Review Article

IDENTIFICATION OF THE CRUCIAL PIECES OF ESOPHAGEAL CANCER PREVENTION AND EARLY DETECTION PROGRAM IN MOZAMBIQUE

IDENTIFICAÇÃO DOS ASPETOS CRUCIAIS DO PROGRAMA DE PREVENÇÃO E DETEÇÃO PRECOCE DO CANCRO DO ESÓFAGO EM MOÇAMBIQUE

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ABSTRACT

Esophageal squamous cell carcinoma (ESCC) poses a significant health burden in Mozambique, with high incidence rates and late-stage diagnoses contributing to its lethality. This comprehensive review examines the epidemiology, risk factors, and potential preventive strategies for ESCC in Mozambique. Key risk factors identified include tobacco smoking, alcohol consumption, dietary factors, hot beverage consumption, infections (such as HPV and HIV), environmental chemical exposures, and dental fluorosis. Geographic variations in EC incidence highlight the need for region-specific intervention. Poverty, gender, and age disparities further complicate prevention efforts. Implementing evidence-based interventions, such as tobacco control measures, dietary diversification, and early detection programs, is essential for reducing EC morbidity and mortality in Mozambique. The Mozambican National Cancer Control Plan (NCCP) provides a framework for integrated prevention and early detection initiatives. Collaborative efforts involving policymakers, healthcare providers, and communities are crucial for addressing the multifaceted challenges EC poses in Mozambique and improving cancer outcomes.

Keywords: *esophageal cancer; risk factors; prevention; early detection; Mozambique.*

RESUMO

O carcinoma espinocelular do esófago (ESCC) representa um significativo problema de saúde em Moçambique, com elevadas taxas de incidência e diagnósticos em estádios avançados que contribuem para a sua letalidade. Esta revisão abrangente examina a epidemiologia, fatores de risco e estratégias preventivas potenciais para o EC em Moçambique. Os principais fatores de risco identificados incluem o consumo de tabaco, consumo de álcool, fatores dietéticos, consumo

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de bebidas quentes, infeções (como HPV e HIV), exposições químicas ambientais e fluorose dentária. As variações geográficas na incidência de EC destacam a necessidade de intervenções específicas para cada região. A pobreza, disparidades de género e idade complicam ainda mais os esforços de prevenção. Implementar intervenções baseadas em evidências, como medidas de controlo do tabagismo, diversificação dietética e programas de deteção precoce, é essencial para reduzir a morbilidade e mortalidade do EC em Moçambique. O Plano Nacional de Controle do Cancro (NCCP) de Moçambique fornece a estrutura para iniciativas integradas de prevenção e deteção precoce. Esforços colaborativos envolvendo legisladores, prestadores de cuidados de saúde e comunidades são cruciais para enfrentar os desafios multifacetados colocados pelo EC em Moçambique e melhorar os resultados do tratamento do cancro.

Palavras-chave: *cancro do esófago; fatores de risco; prevenção; deteção precoce; Moçambique.*

1. INTRODUCTION

Esophageal squamous cell carcinoma (ESCC) is one of the most common and deadly cancers in most Eastern and Southern African countries including Mozambique[1]. There are early reports of esophageal cancer (EC) in Southern Africa, back from 1971 in South African gold mines[2]. In Western countries and China, the incidence of EC has fallen slightly[3,4]. It has been well-established that tobacco, smoking and alcohol drinking[5] are the main risk factors for ESCC5. Dietary carcinogens and insufficiencies of micronutrients were also found to be important risk factors[6]. Consumption of beverages and food at high temperatures, which causes thermal damage to the esophageal epithelium, has been documented to increase the risk of EC[7]. The incidence of EC has decreased in Europe, following a concomitant decrease in tobacco and alcohol consumption[3,8]. EC early detection (or their precancerous lesions) is highly desirable since surgical and endoscopic resection offers the only possible cure for esophageal cancer[9]. Therefore, eradicating or reducing exposure to putative risk factors for EC and early detection of precancerous lesions are the most logical approaches to prevention[5]. Prevention also offers the most cost-effective long-term strategy for cancer control. An issue that is of extreme importance in low-income countries.

The African Esophageal Cancer Consortium (AfrECC) has been conducting, a remarkable research program on putative risk factors, to identify them and design strategies to mitigate the number of cases of this malignancy[10]. Overall, it was suggested by this research group that risk reduction strategies would include cessation of tobacco use, reducing alcohol intake, promotion of clean cooking stoves and ventilation in cooking and sleeping areas, drinking hot beverages at lower temperatures, and bio-fortification to improve crop nutrient levels[11]. However, the cultures and customs of several African ethnic groups, quite different, may promote the concealment of some local risk factors involved in esophageal carcinogenesis. Thus, knowing the local modifiable risk factors is essential to establish a proficient prevention program. What can we know in Mozambique considering these putative risk factors, and what should we do to reduce the impact of this cancer disease? To address EC in Mozambique, this narrative review explores these risk factors and potential preventive measures.

2. METHODOLOGY

This narrative review aims to examine the epidemiology, risk factors, and preventive strategies for ESCC in Mozambique. The methodology adopted involved several key steps to ensure a comprehensive and critical understanding of the topic.

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Selection of Sources

Information sources were selected from a wide range of materials, including:

- Scientific Articles: Research published in peer-reviewed academic journals.
- Public Health Reports: Documents published by health organizations such as the Ministry of Health of Mozambique and the World Health Organization (WHO).
- Books and Book Chapters: Relevant works on esophageal cancer and public health in African contexts.
- Electronic Databases: Searches were conducted in PubMed, Scopus, and Google Scholar databases to identify relevant studies.

Inclusion and Exclusion Criteria

Inclusion criteria:

- Studies addressing the epidemiology, risk factors, and prevention of ESCC.
- Publications specifically discussing the context of Mozambique or similar regions in Sub-Saharan Africa.
- Works published in the last 10 years to ensure the relevance of the information.

Exclusion criteria:

- Publications without peer review or with insufficient data.

Analysis and Synthesis of Information

The analysis of information followed these steps:

1. Critical Reading: Each source was critically read to identify key points and relevant information. All authors participated in the review of the chosen articles.
2. Identification of Themes: Information was categorized into main themes such as risk factors (smoking, alcohol consumption, dietary factors, etc.), epidemiology (incidence rates, geographic variations), and preventive strategies (tobacco control measures, early detection programs).
3. Qualitative Synthesis: The information was synthesized qualitatively, discussing the implications of findings and identifying gaps in the current literature.

Limitations

Acknowledged limitations of the narrative review include:

- Potential bias in the selection of studies due to the lack of a rigorous systematic methodology.
- Reliance on published studies, which may exclude unpublished data or grey literature.
- Temporal and geographic limitations of sources, focusing predominantly on recent studies specific to Mozambique.

The methodology adopted in this narrative review allowed for a comprehensive and critical analysis of EC in Mozambique, highlighting risk factors, epidemiological patterns, and essential preventive strategies to improve health outcomes in the country.

3. POVERTY AND ESOPHAGEAL CANCER IN MOZAMBIQUE

According to McKeown[12], diseases of poverty are diseases manifested after birth that are attributable to deficiencies or hazards related to a lack of the essentials for life. This author stressed that poverty was not a direct cause of disease, but it was the main determinant of influences that led to disease[12]. In 1989, Dr. Samuel Broder, who was then director of the US National Cancer Institute, suggested that "poverty is a carcinogen," a cancer-causing agent[13]. Mozambique is one of the

poorest and most underdeveloped countries in the world. However, this country has reduced poverty in all forms measured in the last 15 years[14-16]. Recent poverty assessments all show a decline in monetary poverty rates from 60.3% to 48.4%, a reduction in multi-dimensional poverty rates from 92.8% to 71% and a reduction in poverty using the international poverty line from 78.5% to 62.9%[17,18]. According to the World Bank, Mozambique lives an economic update characterized by less poverty, but more inequality. The poverty rate has declined on average by 1 % per year, but rural areas continue to lag behind urban areas. The Gini coefficient, which measures inequality, increased from 0.47 to 0.56 between 2008 and 2014. Mozambique's Gini coefficient has consistently remained above 0.4 even in rural areas, a high level of inequality per regional standard. Therefore, rural Mozambique is still poor[17]. Poor housing, for instance, was found to be an independent predictor of esophageal cancer in a study done in Kenya[19]. Mozambique needs inclusive growth, which invests in people, education, electricity, housing, sanitation, and water. These policies can have an impact on the prevention of EC as they can reduce the exposure of populations to various risk factors and create conditions to grow self-awareness related to EC.

4. GENDER AND AGE STATISTICS IN MOZAMBIQUE

Age-standardized rates (ASR) of EC incidence in Africa are generally higher in men than in women, according to a systematic review and meta-analysis of EC in Africa[20]. An analysis of the subgroups (regions) suggests that the incidence of EC is similar in males and females in Northern Africa, but higher in men in Western, Middle, Eastern, and Southern Africa[20].

Focusing on Mozambique (Figure 1), a series of 522 consecutive patient cases of EC admitted and treated at Maputo Central Hospital (Figure 1) were studied and the median patient age was 56.1 years (range, 27 to 97 years) while the gender ratio was slightly higher for women, 291(55.7%). ESCC was the most prevalent subtype, and the stage was

Figure 1 – **Republic of Mozambique**

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advanced at the time of diagnosis[21]. These values agree with observations described in Maputo's population-based cancer registry (2003-2008) with EC being a Prevalent tumor in the Maputo region in both genders, but the incidence rate being slightly higher in the female gender (ASR 8.7 in men and 9.9 in women)[22]. The number of cases, crude and age-standardized incidence rates for the most frequent cancers in both sexes, excluding in situ cancers and nonmelanoma skin cancer, were studied among patients from Maputo City in 2015–2016, the authors found an ASR for esophageal cancer of 7.0 in males and 9.4 in females[24].

In opposition, data reported by another cancer registry in Mozambique (Beira Cancer Registry), revealed a higher rate of incidence in males[23]. Data from the recent publication Cancer in Sub-Saharan Africa Volume III referring to Mozambique show that at the Beira ASR, it is 9.5 in males and 8.5 in females, in Maputo, ASR is 7.4 in males and 10.5 in females[25a] all these registries seem to be indicating a growing increase since 2003 of ASR in females in Maputo region. This picture contrasts with other areas of Sub-Saharan Africa, however, a possible female excess has also been reported for Sudan and Ethiopia[25b].

Concerning age, ESCC incidence rates increase steeply with age, thus an estimated 80% of EC cases (all histologies) in Eastern Africa occur in people aged 50 and over[26]. Data from Beira (2014–2017) shows that 56.8% of esophageal cancer (EC) cases occur in males aged 50 or older, and 44.7% in females[23]. Data from Maputo (2015–2017) shows that 80.3% of EC cases in males and 70.9% in females occurred in those aged 50 and above[25b]. What epidemiological significance may be associated with these local differences?

5. IS THERE GEOGRAPHIC VARIATION IN EC OCCURRENCE IN MOZAMBIQUE?

According to Asombang AW et al[28], over time there have been significant geographic variations in the African prevalence of EC within and between countries. Nowadays within Sub-Saharan Africa, there is a lot of geographic EC incidence variability[28]. Differences in the number of cases from Mozambican population-based cancer registries, namely Beira (central) and Maputo (southern), suggest regional differences in incidence and capacity of diagnosis[23]. The study by Come J et al. revealed that most patients (80.1%) were born in southern regions of the country[29]. It is necessary to verify whether these regional changes are real and if early diagnoses are possible. There is a need to risk-stratify the population so that higher-risk people can benefit from screening endoscopy[20].

6. RISK HABITS AND DIET IN MOZAMBIQUE

6.1. Alcohol

The American Cancer Society considers alcohol as a Group 1 carcinogen[30,31]. The most recent IARC monographs found sufficient animal and epidemiological evidence to conclude that alcohol consumption plays a causal role in EC[32]. Alcohol consumption was found to be significantly associated with EC in Africa[20]. In Africa, 3.7% of male deaths and 1.0% of female deaths were attributable to alcohol consumption and it is estimated that it was responsible for 2.1% (3.4% in men and 0.8% in women) of the disease burden in 200433. 30% of the adult population in Africa drink alcohol and there is an expected increase in the number of potential new alcohol consumers, especially young people and women[33]. Two published studies with representative samples of Mozambicans aged 25–64 found that 24.2–28.9% of women and 48.7–57.7% of men were current drinkers; ~60% of current drinkers consumed alcohol frequently[34,35.] Most drinkers reported consuming more affordable homemade traditional alcoholic beverages (e.g., cabanga), which was strongly associated with binge drinking. A recent study conducted among female

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heads of household living in rural Mozambique from Zambezia Province, located in central Mozambique, revealed a prevalence of current alcohol consumption among female heads of household of 15% and women considered "hazardous drinkers" was 8%[36]. Consumption was higher among men, the spirits consumption rate was relatively high[34,35] and the prevalence of current drinking increased with age and education among women and with income among men. Alcohol consumption globally is one of the major avoidable risk factors, and steps for reducing alcohol-attributable burden and costs should be initiated[33]. A recent review confirmed previous observations of Africa as a target market of alcohol companies due to its relatively high number of lifetime abstainers, particularly among women, increased population growth and urbanization, and relatively weak alcohol controls[37]. It is imperative to adopt policies and interventions to reduce or restrict alcohol consumption in Mozambique.

6.2. Tobacco

Epidemiological evidence of the association between cigarette smoking and cancer began to emerge in the 1920s, and by the 1950's the causal relationship with lung cancer was established[38,39]. The 2004 report of the US Surgeon General on the health consequences of smoking concluded that there is sufficient evidence for a causal relationship between cigarette smoking and EC[40]. Tobacco smoking and chewing are major risk factors for EC across many African countries[20]. Data from the 2003 National Health Survey, showed that among the Mozambican adults, nearly 40% of men and 20% of women were consumers of at least one type of tobacco product, although the patterns of consumption differed across the place of residence. Hand-rolled cigarettes and smokeless tobacco were the main types used by men and women, respectively, both prevailing in rural areas, while manufactured cigarette smoking was much more common in men and was more frequent in urban areas. Additionally, hand-rolled cigarette consumption predominantly occurred in the Northern provinces and rural settings, whereas manufactured cigarette consumption predominated in the south and urban areas[41]. According to Padrão P et al. in Mozambique for 3 323 individuals (25-64 years) in 2005, daily smoking was reported by 9.1% (95% CI = 5.0-13.1) of women (manufactured, 3.4%; hand-rolled, 5.6%) and 33.6% (95% CI = 29.3-38.0) of men (manufactured, 18.7%; hand-rolled, 14.8%)[42]. Although there is no national data on smoking-attributable mortality or lung cancer mortality[42], interventions aimed at controlling tobacco consumption may effectively prevent many smoking-attributed deaths from ever occurring in the country. Otherwise, the increasing urbanization and globalization, together with the weak policy for tobacco control and the recent increase in tobacco production in Mozambique, enhance the susceptibility to rising overall tobacco use[42].

6.3. Diet

Dietary factors, such as deficiencies of specific micronutrients or contamination by carcinogens have been implicated in EC development[43,44]. Deficiencies in vitamins A, B2, C, and E have been shown or suggested to enhance carcinogenesis in human populations and experimental animal models[43,45,46]. A study published in 1993 in the population of Linxian, a rural county in China with one of the world's highest incidence and mortality rates of EC, exceeding the Chinese national average by 10-fold and the American average for Whites by 100-fold, revealed consistently low blood levels of various micronutrients, including retinol, beta carotene, riboflavin, vitamin C, and vitamin E in that population[43,45]. Rensburg S et al. proposed that the primary determinant of EC susceptibility worldwide, are changes induced in the epithelium by chronic multiple micronutrient deficiencies[47].

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In Africa, countries with higher EC incidence rates tended to have lower estimated dietary supplies of Fe, Mg, Zn and Se[20]. The results of a 2013 meta-analysis suggest that the intake of fruits and vegetables is associated with significant reductions in the risk of EC48. A South African study has shown an inverse association between vegetable and fruit consumption and EC risk. The consumption of green leafy vegetables was associated with decreased odds of EC development, whereas green legumes like peas and green beans were only found to be associated with lower risk for females with no significant association for males49. A Mozambican representative sample (n 3323) of subjects aged 25-64 years was evaluated in 2005 following the WHO Stepwise Approach to Chronic Disease Risk Factor Surveillance, which included an assessment of usual fruit and vegetable consumption (frequency and quantity). This study found less than 5% of Mozambicans reported a daily consumption of at least five servings of fruit and vegetables. For rural Mozambican adolescents, higher income, and good education were predictive variables for the consumption of fats, beans, meats and eggs, cereals, and sugars. Higher education and higher income were also associated with lower consumption of vegetables, roots and tubers, fruits, chestnuts, and walnuts. The Food and Agriculture Organization of the United Nations, studying the nutritional profile of Mozambique, describes that the Mozambican diet is mainly composed of cassava – a staple with low protein content – in the northern part of the country, and maize in the central and southern parts. Except for green leafy vegetables which often accompany the staples, the supply of micronutrient-rich foods (other vegetables, fruit, and foods of animal origin) is dramatically low. In urban areas, where street foods, snacks and sugar-rich foods are becoming more common, the nutrition transition is currently underway. Cereals and starchy roots provide almost 80% of the dietary energy supply; this very poor level of dietary diversification has not improved for the last 40 years and is currently the lowest in the region[51].

The importance of micronutrient deficiencies in the population can be directly linked to a diet that is extremely poor in micronutrients[51]. In rural areas, where most of the population lives, the main constraint to food security is physical access to food: the country's infrastructures, both markets and roads, are still inefficient[51]. Floods (in the Zambezi Valley in particular) and drought (in the southern and central provinces) regularly affect agricultural production[50].

Thus, we should screen the populations with high rates of EC for vitamin and micronutrient deficits. This seems important given that the potential preventive possibilities are real, through dietary diversification and increased consumption of animal-based or other rich sources of Zn, as an example[52]. Dietary diversification or modification is a sustainable long-term approach to improving the intake of several nutrients simultaneously. Dietary diversification or modification strategies at the community or household level have the potential to increase the intake of bio-available zinc. Such strategies include (1) Agricultural interventions (2) Production and promotion of animal-source foods through animal husbandry or aquaculture (3) Processing strategies at the commercial or household level to enhance zinc absorption from plant-based diets[52,53]. A study found that Tanzania's drinking water presented several opportunities for delivering greater than 10% of the estimated average requirement (EAR) for micronutrients. For example, 1 to 56% of the EAR for I and up to 10% for Se or 37% for Zn could be contributed via drinking water[53].

Poor water/sanitation remains an important contributor to chronic undernutrition in Mozambique[54]. The water, sanitation and hygiene (WASH) needs in Mozambique are significant. The Joint Monitoring Program (JMP) estimates that in 2019 only 56 per cent of the Mozambican population, 84 per cent of urban households, and 40 per cent of rural households have access to at least basic water service[55].

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6.4. Hot beverage consumption and thermal injury

Hot beverage consumption has been associated with ESCC. According to the International Agency for Research on Cancer (IARC), hot foods/beverages (>65°C) are considered Group 2A carcinogens for humans, as they cause thermal damage to the cells of the esophageal mucosa, which mutate over the long term[30,31,56]. In May 2016, a Working Group of 23 scientists from 10 countries met at the IARC and concluded that there is little evidence in humans for the carcinogenicity of drinking very hot beverages and inadequate evidence in humans for the carcinogenicity of drinking mate that is not very hot[56]. A recent study investigated hot tea drinking habits in Northern Tanzania and found that participants consumed their tea at a mean temperature of 70.6 degrees Celsius. Hot tea consumption, especially milky tea, may be an important and modifiable risk factor for EC in Tanzania and the contribution of this habit to EC risk needs to be evaluated in this setting, jointly with that of the many risk factors acting synergistically in this multi-factorial disease[57]. A case-control study in Kenya found a progressively increased E C risk associated with drinking 'hot' and 'very hot' beverages (predominantly tea) relative to 'warm' beverages[58]. These findings provide further evidence for the role of this potentially modifiable risk factor in EC aetiology. There are no studies in Mozambique regarding the consumption of hot drinks. We only found a reference to the usual consumption of hot tea in a book published by George Ndege on Culture and Customs of Mozambique[59]. This aspect should be investigated as it may be a factor to be modified.

7. INFECTIONS

According to INSIDA 2021, the prevalence of HIV among Mozambican adults was 12,5%, meaning around 2 097 000 lived with HIV. The prevalence was greater among women (15,0%) than in Men (9,5%)[60]. A study conducted in the USA concluded that Cancer-specific mortality was significantly elevated in HIV-infected compared with HIV-uninfected patients for many cancers[61-63]. Would HIV high prevalence rates be associated with high prevalences of EC in Mozambique? There's a clear need for studies accessing that. Human papillomavirus (HPV) infection was observed to be associated with an increased risk of EC[64]. The first description of oral lesions associated with HPV was by reports that suggested the involvement of viruses in the development of benign and malignant lesions of the squamous epithelium of the esophagus in Brazil[65]. In opposition, Kayamba V et al. conducted a case-control study to explore risk factors for EC in Zambia, finding that HPV infection does not appear to play a large role in EC in Zambia66. At a population level, a 2010 study, performed in southern Mozambique showed the prevalence of genital HPV infection very high, especially in the youngest age group (over 50% were infected)[67]. However there is no study yet in Mozambique regarding HPV as a risk factor for ESCC. A consensus on the role of HPV in the development of ESCC[66] should be reached especially in countries with high prevalences of EC like Mozambique.

8. ENVIRONMENTAL CHEMICAL EXPOSURES (PAHS, NITROSAMINES AND MYCOTOXINS)

PAH (Polycyclic Aromatic Hydrocarbons) is a group of chemicals arising from partial combustion of organic matter (biomass smoke)[68]. Particulate matter, PAHs, carbon monoxide, nitrogen oxides, sulfur oxides and other pollutants associated with cooking are the result of incomplete fuel combustion. The magnitude of pollution exposure is affected by many variables including fuel choice, stove design, kitchen ventilation and proximity to main living areas[69]. An estimated 3 billion people

cook and heat their homes using biomass fuel obtained from animal or plant materials, such as wood, charcoal, dung, or crop residue[70]. Exposure to biomass smoke is associated with EC in Africa, according to Kayanba et al[71]. In Mozambique wood, charcoal, dung and maize cobs are the primary fuel source for the poorer communities[72]. Exposure to PAH is constant in rural areas. Housewives have the highest exposure since they are largely responsible for cooking and in stoves using this type of fuel. House heating also often relies on PAH[72]. Similarly, in Tanzania, PAH exposures are higher for females due to time spent cooking indoors with poor ventilation[69]. Toxicological data have proven that nitrosamines can induce tumors in the esophagus of experimental animals[73]. Several epidemiological research have been carried out to explore the relationship between human EC and nitrosamines[74,75]. In smokeless tobacco, the major and most abundant group of carcinogens are the non-volatile alkaloid-derived tobacco-specific N-nitrosamines and N-nitrosamine acids[76]. The prevalence of use of non-cigarette tobacco among students aged 13–15 years in Maputo and Gaza provinces is higher among girls than boys[77]. Nitrosamines can also be found in water and alcoholic spirits[74,78] Nitrosamines have been identified in African traditional alcoholic spirits[79]. Several studies suggest that nitrosamines are potential carcinogens for the EC, but this association has not been rigorously established in Africa[79]. Mycotoxins include a broad class of toxic fungal metabolites. The fumonisin contamination of maize and other crops has been elucidated during the last three decades. Maize has become an important food for humans and feed for domestic animals throughout the African continent. In Sub-Saharan African countries, maize cultivation has grown to a level where maize is the most important cereal crop and contributes up to 40% of the total daily food intake for humans[80]. Fumonisin contamination of maize is increased by stress during the growing season, delayed harvest, and humid storage facilities[80]. The regulatory limits for fumonisins in maize and its by-products were established by the European Union and Food and Drug Authority to prevent exposure of individuals to these fungal toxins is 200–4000 μg kg−1. The fumonisins content in unprocessed maize for human consumption is not permitted to exceed 4000 μg kg−1 in the EU[80-82]. The study "Fumonisins in African Countries" found that Maize samples from Zimbabwe had the highest total fumonisins content with 2735 μg kg−1, and in South Africa, the mean level of fumonisins in home-grown maize was determined to be 1142 μg kg−1, while in commercial maize the mean level was 222 μg kg−1[80,83]. Fumonisin contamination in Mozambique was detected in 92% of the maize samples, and the median FB1 content was 869 μg kg−1[80,84]. In the Transkei region of South Africa, the association between the consumption of fumonisin-contaminated maize and the incidence of human EC was confirmed[85]. There is a clear need for further studies to determine the role of fumonisin as a risk factor for EC.

9. DENTAL FLUOROSIS

Tooth loss, periodontal disease, and other markers of poor oral hygiene have been associated with increased risks of EC and its precursor lesion, esophageal squamous dysplasia (ESD)[86]. Dental fluorosis is an important clinical and public health problem in several parts of the world, especially in the Great Rift Valley that extends from northern Syria to central Mozambique in East Africa[87]. Dental fluorosis can lead to eventual loss of tooth surface attrition and pitting. The severity of dental fluorosis depends on several factors associated with fluoride dose, length of exposure, altitude, and individual differences including health and nutritional status[87]. Menya D et al. conducted the first EC case-control study in Eastern Africa that addresses Dental fluorosis and oral health. In this study, the EC-dental fluorosis association appeared to be concentrated

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in individuals who also had tooth decay or tooth loss[86]. Menya D et al. after adjusting for the other factors, found 40% of EC cases had moderate/severe fluorosis, odds ratio (OR) 9.4, 95% confidence interval: 4.6-19.1 and 43 % cases with mild fluorosis, OR 2.3, 95%CI: 1.3-4. Cases of malnutrition were found in more suburban schools (n = 109; 36.22%) than in urban schools (n = 66; 22.00%) (p = 0.03)[86]. The frequency of sugar consumption was higher among urban children compared to suburban schools (p <0.00). The level of fluoride in water consumption in urban schools was 0.4 ppm F, above the level of fluoride in suburban schools, 0.2 ppm F[86]. An association of dental fluorosis with EC risk was found86. However, research on oral dysbiosis or other biological mechanisms is still needed. Mapengo M et al. studied dental caries in adolescents from public schools in Maputo and the authors concluded that children in urban schools showed less dental caries (0.8 +/- 1.49 SD) than children in suburban schools (1.1 +/- 1.80 SD, p = 0.03). Only 8.15% had very mild to moderate fluorosis but most presented poor oral hygiene[88]. A diet rich in calcium, magnesium and antioxidants is known to reduce fluoride bioavailability and/or ameliorate fluorosis progression[89]. It is crucial to develop strategies that help in reducing the risk of fluorosis.

10. PREVENTION AND EARLY DETECTION PROGRAM

The Ministry of Health and the First Lady of Mozambique have launched the National Cancer Control Plan (NCCP) 2019-2029[90]. During the launching, the First Lady underlined the importance of education, prevention and health promotion[91]. NCCP is the most effective instrument for prevention and early detection since it integrates existing health systems and related services, the different programs that ensure systematic and equitable implementation of control strategies across the continuum of prevention, early detection, treatment and palliative care as set out in WHO's guidelines. "Key Prevention and Control Interventions for Reducing Cancer Burden in the WHO African Region" is a useful WHO publication to help in organizing cancer prevention and early detection national programs[92]. The goal of primary prevention is to reduce or eliminate exposure to cancer-risk factors, which include modifiable factors. The main objective of early detection is to detect precancerous changes or early-stage cancers when they can be treated most effectively. Therefore, EC cancer morbidity and mortality could be prevented by implementing evidence-based interventions to reduce cancer risk factors and increase early detection of cancer.

10.1. Recommended interventions

10.1.1. Policy and Strategic Planning

- Formulate a National EC Cancer Policy and Strategic Plan that also addresses advocacy and cancer awareness.
- Develop a clear policy for diagnosis, referral, treatment, and follow-up of all cancer cases (including EC).

10.1.2. Education and Public Awareness

- Provide global education on EC risks and prevention and incorporate these concepts into health schools' curricula.
- Disseminate information on EC cancer prevention to the public, including environmental and domestic occupational carcinogens.
- Advocate for behaviours favoring EC cancer prevention such as healthy diet, oral hygiene, reducing alcohol intake, stopping smoking, adopting policies that provide good drinking water, rural well-ventilated grain silos, alternative energy sources to PAHs,

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food preservation safety, and better housing conditions.
- Direct educational programs at schools and workplaces on esophageal cancer.
- Avoid chronic consumption of drinks/food at high temperatures.

10.1.3. Training and Capacity Building

- Educational/training programs for health providers regarding EC, including learning about modifiable risk factors and clinical signs that ensure early diagnosis.
- Train gastroenterologists in the diagnosis of premalignant esophageal lesions.
- Facilitate capacity building in EC research at various levels of the health system, including genetics.
- Promote collaboration between various stakeholders involved in EC research.
- Enhance EC research capacity in the country.

10.1.4. Early Diagnosis and Screening

- Promote early diagnosis by creating increased awareness of early signs and symptoms of detectable and curable tumors that have a high prevalence in the community, such as breast, cervical, prostate, and esophageal cancers.
- Design a dysphagia alert program that includes awareness that "an episode of dysphagia in people over 39 years of age", "living in high-risk places (of any age)", or "anyone with episodes of recurrent dysphagia" should be clinically investigated.

10.1.5. Data Collection and Integration

- Establish/reinforce reliable and sustainable sources of EC data collection, particularly cancer registries (hospital or population-based). Identify the regions where EC is most prevalent in Mozambique.
- Integrate and collaborate with other health programs, e.g. malaria, HPV, schistosomiasis, AIDS control, hepatitis B, etc., to strengthen both results.

10.1.6. Control Measures

- Apply effective tobacco control measures; Mozambique has signed the WHO Framework Convention on Tobacco Control.
- Apply effective alcohol abuse control measures.
- Apply effective food safety control measures.
- Apply an effective drinking water safety plan.

10.1.7. Research and Funding

- Identify research priorities for EC in the country.
- Mobilize funds from sustainable sources for funding research.

11. CONCLUSIONS

Esophageal cancer (EC) poses a major public health challenge in Mozambique, with high incidence rates, late diagnoses, and poor outcomes. Despite progress in poverty reduction and healthcare infrastructure, persistent socioeconomic disparities exacerbate EC risk factors and hinder early detection. Evidence-based interventions are crucial to mitigate EC incidence and mortality, addressing modifiable risk factors such as tobacco and alcohol use, dietary habits, hot beverage consumption, infections, environmental exposures, and dental fluorosis. Geographic variations in EC incidence necessitate tailored prevention strategies for high-risk populations and regions. National policies

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should focus on reducing exposure to risk factors, raising awareness, and promoting healthy lifestyles. The National Cancer Control Plan (NCCP) offers a comprehensive framework for prevention and early detection, emphasizing education, advocacy, and cross-sector collaboration. Strengthening healthcare systems, promoting health literacy, and fostering community engagement are essential for meaningful progress in EC prevention and control.

Prioritizing preventive measures, early detection programs, and multidisciplinary approaches can help Mozambique reduce the burden of esophageal squamous cell carcinoma and improve cancer outcomes for its population.

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