International Journal of Celiac Disease, 2019, Vol. 7, No. 1, 9-12
Available online at http: //pubs.sciepub.com/ijcd/7/1/3
Published by Science and Education Publishing
DOI: 10.12691/ijcd-7-1-3

The Underdiagnosed Enemy: Africa Goes Celiac?

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Received December 11, 2018; Revised January 14, 2019; Accepted February 26, 2019

Abstract Celiac disease incidence is continuously increasing worldwide and in Africa, where a clear North to South gradient is apparent. At least in the Maghreb region, the disease features resemble its European neighbors, but some aspects are completely different. The present review highlights the underdiagnosis and the inadequate nutritional therapy for celiac disease patients and summarizes the local special circumstances that should be address to coop with the contemporary load and future burden of the disease.

Keywords: *celiac disease, incidence, Maghreb, Africa, wheat, HLA, burden*

Cite This Article: Lerner Aaron, Lopez Francois, Schmiedl Andreas, and Matthias Torsten, "The Underdiagnosed Enemy: Africa Goes Celiac?" *International Journal of Celiac Disease*, vol. 7, no. 1 (2019): 9-12. doi: 10.12691/ijcd-7-1-3.

1. Introductive Update on the Last Decade 2008-18

Celiac disease (CD) prevalence is increasing constantly worldwide [1], parallel to the general trend in multiple autoimmune diseases [2]. In the past, mainly in the developing countries where infectious diseases were a major contributor to morbidity and mortality, autoimmune diseases were neglected and seldom reported. Being an autoimmune condition, CD was equally underestimated, underdiagnosed and gluten free diet was an exception. Since then, "many rivers have flowed into the oceans", including in Africa. In the last decade, the awareness, rate and mode of diagnosis, normal and at risk population screening, public and professional education and the gluten free product's market changed substantially. The present narrative review intend to update on the new development in CD, in the African continent, during the last decade, from 2008 to 2018. Suffice it to look on the gradual increase in the publications on the subject (Figure 1, from Pubmed.gov) [3], in the recent decades and to conclude that things are moving forward and for the better for CD in Africa.

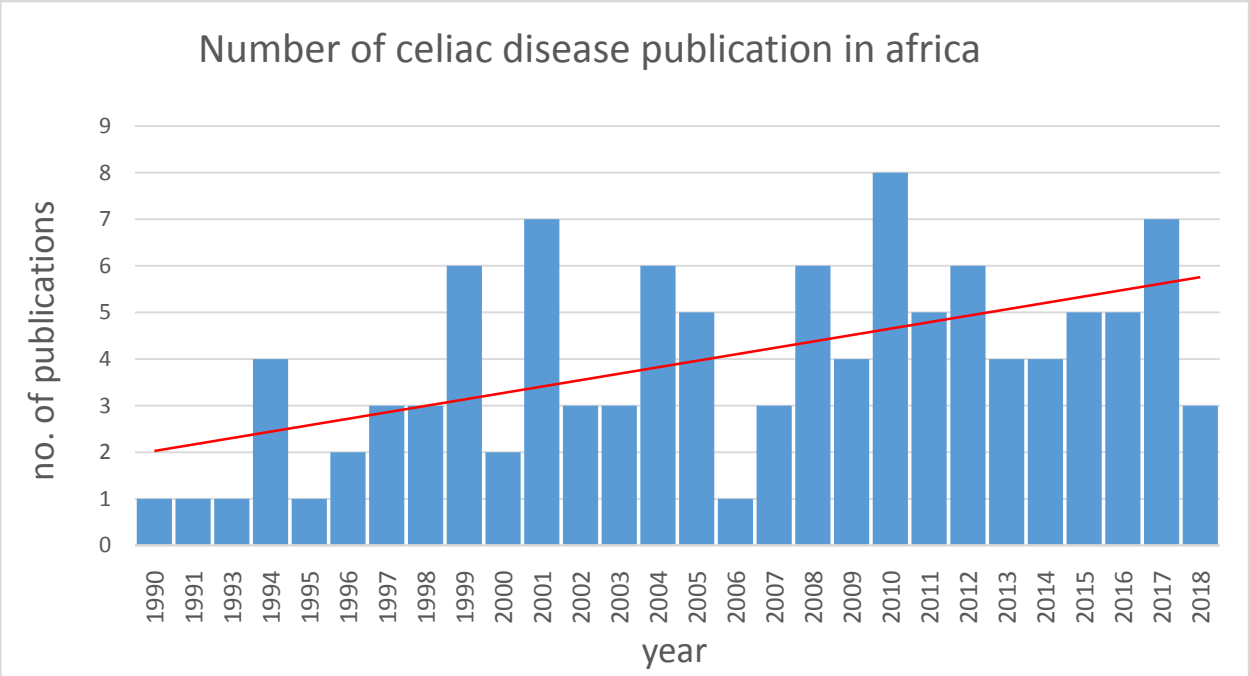

Figure 1. The increased number of Medline publications in the last decades on celiac disease in Africa. (Adapted from Pubmed.gov)

2. Recent African Geo-epidemiology of CD

2.1. Incidences and Geographical Gradient

The true incidence of CD in Africa is unknown, but for sure, it is underestimated for multiple reasons. Lack of awareness, limited resources, unexperienced nursing and medical stuff, lack of diagnostic laboratories and equipment, biased epidemiological screening of low/high risk CD populations are some of the suggested reasons [4,5,6,7,8]. Contrary to the developed world, serious informative gaps in the prevalence rates of CD exist in the developing countries in Africa. In a recent systemic review and meta-analysis the prevalence rates for CD were 0.5% in Africa, compared to 0.4% in South America, 0.6% in Asia and 0.8% in Europe and Oceania [9]. According to Lionetti et al, the reported prevalences from North Africa were 0.5% from Egypt, 0.8% from Libya, and 0.6% from Tunisia [10]. An exception was reported from Burkina Faso with 0% and the surprise came from Algeria- the Saharawi population of Arab-Berber origin had the world record CD incidence of 5.6% [10,11,12,13,14]. It appears that the differential incidence follows a North-South gradient in Africa which remind on the North-South trend in CD [1] and in autoimmune diseases in general [2]. Interestingly, the West –East CD gradient was not described in Africa [9]. Most of the reported CD African studies originated from the Northern parts and very few were done in its Central-Southern half of the continent [9,15].

2.2. HLA-DQ 2/8 and Wheat Consumption Distributions

Lack of resources needed to perform HLA genotyping prevent multiple African countries to apply the new ESPGHAN diagnostic criteria [16]. In fact, in a recent Mediterranean study, no one of the four participating African countries performed HLA, for CD diagnosis [7].

In a seminal study, the HLA-DQ2/8 was reported [10]. The frequency of DQ2 was increased in Northern African populations: Saharawi (39%), Libya (34%), Algeria (28.3%), Tunisia (23.4%), Morocco (25%), compared to sub-Saharan countries: Rwanda (15.5%), Tanzania (13.5%) and Cameroon (7%). The North-South HLA-DQ2 gradient follows in parallel the wheat intake in the corresponding countries. North African populations consume higher gluten rich diets [10]. It can be concluded that the majority of the sub-Saharan countries are less susceptible to CD than the Northern African states. The higher prevalence in the North are not surprising since wheat and barley are major staple foods for the Maghreb populations. Most probably, the current trend of dietary Westernization in Africa will induce a surge in CD diagnosis in the central and Southern part of the continent. As forwarded by Catassi et al, we are witnessing a recent evolutionary event that started 10000-14000 years ago, when wheat was discovered and domesticated in the Fertile Crescent and diffused through the Middle East into Africa [17,18]. Finally, most recently the African orphan crops that evolved under abiotic stresses display beneficial traits, being gluten free: Tef and Millets, thus opening hopes to facilitate local compliance to gluten free diet [19,20].

2.3. Clinical Presentation

It is difficult to sort out the major clinical manifestations in each country along Africa, but it seems that the most prevalent symptoms are gastrointestinal. Summarizing Libya and Egypt, the most prevalent clinical presentations were weight loss and failure to grow (57-100%), followed by diarrhea (45-59%), abdominal distension and flatulence (18-61%) and the short stature (7.7-45%) [5]. Screening four African Mediterranean countries and additional 10 non-Africans centers for CD symptoms, diarrhea or no symptoms stood out (21-25%), followed by failure to thrive (17%) and abdominal pain (12%) [7]. A glimpse on African CD symptomatology can be withdrawn form a Mediterranean survey were 5 north African centers participated [6]. The frequencies of symptoms in the African countries were: vomiting (62%), chronic diarrhea (54%), weight loss (37%), food refusal (30%) and anemia (17%). Intriguingly, between the CD affected Saharawi refugees, abdominal pains and height-for-age were significantly more common compared to local controls, and hemoglobin levels tended to be lower [13]. It appears that the symptomatology between the Saharawi children is particularly severe, manifested by chronic diarrhea, anemia, stunting, lactose intolerance, dental abnormalities, abdominal pains, infertility in adults and multiple nutritional deficiencies [13].

The above cited symptomatologic % are biased since the areas are heavily contaminated by infectious agents, malnutrition is prevalent and medical resources surveys are limited.

2.4. Diagnosis Is Underestimated

It is generally cited that the diagnosed/undiagnosed is 1/7-9 in the Western societies. It will be logical to assume that the ratio is lower in the African continent. Multiple raisons may explain this diagnostic gap. Lack of CD awareness, poor counties with minimal resources, unexperienced medial stuff, limited serological and genetic laboratories, overlap with local infections, malnutrition and stunted growth, differential genetic phenotypes and non-compliance with ESPGHAN diagnostic criteria, are some of them.

2.5. Compliance to Gluten Free Diet

Under the African contexts, Gluten free diet is often based on the available nutrients, most of them uncertified, as compared to the developed countries. The “tough alley in torrid time” of the diet in the Western world is more pronounced in Africa [20]. More so, cross-contamination with gluten or hidden gluten is difficult to avoid, a phenomenon extensively described even in gluten free oat products [21]. The inadequacy and low availability of gluten free products intermingles with the shortage of economical means and the lack of CD oriented dietician network, facing present and future CD burden [4,5]. A very interesting study explored the Saharawi CD children salivary microbiota when their diet was switched from African to Italian-style gluten free diet [22]. The initial African microbiotic equilibrium was perturbated, microbial diversity reduced and the metabolome distorted toward metabolic dysfunction. The study highlight the close interaction between human diet and its microbiome and

stress the consequences of dietary westernization in Africa [22]. Taken together, gluten withdrawal is more problematic in Africa, especially in the northern countries were wheat and barley are the major staple foods and more research should be implemented before applying Western gluten free products on the African CD patients. It is conceivable that adopting local African gluten free prolamins might be the solution [19,23].

2.6. Autoimmune Disease Associations/Complications

When CD associated conditions were review in the Mediterranean countries, where 4/14 were from North Africa, thyroiditis (5.7%), type 1 diabetes (3%) and dermatitis herpetiformis (1.5%) were found [7]. In Egypt, the serological prevalence of CD in type 1 diabetes patients was 5.48%, interestingly no CD was depicted between autoimmune thyroid patients [24]. Comparable prevalence was reported recently in South Africa [25] and Tunisia [26]. The prevalence of Graves' disease was 1.86% in biopsy proven CD in Tunisia [27] and association of CD with rheumatoid arthritis, from Morocco [28,29] and severe osteomalacia from Morocco and Tunisia were described [30,31,32]. Polyautoimmunity encompassing CD, diabetes and Crohn's disease from Algeria [33], CD and aplastic anemia from Tunisia [34], reproductive disorders from Morocco [35], cardiomyopathy and pleuro-pericarditis from Tunisia [36,37,38,39] and CD associated malignancies from Morocco and Algeria [40,41], were reported. Another gluten depended condition, gluten ataxia was recently documented in Algeria [42]. Interestingly, many of those case or series reports were published in the CD dedicated International Journal of celiac disease. Some more CD complications described from Africa are listed in Barada et al [5]. Finally, transient post infectious, false positive CD serology was described in two children from Algeria [43]. The false positivity of IgA anti transglutaminase antibodies was well reported [44,45].

2.7. CD Burden

Few reports addressed the future burden of CD in Africa [4,5]. They predict that in the near future, even in the present decade, CD burden will increase tremendously. Only few African countries are ready to face the coming CD epidemic alone. According to Greco et al, the population growth rates in Algeria (1.2%), Egypt (2%), Libya (2.2%), Morocco (1.1%), and Tunisia (1%), will keep the African populations young and those growth rate are far above the average around the Mediterranean see [4]. Taken, for example Egypt, the estimated number of celiac patients in 2011 was 817135. In 2021, there will be an estimate of 999311 CD patients, one third being in the pediatric age group. The total cost (in Euro) of symptomatic CD patients in 2021 is estimated to be 123,410,460 in Algeria, 277,930,013 in Egypt,49,308,935 in Libya, 80,872,769 in Morocco, and 45,583,796 in Tunisia [4]. When Egypt is taken as an example, the excess celiac deaths in 2021 is estimated to be 39,013 people. Multiple raisons exist for this huge burden and the difficulties of the corresponding authorities to coop with its consequences. The fast growing populations, the increase % of young citizens, the unawareness of CD diagnosis, the lack of health infra-structure and medical, nursing and dieticians CD oriented professionals, the lack of economic resources, the rate of malnutrition and infectious diseases that mask CD clinical manifestations, the quantity and quality health provision gaps between the urban and the rural areas and the lack in diagnostic laboratory contribute to enormous morbid and mortal human cargo that the African CD population will impose on the responsible heath authorities and the national governments.

3. Conclusions

African continent is emerging in the last decades. A lot of local and international effort are dedicated to combat the infectious load and improve public health and quality of life. But, as in the Western societies, allergic, cancer and autoimmune diseases are increasing. The same trend is evolving in CD. At least in the Maghreb countries the disease incidence, phenotype and epidemiology appear to resemble the developed world. However, lack of awareness, resources and qualified health care professionals, change of dietary habits, poverty, illiteracy, malnutrition and infectious load are at the heart of the problematic situation. Lack of deliberate policy toward coping with the current underdiagnosis and inadequate nutritional therapy of CD and the future disease burden should be addressed as early as possible. It is hoped that the present review will encourage mapping CD geo-epidemiology, aiming to improve the ways to deal with the African CD enigma.

Statement of Competing Interests

No grant support and no conflicting interests.

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