relative percentage with respect to all sites. (Figure 2) shows the five years Age adjusted rates for site as well as morphology wise. Table 2.1 and 2.2 shows trend-analysis results, as evaluated by relative change model, with an estimation of the percentage change for the period 1982–1986 and 2002-2007 and also gives 95% confidence limit.

Overall, these data enabled two different periods to be discerned in the time trends of these tumors by histology. Hence, during the first decade of the study, there was a sharp decrease in
the proportion of unspecified tumors, paralleled by a marked increase in the rates of neoplasms with specified site or histology. During the 1990s, the proportion of unspecified cancers continued to decline. Relative percentage change and histological types would reflect improvements in data quality. Among men, age-standardized oesophageal cancer incidence rates registered a significant increasing trend over the study period while in females it showed no trend. In terms of morphology, squamous cell carcinoma rose sharply between the periods 1982 to 1992 with a significant increase in males and showed no trend in females while adenocarcinoma in both men and women showed increasing trend.

Among women, oesophageal rates were 7.67 per 100,000 person-years in 1982–1986 and 6.96 in 2002–2007. Although oesophageal cancer in

<table>
<thead>
<tr>
<th>Sites/Morphology</th>
<th>AAR (1982-1986)</th>
<th>AAR (2002-2007)</th>
<th>Relative Change in %</th>
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<th>CI Upper</th>
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<tbody>
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<td>7.58</td>
<td>11.7</td>
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<td>-42.4</td>
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<td>2.39</td>
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<td>9.45</td>
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<td>10.64</td>
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<td>1.80</td>
<td>-46.1</td>
<td>2.85</td>
<td>3.83</td>
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Table 2.1: Trend changes evaluated using change-point models for the period-Males (1982-2007)

<table>
<thead>
<tr>
<th></th>
<th></th>
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<td>Oesophagus</td>
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<td>6.96</td>
<td>-9.34</td>
<td>6.87</td>
<td>8.47</td>
</tr>
<tr>
<td>Adeno carcinoma</td>
<td>0.13</td>
<td>0.22</td>
<td>66.88</td>
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<td>Squamous cell carcinoma</td>
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<td>4.44</td>
<td>-10.81</td>
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<td>5.64</td>
</tr>
<tr>
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<td>0.32</td>
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<td>-41.34</td>
<td>1.56</td>
<td>2.09</td>
</tr>
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</table>

Table 2.2: Trend changes evaluated using change-point models for the period-Females (1982-2007)
female is extremely infrequent, and site and morphology incidence rates were more unstable, it showed similar trends to those of men in general (Figure 1). Squamous cell carcinoma incidence in females however decreased by 10% over the entire study period although there was a statistically significant change in adenocarcinoma by increasing to 67% during the study period. The male: female ratio was slightly higher for adenocarcinoma than for Squamous cell carcinoma (7:3 and 5:5, respectively in the last 6-year period). Overall, gastric cancer decreased from 9.81 cases per 100,000 person-years in 1982–86 to 9.45 in 2002–2007 among men.

Among women, gastric cancer rates fell by 4.1% between the two periods. Morphology trends were found non-significant except adenocarcinoma in case of male. All other morphologies showed constant in trend while male: female ratio was more than two times higher for adenocarcinoma (7:3). Cancer incidence rates for the oesophago-gastric region rose in men, particularly during the early 1980s, reflecting the above-mentioned problems of data quality.

Figure 1: Ten Leading Sites of Cancer based on relative percentage- Bangalore (2002-07)

Figure 2: Trends in age-standardized incidence rates (World Standard Population) of oesophageal Cancer by histology: 1982–2007.

Figure 3: Trends in age-standardized incidence rates (World Standard Population) of Stomach Cancer by histology and site: 1982–2007.

Discussion

This paper reports the most recent data on Oesophageal and stomach cancer incidence by site and histology in Bangalore registry. Overall, our results show that while the incidence of oesophageal cancer remained stable among Bangalore men and women across the study period, gastric cancer incidence decreased in both sexes, with a stronger decline among women. Until the early 1990s, most cases were registered
in ill-defined categories; reclassification of classes due to improvements in data quality caused facts in time trends which render the trend during the early 1980s difficult to interpret from an epidemiological and etiological standpoint. In brief, whereas squamous cell carcinoma has been declining since the mid-1980s among men and in 1993 started falling among women too, oesophageal adenocarcinoma rates increased markedly in both sexes. Possible limitations of this analysis relate to the data quality of the cancer registry. Although most of these provide regular data to the Cancer Incidence in Five Continents database and undergo validity checks, data quality is nonetheless affected by the analytical and diagnostic methods used by pathologists and clinicians. During recent decades, the number of endoscopies has gradually increased and the quality of diagnostics has improved accordingly, leading in turn to a dramatic decrease in unspecified site and morphology in both oesophageal and gastric cancers.

Simultaneously, different studies have highlighted the difficulty of distinguishing the organ of origin in adenocarcinomas situated at the oesophagus and gastric cancer, the transition zone between the squamous epithelium of the distal oesophagus and the glandular epithelium of the cardias. Consequently, misclassification might not be trivial and caution is called for when it comes to interpreting incidence trends by histology and anatomical subsite, as classification proposals for these lesions are still very recent. Overall, our results are in agreement with previous findings in other Western countries. In Bangalore, oesophageal squamous cell carcinoma have been increasing since the mid-1980s and starts to decline in 1996 onwards among men but this decrease is non-significant in line with reported changes for other smoking-related cancers in this country, and have remained stable since 1994 among women. In other European countries, as well as in the USA and Canada, a similar declining trend was observed among males in recent decades, while a significant rise was noted among women in Scotland, Switzerland, Canada and Australia. This histological type accounts for the majority of oesophageal cancers (68% in men and 63% in women in the most recent quinquennium), with a 10-fold difference in age standardized incidence rates between males and females probably reflecting differences in the main risk factors, i.e. smoking, alcohol consumption and a low intake of fruit and vegetables. In other countries, this decrease in the incidence of squamous cell cancer accompanied by the increase in oesophageal adenocarcinomas has led to a change in the predominant morphology. While similar rates are now being seen for both histological cancer types in Australia, adenocarcinoma has already become the most frequent histological type of oesophageal cancer in Denmark, Scotland and the USA. Insofar as cancers of the oesophago-gastric region are concerned, a moderate increase has been observed in men since the early 1980s, whereas in women these tumors have declined by 2% since the mid-1990s. This joint category summarizes two diverging trends: oesophageal adenocarcinomas, which account for 20% of all cancers of this organ (using Spanish data), steadily increased at a rate of 6% per annum in both sexes since the mid-1980s; gastric cardia adenocarcinomas on the other hand have remained stable among Spanish males since the early 1980s and decreased at a rate of 5% among women since the early 1990s. Similar results have been reported in recent decades from Finland, England and Wales, Switzerland and Australia, where a continuing rise in the incidence of oesophageal adenocarcinoma was observed and no increase in gastric cardia carcinomas have been observed. In the USA and in some parts of Europe however, an increase in incidence of both adenocarcinoma of the oesophagus and gastric cardia has been recorded. Whether or not the positive trend reported for oesophageal adenocarcinomas reflects a real increase in disease burden is a matter for debate. Various factors may be determining the observed trends in the incidence of oesophageal adenocarcinomas, such as the opposite trend in oesophageal cancers with unspecified morphology, and the reclassification of gastric cancers. Most European countries did not start using a code for cardia cancer until the late 1970s, and until 1999 there was no consensus as
to the definition of gastric cardia.\(^{(23)}\) Currently, adenocarcinomas that straddle the junction are supposed to include many tumors that were formerly designated cancers of the gastric cardia\(^{(24)}\) and, indeed, combining these tumors seeks to avoid the problems posed by reclassification changes over time.\(^{(20, 25)}\) In some countries, where both oesophageal adenocarcinomas and gastric cardia cancers are rising, it has been argued that even if these trends were to be partially explained by improvements in the accuracy of histological diagnosis, we would nevertheless be facing a genuine upward trend in disease burden.\(^{(26–28)}\)

Other authors, however, state that, before concluding that adenocarcinomas of the oesophagus and gastric cardia are on the rise, it is crucial to address whether the observed increase can be explained by a shift in classification.\(^{(20, 23)}\)

The main risk factors for the subgroup of cancers displaying the greatest increases, namely those of the oesophagus and stomach cancers, includes smoking, Oesophageal and stomach reflux, obesity and the presence of Barrett’s oesophagus. Despite the fact that the etiology of these groups of cancers is insufficiently understood and the question of whether these cancers represent just one or two distinct entities continues to be an open issue of discussion,\(^{(29, 30)}\) some authors suggest that adenocarcinomas of the distal oesophagus and gastric cardia might represent biologically different malignancies and have different risk factors.\(^{(31)}\) Whereas the main accepted risk factors for adenocarcinomas of the oesophagus are smoking, Oesophageal and stomach reflux, obesity and the presence of Barrett’s oesophagus, gastric cardia adenocarcinomas are associated with smoking and obesity. In this respect, the divergent trends in oesophago-gastric region cancers might, in part at least, be attributed to changes in the prevalence of etiological risk factors. If tobacco use is indeed decreasing among men, and obesity is a risk factor for both oesophageal adenocarcinomas and gastric cardia cancers, Oesophageal and stomach reflux and Barrett’s oesophagus should account for most of the excess risk of oesophageal adenocarcinomas. Over-diagnosis due to increased diagnostic intensity, particularly among patients with Oesophageal

and stomach has also been suggested as a contributory factor to the upward trend in oesophageal adenocarcinomas reported in some countries. Some authors make the point however that it would seem somewhat implausible that an increase in the prevalence of these two disorders could account for the sharp increase in this cancer type.

The stomach (8.7 % according to our data), has declined by 2% per annum since the mid-1982s. Similar trends by subsite (cardia/non-cardia) were described in Sweden where the decline in gastric adenocarcinoma has been attributed to a decrease in tumors located distal to the cardia region\(^{(13)}\) with cardia cancer rates remaining stable. Although cardia and non-cardia adenocarcinomas seem to be two different entities with different epidemiological characteristics, these two groups nevertheless share epidemiological features, such as trends over time and sex distribution. Helicobacter pylori infection and diet are the main accepted risk factors for non-cardia gastric cancers, though not enough is currently known about the cofactors needed to transform gastric mucosa infected with this very prevalent microorganism into a malignant tumor in a small percentage of people. In spite of the uncertainties that continue to surround the study of oesophago-gastric cancers, some authors have indicated that a short list of risk factors would probably account for the majority of oesophageal and gastric cancers, so that reducing the prevalence of smoking, Oesophageal and stomach reflux and overweight, and simultaneously increasing the intake of fruit and vegetables would help to reduce the incidence of these cancers.\(^{(32)}\) It is more than likely however that difficulties in classification are still hampering correct assessment of epidemiological risk factors in this group of cancers since many of the studies published in previous decades might have been affected by this very problem.

**Conclusion**

The overall incidence of oesophageal cancer increased in males and decreased in females over the 26-year study period, among men and women alike, yet gastric cancer continued to decline.
While examination of oesophago-gastric cancer trends by morphology shows that oesophageal squamous cell carcinoma rates remained stable or decreased slightly among men, the reported increase plotted by oesophageal adenocarcinomas in other Western countries has likewise been confirmed in Bangalore. Similarly, during the same period, gastric cardia cancer registered a more moderate increase among men. Non-cardia cancer rates, on the other hand, have also been declining since the mid-1980s. In our opinion, however, the changes in classification had such a strong influence on the trends described for the different types of oesophago-gastric tumor that at this point in time, it is almost impossible to elucidate which changes are attributable to differences in the distribution of causal factors. This is no doubt something that will be easier to study in the future when more accurate subsite and morphological recording is in place.

References


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