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Research Article

A Mixed Cross-sectional and Case-control Study to Investigate the Risk Factors of Noma (A Psychologically Debilitating Disease) in Ethiopia

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ABSTRACT

Noma is a polymicrobial gangrenous facial disease affecting people living in the most impoverished areas of low- and middle-income countries. The condition is associated with varying levels of psychological, functional, and social morbidity. Several risk factors are reportedly claimed to favor the development and progression of the disease. A cross-sectional and case-control study was conducted to assess the risk factors of Noma in Ethiopia. The raw data of the cases were obtained from three major Noma treatment centers in Ethiopia. Three controls were selected per single case. Odds Ratios (ORs) and Chi-square tests were calculated. A total of 64 cases were selected for the case control study. Considering the 1:3 case to control ratio, 192 matching controls were identified. Malaria, helminths, measle, diarrheal diseases, and living with domestic animals were found to be risk factors for Noma with a respective p-value<0.01. Contrarily, the analysis has identified vaccination (p<0.01) as a protective factor. Poverty-related diseases such as malaria, helminth infection, measle, diarrheal diseases, and unfavorable living conditions were identified as risk factors for Noma. As such, the disease is preventable. Therefore, in addition to other healthcare-related preventive measures, long-lasting economic development should be considered to effectively and sustainably reduce the burden of the disease.

Keywords: Malaria; Helminth; Measle; Cancrum oris; Diarrheal Diseases; Poverty

Abbreviations: ORs: Odd Ratio; AIDS: Acquired Immunodeficiency Syndrome; CRFs: Modified Case Report Form; WHO: World Health Organization

INTRODUCTION

Noma was quite prevalent in the past in the southwest; however, following the increasing economic and educational advancement, there has been a steady downward trend, except for some sporadic cases [1]. On the contrary, the disease remains more prevalent in the northwest, where poverty is much more prevalent, and illiteracy rates are much higher [2-4]. However, various studies have reported a bunch of pathogens that can potentially cause the disease, with Fusobacterium Necrophorum being the most common [5-9]. Noma is commonly seen in a population with extreme poverty, severe malnutrition, unsafe drinking water, poor sanitation, poor oral health practices, limited access to high-quality health care, and intrauterine growth retardation [10]. Recently, an increased incidence of Noma has been reported in patients with Human Immune Deficiency Virus (HIV) infection, cyclic neutropenia, leukemia, Down's syndrome, Burkett's Disease, and Herpetic Stomatitis [11]. Malnutrition is considered a significant risk factor for Noma [12]. In Africa, most cases were reported during the dry season when food is scarce and the incidence of measles is at its peak [13]. Studies, which were conducted to assess the risk factors of Noma in Nigeria revealed severe malnutrition, recent respiratory or diarrhoeal syndrome, the number of previous pregnancies in the mother, an altered oral microbiota, lack of maternal care, malnutrition, and the absence of chickens at home as predictors of Noma [14,15]. Immunodeficiency disorders, including AIDS, down syndrome, malnutrition, dehydration, poor oral hygiene, recent orofacial and systemic illness, unsafe drinking water, poverty, malignancy, and living

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near domestic animals are also reported to be the other predisposing factors [16-19]. However, on many occasions, debilitating conditions like measles (commonly), herpès simplex, varicella, scarlet fever, malaria, gastroenteritis, tuberculosis, and bronchopneumonia commonly appear to set the initial stage for the development of Noma [1,18,20]. Most Noma cases die and the remaining few survivors suffer from severe functional impairments [21]. The condition is also psychologically debilitating leaving survivors with severe cosmetic disfigurements [22,23]. Yet, the disease is not studied well and very little is known about the risk factors of the disease [24,25]. Certainly, this explains the extent to which the condition is neglected [26,27]. This study was initiated to assess the risk factors of Noma in Ethiopia.

MATERIALS AND METHODS

Research design

A mix of cross-sectional and case control study approaches was used to identify the possible risk/predisposing factors that could potentially be associated with the development of Noma in this study. The study matched three controls for each corresponding case in terms of geographic location, gender, and age.

Sample and setting

The cross-sectional and case-control studies were conducted in different parts of the country, including Addis Ababa depending on the findings of the demographic-geographic data obtained from patients' medical records review. All the patients' medical records were obtained from the main offices of the three major Noma treatment centers in Addis Ababa. Cases were patients diagnosed with Noma and treated in Yekatit 12 Hospital, Facing Africa Ethiopia or Harar Project Ethiopia, between March 2004 and December 2020. The cases were identified via the cross-sectional study. Controls were individuals matched to cases by the village of residence, current age (± 2 years), and sex.

Case and control definitions

Definition of case: In this study, cases are individuals diagnosed with Noma in Ethiopia between January 2004 and February 2020. To be ascertained as a case of Noma, an individual should have facial edema, intraoral necrotizing stomatitis, metallic taste, typical halitosis (often considered pathognomonic), bluish discoloration of the skin, gangrenous demarcation, tissue necrosis, and sloughing. Moreover, the subjects need to be diagnosed with Noma. Three or more of the following were also considered: A history of malnourishment, a history of poor oral hygiene, a history of poverty, a history of poor sanitation and living close to domestic animals, and a history of debilitating and immunocompromising diseases such as measle, tuberculosis, AIDS, leukemia.

Definition of control: Controls are individuals who were never diagnosed with Noma. Furthermore, the controls must be matched to cases by the village of residence, current age (± 2 years), and sex.

Instruments: To answer the research questions, the investigator needed to review the medical registry of Noma cases for the 2004-2020 period, including patients' photos with relevant clinical and demographic information. A modified Case Report Form (CRFs) consisting of demographic and clinical sections was used to collect the relevant demographic and clinical data. The demographic section of the CRFs contains the name, gender, age, physical address (geographic location), telephone address, and year of admission of the patients. On the other hand, the clinical section of the CRFs primarily subdues the localization of Noma-induced anatomical lesions, medical history, dietary information, vaccination details, living stands, and functional impairments data.

Similarly, a questionnaire with a set of questions was used to interview the cases (caregivers or guardians) and controls (caregivers or guardians) to complete the case control study. Therefore, information regarding the possible risk factors for Noma was obtained using a structured written questionnaire and reviewing patients' medical charts. The questionnaire also consisted of demographic and clinical (risk factor) data. Both the CRFs and questionnaire were made to be valid. The researcher verified the validity of the CRFs and the questionnaire. Furthermore, pre tests were conducted to assess the validity and reliability of the data collection instruments used in this case-control study.

On the other hand, the contact information of the cases, including patient name, telephone number, and home address, was obtained from the CRFs and used to select neighboring controls. The controls were explored for the necessary demographic and clinical information to carry out the case-control study.

Data analysis: The data analysis of the case-control study follows the entry of relevant clinical and demographic data of the cases and controls into an excel sheet. Descriptive analysis was used to determine the characteristics of cases and controls. The Odds Ratio (or) was calculated to rule out the existing association between the possible risk/predisposing factors and the disease. A chi-square test was carried out to test the statistical significance of the associations observed between the predisposing factors and the condition.

RESULTS

The case-control study was employed to identify the possible risk factors for developing Noma among the cases. The cases were selected from the medical records obtained from the three Noma treatment centers (Yekatit 12 Hospital, Facing Africa, and Harar Project). Completeness of medical records, availability of pertinent contact information (at least phone number), and patient age during admission were the criteria for selecting the 64 cases.

Of the 163 Noma patients who sought care in the programs between March 2004 and December 2020, 68 were eligible for inclusion in the case-control study. Four could not be reached for logistical reasons, and the researcher managed to interview the study participant via phone. Thus, the final analysis included 64 Noma cases and 192 controls. All cases and

controls were under 41 years old. The age restriction was considered to avoid recall bias. The assumed potential risk factors were living with domestic animals, having diarrheal disease, having a helminthic infection, exposure to malaria infection, being inflicted with measle infection, and drinking river (Tables 1-6).

Categories	Cases	Controls	Total
Present	35	43	78
Not-present	29	149	178
Total	64	192	256

Table 1: Domestic animals at home.

Categories	Cases	Controls	Total
Present	35	43	78
Not present	29	149	178
Total	64	192	256

Table 2: The assumed potential risk factors with diarrheal disease.

Categories	Cases	Controls	Total
Present	31	12	43
Not present	33	180	213
Total	64	192	256

Table 3: The assumed potential risk factors with helminthic infection.

Categories	Cases	Controls	Total
Present	21	14	35
Not present	43	178	221
Total	64	192	256

Table 4: The assumed potential risk factors with malarial infection.

Categories	Cases	Controls	Total
Present	13	14	27
Not present	51	178	229
Total	64	192	256

Table 5: The assumed potential risk factors with measle infection.

Categories	Cases	Controls	Total
Drinks	15	41	56
Not drink	49	151	200
Total	64	192	256

Table 6: The assumed potential risk factors with drinking river water.

On the other hand, vaccination was regarded as a potential protective factor based on the literature review (Table 7).

Categories	Cases	Controls	Total
Vaccinated	14	104	118
Non-vaccinated	50	88	138
Total	64	192	256

Table 7: The assumed potential risk factors with vaccination.

The clinical information obtained from the patient's medical records was the main guiding principle to consider these as potential risks and protective factors for Noma. Accordingly, each possible risk factor and the vaccination as protective factors were assessed for having a statistically significant association with the occurrence of Noma.

In conclusion, malaria, helminthic and measle infections, living with domestic animals, and diarrheal diseases are identified as risk/predisposing factors for developing Noma. On the contrary, drinking river water has shown no significant association with the development of Noma among the cases. On the other hand, vaccination is found to be a protective factor not developing Noma among the controls (Table 8).

Risk/protective factor	Odd Ratio (ODs)	Chi-square (χ^2)	p-value
Malaria	6.2	24.37	8E-07
Helminthic infection	14.1	58.11	1E-10
Measle infection	3.2	7.3	0.007
Diarrheal diseases	4.2	22.1	0.000003
Domestic animals	4.1	22.13	0.000002
River water	1.13	0.03	0.9
vaccination	0.24	21.46	0.000004

Table 8: Summary of risk and protective factors.

DISCUSSION

Most of the Noma cases live in the most deprived and remote regions of sub-Saharan Africa [28]. Historically, Noma was most prevalent in the Noma belt region that extends from Senegal to Ethiopia [5]. In countries where the condition is widespread, risk factors such as malnutrition, debilitating diseases like malaria and measles, and close residential proximity to livestock are reported [29,30]. Moreover, respiratory or diarrheal syndrome and altered oral microbiota have been reported as risk factors for Noma [14]. The AIDS pandemic increases the number of cases outside the Noma belt region and is considered a viable risk factor for the disease [31]. Other risk factors that have been reported in several articles include the absence of breastfeeding, unsafe drinking water, limited access to high-quality health, and food security [1,32,33].

On the other hand, childhood vaccine coverage has been reported as a protective factor in not developing Noma [34]. Diarrheal diseases, drinking river water, living with domestic animals, vaccination coverage, measle, malaria, and helminthic infections were tested for possible significant association with the development of Noma in this study. The findings of this study supported the above argument. In other words, measles, malaria, helminthic infections, diarrheal diseases, and domestic animals at home have been identified as potential risk factors for developing Noma among the cases. On the other hand, vaccination coverage has shown a statistically significant protective effect not developing Noma among the controls.

Malnutrition is considered an important risk factor for Noma [35,36]. In Africa, most cases were reported during the dry season when food is scarce, and the incidence of measles is the highest [37]. The debilitating diseases such as malaria and measles have shown a statistically significant association of being precursors to Noma in this study. Hence the periodicity of onset of the disease in this study could be explained by the dry seasons, as food is scarce, and the incidence of measles and malaria often increases [38]. Measles and malaria could also be significant risk factors because of the associated immunosuppression [39,40]. Furthermore, malnutrition could be regarded as a confounding factor in these associations. However, a further in depth investigation needs to be carried out.

The proportion of vaccination coverage in many developing countries is below the standards recommended by the World Health Organization [41]. There is evidence that the occurrence of vaccine-preventable diseases and malnutrition precedes the onset of Noma. The low coverage of vaccination not only increases the risk of morbidity and mortality from vaccine-preventable diseases but is a contributing factor in immunosuppression, which is thought to play a vital role in the sequence of events for Noma development [42]. Measle, the only vaccine-preventable disease identified as a risk factor for Noma in this study, could cause immunosuppression among the cases described [43]. The diarrheal and helminthic infections identified in this study could also cause immunosuppression. This immunosuppression could be generally confounded by low coverage of vaccination.

On the contrary, the protective effect of vaccine coverage identified in this study could be regarded as a positive factor in reducing the burden of the disease. Living with domestic animals is the other risk factor of Noma among the cases studied in this study. This factor could be explained in terms of the lack of proper sanitation. On the other hand, drinking river water has shown neither protective nor causative effects on the development of Noma in this study.

The tropical climate, lack of education, rural condition, poor sanitation, and poverty are the leading risk factors for the occurrence of Noma [11,44-47]. Furthermore, several studies have shown that in countries where the condition is widespread, risk factors such as malnutrition, debilitating diseases like malaria and measles, respiratory or diarrheal syndrome, altered oral microbiota, and close residential proximity to livestock are reported [48, 49, 27, 50-54].

CONCLUSION

The risk factors of Noma are highly related to poverty. Simply, Noma can be considered an excellent biological parameter of extreme poverty. Hence, policymakers need to be aware that activities against extreme poverty can inevitably avert the occurrence of the disease and its associated ill sequela in developing countries. The importance of awareness rising initiatives, execution of timely and appropriate medical intervention, providing physical and psychological rehabilitation, and increasing immunization coverage should also be underscored.

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