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An Update on the Risk Factors of Noma (Facial Gangrene) in Ethiopia

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Abstract

Noma is a severely disfiguring and highly morbid mouth and facial region disease. The condition is most prevalent in developing countries and primarily affects children under the age of 10. The specific trigger of the disease is unknown. However, several risk factors are reported to favor the development of Noma. A cross-sectional and case-control study was conducted to determine the risk factors for Noma in Ethiopia between January and February 2021. The current study was conducted in February 2023 to update the previous study. Raw case data were obtained from three major noma treatment centers in Ethiopia. Three controls were selected for each individual case. Odds ratios (ORs) and chi-square tests were calculated. P values for each potential risk factor were also determined, considering a degree of freedom (df) of 1. A total of 64 cases were selected for the previous case-control study. Considering a 1:3 ratio between cases and controls, 192 matched controls were determined accordingly. This updated study included 73 cases and 219 controls, including the newly recruited 9 cases and 27 controls. Similar to the previous survey, this updated study identified malaria, helminths, measles, diarrheal diseases, and living with pets as predisposing factors for Noma with a respective p-value of <0.01. In contrast, vaccination was found to be a protective factor (OR = 0.30 & $p < 0.01$) for the absence of noma disease in both studies. However, unlike the earlier studies, drinking river water ($p = 0.04$) was found to be a risk factor for noma in this updated analysis. In general, all risk factors identified in both studies are predominantly associated with poor living standards due to poverty. Therefore, long-term economic development should be considered along with other health-related preventive measures to effectively and sustainably reduce the burden of the disease.

Keywords: Malaria, Helminths, Measles, Diarrheal diseases, Poverty

Abbreviations:

ORs: Odd Ratio

AIDS: acquired immunodeficiency syndrome.

CRFs: modified case report form

WHO: World Health Organization

Introduction

The word Noma is derived from the Greek term nomein, which means to devour (eat quickly) [1]. Noma is a rapidly progressive, polymicrobial, opportunistic, gangrenous infection of the oral cavity, most likely caused by certain species of bacterial flora that become pathogenic when the host immune system is weakened [2]. The disease is reported to be more common and fatal in children under ten years of age [3, 4]. Few affected children seek medical

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attention during the acute stage of Noma, due in part to the very rapid progression of the disease but also to lack of knowledge, stigma, and the absence of a functioning health care system in affected and usually particularly disadvantaged areas [5]. For early recognition and diagnosis, a history of previous infections or debilitating illnesses with recurrent fever, still persistent severe stunting and emaciation, malnutrition, diarrhea, and currently present facial swelling, foul-smelling breath, excessive salivation, oral mucosal ulceration with the exposed bone are important clues [6]. Other ulcerative lesions to consider in the differential diagnosis of Noma include facial midline granulomas, agranulocytic angina, malignant oral lesions, mucocutaneous leishmaniasis, Buruli ulcer, leprosy, and syphilis, but most of these diseases rarely have facial involvement and/or are uncommon in young children [6-8]. Additional diagnostic tools besides a careful history include microscopy for analysis of the microbiota on smear cultures and various imaging modalities such as magnetic resonance imaging (MRI), radiographs and orthopantomography (OPG), and computed tomography (CT) [9].

If diagnosed early, Noma can be treated, and its progression can be arrested [8, 10]. Critical treatment options for Noma in the early acute phase include correction of dehydration and electrolyte imbalance, nutritional rehabilitation, treatment of predisposing and systemic diseases such as malaria or measles, administration of antibiotics (e.g., e.g., penicillin, metronidazole), local wound care by daily dressing of lesions with oral antiseptic-soaked gauze, and oral hygiene measures such as daily rinsing of the mouth with chlorhexidine digluconate solution if conditions permit [11, 12]. However, enteral or parenteral nutrition may be required in advanced stages because oral feeding may become impossible due to pain or trismus [6]. Debridement of necrotic tissue, reconstruction of the affected anatomic region, and psychological and physical rehabilitation of survivors are the main therapeutic measures for diagnosed noma cases [1, 21].

Because Noma occurs mainly in young children in remote areas of the least developed countries with inadequate health care systems, progresses rapidly, has a high mortality rate, and is stigmatized, it is a poorly understood disease whose cause is still idiopathic today [4, 13]. Because of the possible involvement of bacteria, the transmissibility of Noma must be considered, but epidemiologic patterns and animal studies do not currently support this possibility [8, 14]. Predisposing factors cited include immunodeficiency disease, including AIDS; malnutrition; dehydration; poor hygiene, especially in the mouth; recent orofacial and systemic disease; unsafe drinking water; poverty; malignancy; and living near pets. In many cases, recent debilitating conditions such as measles (general), herpes simplex, varicella, scarlet fever, malaria, gastroenteritis, tuberculosis, and bronchopneumonia appear to set the stage for the development of Noma [13, 14]. Intrauterine growth retardation, Down syndrome, exposure to cytomegalovirus, and preterm birth are also considered predisposing factors for the development of Noma [15-21]. Cases associated with malignancies (e.g., leukemia) are not uncommon [22]. Nevertheless, the disease is poorly studied, and very little is known about the condition's risk factors [23-25]. This certainly explains the extent to which the disease is neglected [26, 27]. This study was initiated to update the risk factors for Noma in Ethiopia.

Materials and Methods

Research Design

The researcher conducted a mixture of cross-sectional and case-control studies to update the risk/predisposition factors for the development of Noma. Potential risk factors were assumed to be living with pets, diarrheal disease, helminth infection, malaria infection, measles infection, and drinking from rivers. On the other hand, vaccination was considered a potential protective factor based on the literature review. In this updated study, for each possible risk factor and vaccination as a protective factor, the researcher examined whether there was a statistically significant association with the occurrence of Noma. The study selected three control subjects for each corresponding case in terms of geographic location, sex, and age.

Sample and Setting

Volunteer Noma cases who have had a clinical follow-up in three major noma treatment centers (Yekatit 12 Hospital, Facing Africa Ethiopia, or Harar Project Ethiopia) were involved in this updated study. Therefore, the cases were patients diagnosed with Noma and those who had have surgical follow-ups at the three centers between March 2004 and January 2023. New cases were identified as part of a cross-sectional study. Controls were individuals matched to cases based on place of residence, current age (+/- 2 years), and sex.

The previous case-control study identified malaria, helminth infection, living with pets, diarrheal diseases, and measle infection as predisposing factors for developing Noma among adults in Ethiopia. The study included 64 cases and 192 controls for data analysis and was conducted between mid of January and the end of February 2021. The cases were obtained from Ethiopia's three noma treatment centers (Yekatit 12 Hospital, Facing Africa, and Harar Project). Completeness of medical records, availability of relevant contact information (at least telephone number), and age of the patient at admission (above 18 and ≤ 41 years old) were the inclusion criteria to select the cases. The age restriction was needed to avoid potential recall biases in the study participants.

Instruments

A modified case report form (CRF) consisting of socio-

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demographic and clinical sections was used to collect the selected cases' relevant demographic and clinical data. The demographic section of the CRFs includes the patient's name, sex, age, address (geographic location), telephone number, and year of admission. The clinical section of the questionnaires primarily contains information on the location of anatomic lesions caused by Noma, medical history, diet, vaccinations, housing situation, and functional impairments.

A structured questionnaire consisting of a series of clinical and socio-demographic questions was used to interview the cases and controls. The questionnaire primarily aimed to extract relevant information concerning the anticipated risk and protective factors for developing Noma among the cases and controls. The researcher checked the validity of the CRFs and the questionnaire by conducting pre-tests.

Data analysis

The IBM SPSS (Statistical Package for Social Sciences) Statistics, version 29 version was used to analyze the collected data. Data analysis of this study was performed after entering the relevant clinical and socio-demographic data of the cases and controls into an Excel spreadsheet. The odds ratio (OR) was calculated to rediscover the existing potential association between the anticipated risk/protective factors and the disease. A chi-square test and determination of p values were performed to test the statistical significance of the observed associations between the predisposing/protective factors and the disease. The analysis considered a statical degree of freedom (df) equal to 1.

Ethical clearance

Ethical approval was obtained from the Addis Ababa Health Bureau Institutional Review Board (IRB) Ethics Committee. Verbal consent was obtained, and all study participants were fully informed of the study and its purpose, the anticipated risks and benefits of participation, and the confidentiality of the information.

Findings

A total of 19 Noma patients, including those who could not be accessed due to various reasons to involve in the previous study, had participated voluntarily in the screening phase of the updated survey. Of these, 9 (6 males & 3 females) new patients fulfilled the inclusion criteria and were selected as cases in February 2023. Accordingly, 27 controls were newly recruited, considering the 1:3 ratio between cases and controls. All the cases and controls underwent rigorous investigations (screenings) to rule out malaria, consuming river water, helminth infection, measle infection, diarrheal diseases, and living with pets as potential predisposing factors for developing Noma in the updated study. The protective impact of vaccination towards not contracting Noma was also investigated. Thus, the post-interview outcomes of the newly recruited study participants were combined with the previous study's findings to come up with the results of this updated study. Therefore, the findings of the current study were found after analyzing the post-interview outcomes of the aggregate study participants [73 (64+9) cases & 219 (192+27) controls]. Female to male ratio was calculated to be 0.66 [i.e., 116 females (29 cases+87 controls) and 176 males (44 cases+132 controls)].

In summary, malaria, drinking river water, helminth infection, living with pets, diarrheal diseases, and measle infection were all identified as risk or predisposing factors for developing Noma. In this updated study, drinking river water has also shown a significant association with the development of Noma among cases. On the other hand, vaccination has been found to be a protective factor against the development of Noma in control subjects (Table 1).

Discussion

Most noma cases live in sub-Saharan Africa's poorest and most remote regions [28]. Historically, Noma was most prevalent in the noma belt region, which extends from Senegal to Ethiopia [5]. In countries where the disease is widespread, risk factors include malnutrition, debilitating diseases such as malaria and measles, and proximity to livestock [29, 30]. In addition, respiratory or diarrheal diseases and altered oral microbiota have been cited as risk factors for noma [14]. The AIDS pandemic increases the number of cases outside the noma belt region and is considered a risk factor for the disease [31]. Other risk factors reported in several articles include lack of breastfeeding, unsafe drinking water, limited access to quality health care, and food insecurity [1, 32, 33].

On the other hand, childhood vaccination protection has been reported to be a protective factor in not contracting noma [34]. Diarrheal diseases, drinking river water, living with pets, vaccination protection, measles, malaria, and helminth infections were investigated in this study for a possible significant association with the development of Noma. The results of this study support the above argument. In other words, measles, malaria, helminth infections, drinking river water, diarrheal diseases, and pets in the household were identified as risk factors for developing Noma in affected individuals. On the contrary, vaccination has shown a statistically significant protective effect against the development of Noma in control subjects. Of note, drinking river water did not show any protective or causative effect on the development of Noma in the previous study. But the current updated study disproved the previous survey; i.e., drinking river water was found to be the risk factor for Noma.

Malnutrition is a significant risk factor for Noma [35, 36]. In Africa, most cases have been 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 as precursors of Noma in this study. Therefore, the periodicity

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Table 1: Summarized findings pertaining to the identified risk & protective factors

Risk & protective factors	Status	Cases	Controls	Total	Odd ratio (ODs)	Chi-square (χ2)	p-value
Malaria infection	Present	28	22	50	5.57	28.96	< .00001
	Not present	45	197	242			
	Total	73	219	292			
Domestic animals at home	Present	41	51	92	4.22	25.92	< .00001
	Not present	32	168	200			
	Total	73	219	292			
Diarrheal disease	Present	42	52	94	4.35	27.11	< .00001
	Not present	31	167	198			
	Total	73	219	292			
Helminthic infection	Present	37	18	55	11.48	61.83	< .00001
	Not present	36	201	237			
	Total	73	219	292			
Measle infection	Present	19	21	40	3.32	11.16	836
	Not present	54	198	252			
	Total	73	219	292			
Drinking river water	Drinks	23	42	65	1.94	4.12	0.042379
	Do not drink	50	177	227			
	Total	73	219	292			
Vaccination	Vaccinated	19	118	137	0.3	18.19	0.00002
	Non-vaccinated	54	101	155			
	Total	73	219	292			

of the disease outbreak in this study could be explained by the dry seasons when food is scarce, and the incidence of measles and malaria often increases [38]. Measles and malaria could also be major risk factors because of the associated immunosuppression [39, 40]. In addition, malnutrition could be considered as a confounding factor in these associations. However, further in-depth studies need to be conducted.

Immunization coverage in many developing countries is below the standards recommended by the World Health Organization [41]. Evidence suggests that the occurrence of vaccine-preventable diseases and malnutrition precedes the occurrence of Noma. Low vaccination coverage increases the risk of morbidity and mortality from vaccine-preventable diseases. It contributes to immunosuppression, which is thought to play a critical role in the sequence of events in the development of Noma [42]. Measles, the only vaccine-preventable disease identified as a risk factor for Noma in this study, could cause immunosuppression in the cases described [43]. The diarrheal and helminth infections identified in this study could also cause immunosuppression. In general, such immunosuppression could be affected by low vaccination coverage [45].

On the contrary, the protective effect of vaccination identified in this study could be considered a positive factor in reducing the disease burden. Living with pets is the other risk factor for Noma among the cases investigated in this study. The lack of adequate sanitation facilities could explain this factor. Tropical climate, lack of education, rural conditions, poor sanitation, and poverty are the most common risk factors for the occurrence of Noma [11, 44-47]. In addition, several studies have shown that risk factors such as malnutrition, debilitating diseases such as malaria and measles, respiratory or diarrheal diseases, altered oral microbiota, and proximity to livestock have been reported in countries where the disease is prevalent [27, 48, 49].

Conclusion

In one way or another, the identified risk factors in this updated study are associated with poverty. Given the need to conduct further in-depth research, the results of this updated study can be considered a good indicator of the link between Noma and poverty. Therefore, policymakers must develop a prevention strategy focusing primarily on poverty reduction. However, the importance of awareness-raising initiatives, timely and appropriate medical interventions, physical and psychological rehabilitation, and increased vaccination coverage should not be overlooked. In general, issuing nutrient-rich foods, promoting exclusive breastfeeding, fostering health education, advocating for proper oral hygiene, distributing vaccinations against debilitating diseases, segregating pets, providing clean drinking

water, raising awareness of the disease and reducing the psychosocial burden on survivors, and facilitating the full social reintegration of noma cases should be included in the overall strategic plan for disease prevention.

Conflict of Interest

The author declares no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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