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TIME TO PRESENTATION AND DIAGNOSIS OF ESOPHAGEAL CANCER IN PATIENTS SEEN AT THE KENYATTA NATIONAL HOSPITAL
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# TIME TO PRESENTATION AND DIAGNOSIS OF ESOPHAGEAL CANCER IN PATIENTS SEEN AT THE KENYATTA NATIONAL HOSPITAL

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## ABSTRACT

*Background:* **Esophageal Cancer (EC) is one of the leading causes of cancer death in Kenya. Majority of the patients with esophageal cancer at Kenyatta National Hospital (KNH) present at an advanced stage limiting their treatment options.**

*Objective:* **To determine diagnostic time lines and factors associated with delayed health care service delivery among patients with established histological diagnosis of EC at KNH.**

*Design and Setting:* **A retrospective diagnostic cohort study was carried out at the Cardiothoracic, endoscopy and radiotherapy units at KNH.**

*Results:* **Eighty-five participants with established histological diagnosis of EC consented and were enrolled into the study. Majority (89.4%) were diagnosed in stage III and IV of the disease. The median time to histological diagnosis of EC was 90 days. The time to first presentation was more than 30 days among 78.8% of subjects. The median time from first consultation to referral to a diagnostic-capable facility was 30 days, with 76.5% of the participants taking more than 30 days to reach KNH. Those who could not afford transport and consultation were more likely to report delay to first presentation (OR 3.6 95% CI 1.2-11.3, p=0.022). Referral delay was associated with residence, with those living in the rural areas less likely to delay (OR 0.2, 95% CI 0.0-0.8, p=0.019).**

*Conclusion:* **Overall this study found that there was significant delay in the diagnostic process of EC patients. Over 75% of the patients delayed in presenting for the first consultation, being referred to higher level facilities, getting an endoscopy done and receiving histological diagnosis. Consequently, about 90% of the patients were diagnosed at an advanced stage of the disease.**

## INTRODUCTION

Esophageal cancer (EC) is the eighth most common cancer and the sixth leading cause of cancer death in the world[1]. In Kenya, EC is the second commonest cancer in males and third in females, after breast and cervical cancers[2]. The most common histological type of EC in Kenya is squamous cell carcinoma which accounts for over 90% of cases[3].

Esophageal cancer carries a high mortality with a five-year survival of less than 10%[4]. About 80% of diagnoses are made in patients presenting with dysphagia and weight loss, clinical findings frequently

observed in patients in at least stage II disease[5]. In developing countries, more than 90% of diagnosis of esophageal cancers are stage II to IV.[4] Only 15% to 30% of patients elected for curative surgery[4]. Diagnosis of early stage lesions is still the best way to improve the chances of cure and survival.

This study aimed to define the timelines for the delay in the diagnosis of cancer of the esophagus at the Kenyatta National Hospital (KNH).

## METHODS

This was a retrospective diagnostic cohort study carried out at the Cardiothoracic, endoscopy and radiotherapy units at KNH between September and November 2016. Patients recruited were aged more than 13 years, with complete case files, confirmed histological diagnosis of Ca-O and receiving treatment in KNH. The exclusion criteria included patients who were acutely ill, who could not give history and with conditions affecting their memory.

The overall delay in the diagnosis and treatment was measured from the date the patient first experienced the symptoms up-to the definitive histological diagnosis of EC. The delay in diagnosis was defined using three time periods:

*Patient delay* - time from the appearance of symptoms to first contacting the healthcare system. The symptoms included any or combination of: difficulty in swallowing, retrosternal pain and pain on swallowing.

*Endoscopy delay* - time from first contacting the healthcare system to endoscopic (OGD) diagnosis. The delay was stipulated as median time in weeks.

*Histology delay* - time from when the endoscopy was done up to receipt of the histological diagnosis

Cancer staging was done using the TNM staging system.[4] Ethical approval was obtained from the KNH/UoN ethics and research committee. Two trained research assistants with clinical background were used during the study.

## RESULTS

A total of 95 participants with established histological diagnosis of esophagus cancer were screened consecutively at the Cardiothoracic, Endoscopy and Radiotherapy units of Kenyatta National Hospital. The total number of patients on follow-up for EC during this period was 150, with an estimated 50% having advanced disease. Among eligible participants, six declined to participate in the study as they were taking part in other studies, and four were too sick for the interview with 85 patients being enrolled in the study.

The mean age of subjects was 59.2 years (SD 14.5 years) at time of the study and 58.7 years (SD 14.6 years) at cancer diagnosis. Majority (64.7%) of participants were males, 80% were married and 62.4% were from urban areas. Approximately 25% of participants were illiterate, 40% had completed primary education and 31.8% had attained secondary level of education. While 47.1 % of the participants were unemployed, 51.8% had a regular source of income. Over 80% of the participants had cancer stage 3 (41.2%) and 4 (48.2%).

The time to the first presentation was more than 30 days among 78.8% of participants. The median time from the first consultation to referral to a diagnostic-capable facility was 30 days, with 76.5% of the participants taking more than 30 days to reach the referral facility. After presentation and evaluation in referral facility, subjects took a median time of 7 days to undergo Endoscopy, with 64.7% taking 14 or more days. Similarly, the pathway from OGD to histological diagnosis took a median of 7 days with 84.7% of the patients taking 14 or more days (table 1)

Overall, the median time from initial symptoms to histological diagnosis was 90 days, with 61.2% of patients experiencing total diagnostic delay of 90 or more days.

**Table 1**

*Timelines in the delay in the diagnosis of cancer of the esophagus*

| Variable | Frequency (%) | 95% CI |
|---|---|---|
| **Time from referral facility evaluation to OGD** | | |
| Median days (IQR) Range | 7 (7-30) | |
| Category, n (%) | 7-90 | |
| ≥14 days | 55 (64.7) | 55.3-74.1 |
| <14 days | 30 (35.3) | 25.9-44.7 |
| **Time from OGD to histological diagnosis** | | |
| Median days (IQR) Range | 7 (7-14) | |
| Category, n (%) | 7-30 | |
| ≥14 days | 72 (84.7) | 77.6-91.8 |
| <14 days | 13 (15.3) | 8.2 – 22.4 |
| **Time from initial symptoms to histological diagnosis** | | |
| Media days (IQR) Range | 90 (30-120) | |
| **Category, n (%)** | 7-120 | |
| Total delay (≥90 days) | 52 (61.2) | 50.6-71.8 |
| No delay (<90 days) | 33 (33.8) | 28.2-49.4 |

*Data are frequencies (percentages)*

Patients who could not afford transport and consultation were more likely to have delayed first presentation (88.6%) than those who could (68.3%), OR 3.6 (95% CI 1.2-11.3), p=0.022. None of the other factors were associated with patient delay (table 2).

The study found that those who lived in the rural village were less likely to experience doctor delay (65.6%) compared to those who lived in urban areas (92%), OR 0.2 (95% CI 0.0-0.8), p=0.019.

**Table 2**

*Factors associated with patient delay in the diagnosis of cancer of the esophagus*

| Variable | Patient delay | | OR (95% CI) | P value |
|---|---|---|---|---|
| | Delayed | Not Delayed | | |
| **Sex:** | | | | |
| Male | 43 (78.2) | 12 (21.8) | 0.9 (0.3-2.7) | 0.845 |
| Female | 24 (80.0) | 6 (20.0) | 1.0 | |
| **Age at diagnosis, mean (SD)** | 59.1 (13.9) | 57.3 (17.5) | - | 0.649 |
| **Level of education:** | | | | |
| None | 17 (81.0) | 4 (19.0) | 1.5 (0.4-6.0) | 0.528 |
| Primary | 28 (82.4) | 6 (17.6) | 1.7 (0.5-5.6) | 0.384 |
| Secondary/Tertiary | 22 (70.4) | 8 (29.6) | 1.0 | |
| **Occupation** | | | | |
| Unemployed | 34 (85.0) | 6 (15.0) | 2.0 (0.6-7.1) | 0.281 |
| Employed | 16 (72.9) | 6 (27.3) | 0.9 (0.3-3.5) | 0.928 |
| Business person | 17 (73.9) | 6 (26.1) | 1.0 | |
| **Marital status** | | | | |
| Single | 3 (60.0) | 2 (40.0) | 1.0 | |
| Married | 53 (77.9) | 15 (22.1) | 2.4 (0.4-15.4) | 0.360 |
| Divorced/Widowed | 11 (91.7) | 1 (8.3) | 7.3 (0.5-111.2) | 0.191 |
| **Residence** | | | | |
| Urban | 22 (88.0) | 3 (12.0) | 1.0 | |
| Urban suburbs | 20 (71.4) | 8 (28.6) | 0.3 (0.1-1.5) | 0.138 |
| Village | 25 (78.1) | 7 (21.9) | 0.5 (0.1-2.1) | 0.331 |

| | | | | |
|---|---|---|---|---|
| **Income** | | | | |
| Yes | 32 (72.7) | 12 (27.3) | 0.5 (0.2-1.4) | 0.154 |
| No | 35 (85.4) | 6 (14.6) | 1.0 | |
| **Distance to health facility, median (IQR)** | 45 (25-70) | 60 (20-80) | - | 0.382 |
| **Income adequate for medical cost** | | | | |
| | 22 (73.3) | 8 (26.7) | 0.6 (0.2 – 1.8) | 0.360 |
| Yes | 45 (81.8) | 10 (18.2) | 1.0 | |
| **Have health insurance** | | | | |
| Yes | 61 (78.2) | 17 (21.8) | 0.6 (0.1 – 5.3) | 1.000 |
| No | 6 (85.7) | 1 (14.3) | 1.0 | |

*Data are frequencies (percentages):*

Almost 9 in every 10 patients (89.7 %) reported Endoscopy delay. Delayed Histology results were cited to be due to inadequate tissue samples (50%) or wrong labeling of samples (12.5%). Indicators of lower socio-economic status (lack of employment, enough money for medical consultation and health insurance) were not associated with overall diagnostic delay (table 3).

**Table 3**
Factors associated with overall diagnostic delay

| **Variable** | **Diagnostic time** | | **OR (95% CI)** | **P value** |
|---|---|---|---|---|
| | **Delayed** | **Early** | | |
| **Sex:** | | | | |
| Male | 36 (65.5) | 19 (34.5) | 1.7 (0.7-4.1) | 0.273 |
| Female | 16 (53.3) | 14 (46.7) | 1.0 | |
| **Age at diagnosis, mean (SD)** | 59.1 (13.6) | 58.2 (16.3) | - | 0.804 |
| **Level of education:** | | | | |
| No education | 16 (76.2) | 5 (23.8) | 2.4 (0.7-8.4) | 0.151 |
| Primary | 19 (55.9) | 15 (44.1) | 1.0 (0.4-2.6) | 0.950 |
| Secondary/Tertiary | 17(56.6) | 13 (43.3) | 1.0 | |
| **Occupation** | | | | |
| Unemployed | 15 (68.2) | 7 (31.8) | 1.4 (0.4-4.7) | 0.609 |
| Employed | 14 (60.9) | 9 (39.1) | 1.0 | |
| Business person | 23 (57.5) | 17 (42.5) | 0.9 (0.3-2.5) | 0.794 |
| **Marital status** | | | | |
| Married | 42 (61.8) | 26 (38.2) | 1.0 | |
| Single/Divorced/Widowed | 10 (58.8) | 7 (41.2) | 0.9 (0.3-2.6) | 0.824 |
| **Residence** | | | | |
| Urban | 14 (56.0) | 11 (44.0) | 1.0 | |
| Urban suburbs | 16 (57.1) | 12 (42.9) | 1.0 (0.4-3.1) | 0.933 |
| Village | 22 (68.8) | 10 (31.3) | 1.7 (0.6-5.1) | 0.322 |
| **Regular income** | | | | |
| Yes | 28 (63.6) | 16 (36.4) | 1.2 (0.5-3.0) | 0.630 |
| No | 24 (58.5) | 17 (41.5) | 1.0 | |
| **Distance to HCF, median (IQR)** | 45 (27.5-70) | 50 (22.5-80) | - | 0.939 |
| Income adequate for medical cost | | | | |
| Yes | 19 (63.3) | 11 (36.7) | 1.2 (0.5 – 2.9) | 0.763 |
| No | 33 (60.0) | 22 (40.0) | 1.0 | |
| **Affordability of transport and consultation costs** | | | | |
| Yes | 24 (54.5) | 20 (45.5) | 1.0 | 0.194 |
| No | 28 (68.3) | 31 (31.7) | 1.8 (0.7-4.4) | |

| | | | | |
|---|---|---|---|---|
| **Health Insurance** | | | | |
| Yes | 2 (28.6) | 5 (71.4) | 1.0 | 0.103 |
| No | 50 (64.1) | 28 (35.9) | 4.5 (0.8-25) | |

*Data are frequencies (percentages)*

## DISCUSSION

Despite recent advances in treatment modalities, esophageal cancer has a uniformly dismal prognosis the world over, with no more than 14% of patients surviving longer than five years from diagnosis[4, 6].A key underlying reason for this low-survival rate is that most patients are diagnosed at an advanced stage. Earlier detection therefore remains a key strategy to improving survival.

This study found that late presentation of EC was common at the Kenyatta National Hospital, with almost 90 percent of patients being diagnosed in stages 3 and 4. The median overall delay of 90 days, found in this study, is similar to Jones et al[7] in Britain but was longer than that found in studies by Wong et al[8] in China and Witzig et al [9] in Germany, both of which reported a median overall delay of 2.2 months. In the surgical department of a large teaching hospital in Britain, Martin et al[10] reported a median delay of more than 4 months from the first symptoms to histological diagnosis. Unique features of health care systems might explain some differences in diagnostic time-lines across these studies. In China, though medical insurance covers only a quarter of the whole population, most people self-refer themselves to large hospitals when they think their disease is severe. This ultimately leads to shorter delays in the diagnosis of esophageal cancer. In Britain, there is full-population medical insurance and developed community health-care system, and all the patients treated by specialists must be referred by General Practitioners in community clinics. Consequently Britons have shorter delay from the first symptoms to first contacting the health-care system for medical services, but might wait longer for referral to specialists for Endoscopy.

The symptom-to-treatment delay is a highly complex variable. Beyond tumor biology, symptom-to-treatment delay reflects the health seeking behavior of the patient, the diagnostic acumen of the physician, the functioning of the health-care system, and sociocultural norms, amongst other factors. This study found that the patients who delayed before presenting for their first medical consultation were those who could not afford transport and consultation charges. As a proxy measure of socio-economic status, these findings are in agreement with previous studies in EC.[8, 11-13]

Referral delay which means taking more than 30 days from first consultation to referral for Endoscopy was high at 76.5%. More than three-quarters of subjects initially sought care at Health centers and Sub-district hospitals where they underwent basic investigations and symptomatic treatment before referral to centers capable of making an EC diagnosis. Some of the reasons underlying delayed referral were alternative diagnoses and need for further evaluation at the same center. Residence in rural settings was identified as a cause for delayed referral. In other studies, misdiagnosis of cancer of the esophagus has been highlighted as one of the main reason for referral delay[14].

In this study, 64.7% of patients had Endoscopy delay whereas 84.7 had delay in histological diagnosis. These delays at the referral centre are considerably longer than what has been reported in other developing countries. Studies in Sri Lanka[15] and China[8] found shorter delays (<20%) in Endoscopy and Histology. These findings show regional differences in relation to efficiencies in the health care facilities. The health care system delay in our study could be attributed to shortage of Endoscopy and Histology facilities resulting in long booking time and delayed Histology results[3].

A 2015 systematic review[16] investigating

whether delays in time to diagnosis and treatment in symptomatic cancer were associated with poorer outcomes identified one study[10] that showed a survival benefit and two studies[17, 18] that reported no association. In the study by Martin et al[10], the median delay was seven weeks for those with stage I and II cancer compared with 21 weeks for those with more advanced cancer, implying that reducing diagnostic delays might improve clinical outcomes.

Interventions to reduce patient delay include promoting health literacy[19], and expanding access to primary care[20] in high incidence areas[3]. Referral delay can be reduced through educating the health care workers on the symptoms EC and the key diagnostic role of Endoscopy. Health care workers should be encouraged to refer the patients to Endoscopy capable centers at first contact[10]. Endoscopy and Histology delays can be reduced by increasing the centers with Endoscopy and pathology services, training of heath care personnel and provision of mobile Endoscopy services in high incidence areas[3].

## RECOMMENDATIONS

More studies on interventions targeting diagnostic delay in this population are urgently needed and their impact on outcomes such as morbidity, health related quality of life and mortality.

## LIMITATIONS

A key limitation of this study is the possibility of recall bias, as the authors were not able to verify all responses through clinical records.

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