



CODEN [USA]: IAJ PBB

ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

<http://doi.org/10.5281/zenodo.1479832>

Available online at: <http://www.iajps.com>

Review Article

PREVALENCE OF CELIAC DISEASE AND ITS ASSOCIATED RISK FACTORS AMONG CHILDREN IN THE KINGDOM OF SAUDI ARABIA: A SYSTEMATIC REVIEW

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Abstract:

Objectives: To assess the epidemiological data for reporting the prevalence, risk factors and the common symptoms of celiac disease among children in the kingdom of Saudi Arabia. **Methods:** Two electronic database named PubMed and Google scholar were used to collect the suitable literature for this systematic review by using appropriate key words and filters were applied in all possible ways. **Results:** A total of 40 literatures were identified from the above mentioned two databases and only 20 were appropriate and after reading the abstract only 7 literature were found to be suitable and one more paper from the references were taken so total of 8 literatures were included in this systematic review. The prevalence of celiac disease on Saudi children varies between 1.5 % to 18.5 % and the common symptoms were found to be abdominal pain, vomiting, diarrhea and constipation. The study also found that children with type 1 diabetes and autoimmune thyroid disease were suffering from celiac disease. **Conclusion:** The prevalence of celiac disease on pediatric population is quite high in the kingdom of Saudi Arabia so there is a necessity for establishing the routine screening among the children especially on the high risk groups in the kingdom of Saudi Arabia for preventing the complications of celiac disease.

Key words: Celiac Disease, Children, Prevalence, Risk factors, Saudi Arabia.

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Please cite this article in press Yasser Awadh Ayed Alasmari et al., *Prevalence of Celiac Disease and Its Associated Risk Factors among Children in the Kingdom Of Saudi Arabia: A Systematic Review.*, Indo Am. J. P. Sci, 2018; 05(11).

INTRODUCTION:

The term celiac disease was initially introduced in the year 1887 and it is defined as the lifelong immune mediated disease. It is also known as the disease that affects multiple systems. The persons who are vulnerable hereditarily are at risk of developing celiac disease and the disease is activated by gluten and other associated prolamins [1-3]. The symptoms of celiac disease considerably not similar from one individual to another. The patients with celiac disease are more likely to have a gastrointestinal symptom that includes diarrhea, vomiting and steatorrhea. Apart from that several other symptoms such as fatigue, irritability, depression, anxiety, dermatitis, herpetiformis, anemia, osteoporosis, neurological problems and dental enamel hypoplasia are also seen among the patients with celiac disease [4-6]. Celiac disease is mainly induced by the protein named gluten that is predominantly high in wheat, rye and barley. The incidence of celiac disease varies from one country to another based on the agricultural patterns. The incidence of celiac disease is quite high in India because wheat is considered to be a basic diet in most of the states [7]. However the cases of celiac disease are also reported highly in Iran due to high consumption of wheat among the population [8,9]. Overall one percentage of the population across the world suffers from celiac diseases however females are three times more likely to develop celiac disease in comparison with male population¹⁰. According to the latest research the prevalence of celiac disease has increased over a period of years and approximately 1-3% of the populations in the European countries are suffering from celiac disease¹. Similarly various studies that have been carried out among the children also reported the prevalence of celiac disease ranges from one case per 93 children to one case per 500 children which was extremely high [11-16]. Likewise the research that was conducted among the pediatric population reported that the average age of diagnosing the celiac disease has sharply increased from less than 2 years and upto 9 years in many developed countries across the globe [17]. More importantly several research studies that were carried out reported that the risk of malignancy among the celiac patients had considerably increased [18-22]. A Cohort study was carried out in the year 2016 among the children in the kingdom of Saudi Arabia which reported that approximately 2.2 % of the children were suffering from celiac disease [23]. The study conducted by Aljabreen et al in three regions of Saudi Arabia named Aseer, Madinah, and Al- Qaseem among the school students aged between 16 to 18 years found a prevalence rate of celiac disease ranges from 1.8 % to 3.2 % respectively [10]. Similarly another study conducted by Maher M. Al

Hatlani in eastern province of kingdom of Saudi Arabia reported a prevalence rate of celiac disease of about 1% among the children aged between 6 to 18 years²⁴. The etiology of celiac disease among the children is not fully known however there is a role of multiple factors such as environmental conditions, infectious agents that includes rotavirus, absence of breast feeding, introduction of food that contains gluten to infants during weaning process etc [25-27]. There is no review done in kingdom of Saudi Arabia which aimed at assessing the Prevalence of celiac disease and its associated risk factors among children. Celiac disease unawareness is common among the patient's especially in children and can lead to serious consequences in spite of lack of symptoms. Therefore the current study aimed at conducting a systematic review of the present epidemiological data in order to report the prevalence of celiac disease among children in the kingdom of Saudi Arabia.

METHODOLOGY:

The literature search was performed by using the electronic database "Pub Med" and "Google Scholar". The key words like Celiac Disease, Children and Saudi Arabia were used. The alternative search terms such as "Anti-tissue transglutaminase IgA (IgA-tTG) and anti-tissue transglutaminase IgG (IgG-tTG), anti-tissue transglutaminase (IgG/IgA) "and Saudi Arabia were used to collect the relevant literature. The filters were set for studies related to humans and the languages were limited to English. The attempt was made to collect all the literature related to celiac disease so the time limit was not set. The articles were screened for relevance by reading the title and abstract. The studies included in the analysis that fulfills the following criteria.

1. Prevalence of Celiac Disease
2. Children with Type 1 Diabetes
3. Children with short stature
4. Dietary Adherence to Gluten-Free Diet among Saudi Children
5. Celiac Disease in Saudi Children

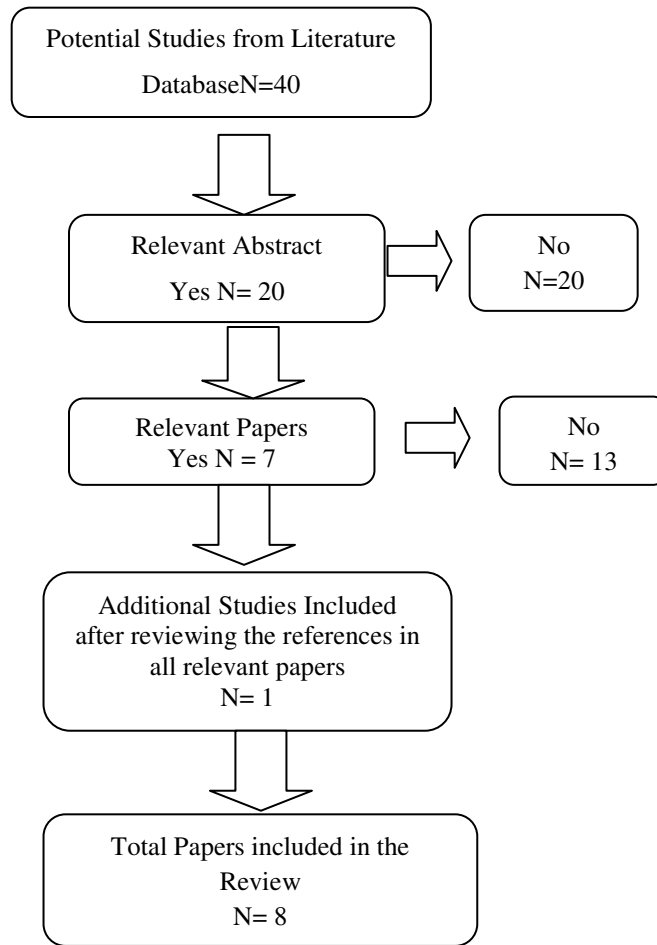
If the studies were not about the above mentioned items they were excluded and in addition to that the studies were excluded if they were

1. Celiac Disease among adults
2. Editorials
3. Overview of Celiac Disease
4. Quality of life among patients with celiac disease
5. Treatment of celiac disease

Data were extracted only from the full text articles which include Sample Size, age of the children, prevalence of celiac disease, risk factors and symptoms of the celiac disease among the target

population.

RESULTS:



[Fig: 1] Process of selection of articles to be included in the review

Two electronic databases named PubMed and Google Scholar were searched and identified a total of 40 records and out of 40 studies only twenty articles were relevant after reading the abstract and the remaining twenty were excluded. Out of 20 abstract screened only 7 were considered to be appropriate and the remaining 13 were excluded because it was Celiac Disease among adults, Editorials, Overview of Celiac Disease and the journal articles related to Quality of life among patients with celiac disease and Treatment of celiac disease. Additionally one more paper from the references was included in the study. Overall a total of eight papers were included in this review.

Study Character

The Eight articles included in the systematic review were original research papers. The earliest study was published in the year 2002 and the latest was published in 2017 so the research studies included in

The review has a research span of about 15 years. Overall information regarding the Sample Size, age of the children, prevalence of celiac disease, risk factors and symptoms of the celiac disease among the target population were extracted from all the original studies.

All of the eight studies were cross-sectional study looking at the prevalence of celiac disease among children in the kingdom of Saudi Arabia. [With reference to Table 1].

The latest study was carried out by Anjum Saeed et al in 2017 found that 59 children had celiac disease and the median age among the children was 8 years and the study also revealed that the mean duration of symptoms before diagnosing the disease was more likely to be 2.3 (± 1.5) years. The study also presented that around 70% of the children belong to high risk

groups who were having risk factors for celiac disease that includes type-1 diabetes, autoimmune thyroiditis, Down syndrome and siblings. The most common symptoms that were reported among those children includes failure to thrive, short stature, abdominal pain and chronic diarrhea. The researchers also carried out laboratory investigation which discovered Anti-tissue transglutaminase antibody was positive among 91.5% of the children. Furthermost there was no statistical significance observed between children with classical disease and non-classical disease. The study concluded that the children with high risk should be screened as early as possible in order to evade the complications that are associated with untreated celiac disease [28].

Another study conducted by Abdulrahman Al-Hussaini et al in Riyadh found that the prevalence of celiac disease among the children was about 1.5% and the mean age among the children was 11.5 years. The quite interesting finding of the study was that more female children were having celiac disease compared to male children. The study also found that the children were having mild gastro-intestinal symptoms that include abdominal pain, vomiting, constipation and diarrhea. This paper also pointed out that around 48% of children with celiac disease were overweight or obese. The study concluded that the prevalence rate of celiac disease among the children in the kingdom of Saudi Arabia was quite high in comparison with the European and North American countries [29].

Similarly a study conducted by Ahmed Al Sarkhy et al in 2015 reported that the mean age of children with celiac disease was 9.9 years and mean age of onset of disease was 5.5 years. The study also presented that the mean age at diagnosing the disease was 7 years. Most important finding of this study was approximately 55% of children reported with celiac disease were females. The study also informed that the children were having more of gastro-intestinal symptoms that include chronic abdominal pain, abdominal distension, gases, bloating and chronic diarrhea. Poor weight gain was also reported among the children with celiac disease. The study concluded that diagnosing the disease at the earlier stage was recommended in order to have an improved rate of adherence [30].

A prevalence study conducted by Maher M. Al Hatlani found one percentage prevalence of celiac disease among the children. The researchers used biopsy as a tool for confirming the celiac disease. The study was carried out in nine public schools of the military campus of National Guard in the Eastern

Province of Saudi Arabia. The school students were screened for celiac disease using anti-tissue transglutaminase IgA (IgA-tTG) and IgG antibodies (IgG-tTG). The study recommended that there is a need for mass screening among the school children for celiac disease and the researcher also advocated that early diagnosis and restricting the diet can prevent the complications that are associated with celiac disease among the children [24].

A study for finding the Seroprevalence of celiac disease among the adolescents was conducted by Abdulrahman M Aljebreen et al in the year 2013. The study has been carried out in three different regions of Saudi Arabia namely Aseer, Madinah and Al-Qaseem. The study reported a higher prevalence of celiac disease in the Al-Qaseem region which was about 3.2% followed by Aseer 2.1% and the least prevalence rate was observed in the Madinah region which was about 1.8%. The study also found that the prevalence rate of celiac disease varies according to the region which was also statistically significant. The study suggested the need for conducting a mass screening among all the school children in the kingdom of Saudi Arabia for early diagnosis of celiac disease [10].

A hospital based study conducted by Nasir A.M. Al-Jurayyan et al revealed that 4.5% of the children were having celiac disease. The study also reported that the children were belonging to the age group ranges between 2.6 to 14 years. The researchers also found that the most common cause of celiac disease among the screened children was genetic and apart from hereditary problems several endocrine and non-endocrine causes were noted among the children. The most important finding of the study was more female children were suffering from celiac disease than male children. The study concluded that there is a necessity for serological examination among all the school children for better diagnosis of celiac disease at the earlier stage [31].

A study conducted by Omar I. Saadah et al described that the prevalence of celiac disease among the screened children was quite high about 11.2%. The median age of children at the time of screening was 10.7 years. The study also presented that female children were more likely having the celiac disease in comparison with the male children. The most common symptom that was observed among all the children with celiac disease was poor weight gain and it was statistically significant. The study also found that anemia, low albumin level and autoimmune thyroid diseasewere the common risk factors among the children reported to be positive with celiac

disease and a positive correlation was also observed between the above mentioned risk factors and the celiac disease. The study projected a valid recommendation of screening the school children with serological examination for better diagnosis of celiac disease [32].

A study done by Rabab Ali Al Attas found that the prevalence rate of celiac disease among the children was 7.6%. The mean age among the screened children was 4 years. The study also revealed that the children with celiac disease were having several risk

factors that include autoimmune hepatitis, autoimmune gastritis and autoimmune thyroid disease. The most common symptoms reported among the children with celiac disease were chronic diarrhea, failure to thrive, chronic abdominal discomfort and short stature. The study also pointed out that the prevalence of celiac disease was quite high among the children with autoimmune thyroid disease. The researchers also described that there is a mandatory need for screening all the children for celiac disease for early diagnosis and outstanding prognosis [33].

Table: 1: Prevalence, Risk factors and Symptoms of Celiac Disease among children in Kingdom of Saudi Arabia

S. No	Authors	Sample Size	Mean/ Median Age of Children	Risk factors for Celiac Disease	Prevalence rate of Celiac Disease	Reported Symptoms of Celiac Disease
1	Anjum Saeed et al, 2017 (28)	318	8 Years	Type-1 diabetes autoimmune thyroiditis and Down syndrome	18.5 % (59/318)	Failure to thrive short stature abdominal pain and chronic diarrhea
2	Abdulrahman Al-Hussaini et al, 2017 (29)	7930	11.5 Years	Type-1 diabetes and overweight	1.5% (119/7930)	Abdominal pain vomiting constipation and diarrhea
3	Ahmed Al Sarkhy et al, 2015 (30)	113	9.9 Years	Family history of celiac disease consanguinity and Insulin dependent diabetes mellitus (IDDM)	6.2% (7/113)	Chronic abdominal pain abdominal distension gases bloating and chronic diarrhea
4	Maher M. Al Hatlani, 2015 (24)	1141	11 Years	Type-1 diabetes and overweight	1 % (10/10)	No Gastro-intestinal symptoms
5	Abdulrahman M Aljebreen et al, 2013 (10)	1167	16.6 Years	Consanguinity and heavy gluten ingestion	2.2% (26/1167)	No Gastro-intestinal symptoms and other symptoms
6	Nasir A.M. Al-Jurayyan et al , 2013 (31)	110	2.6 to 14 Years	Hereditary problems several endocrine and non-endocrine causes	4.5 % (5/110)	No Gastro-intestinal symptoms and other symptoms
7	Omar I. Saadah et al , 2012 (32)	430	10.7 Years	Anemia low albumin level and autoimmune thyroid disease	11.2% (48/430)	Abdominal pain abdominal distension vomiting and diarrhea
8	Rabab Ali Al Attas , 2002 (33)	145	4 Years	Autoimmune thyroid disease	7.6% (11/145)	No Gastro-intestinal symptoms and other symptoms

DISCUSSION:

According to the authors knowledge no systematic review was done to assess the prevalence of celiac disease and its associated risk factors among children in the Kingdom of Saudi Arabia. Thus the result of the systematic review showed that the prevalence of celiac disease among the children in the kingdom of Saudi Arabia varies from 1.5 % to 18.5 %. The current study prevalence is much higher than the prevalence rate among Asians [34]. A study conducted in Sweden among the children regarding the celiac disease reported a prevalence rate that ranged between 0.35 % to and 1.3% which was comparatively lesser than the current study results [35]. Similarly a study conducted among the Italian school children which reported a prevalence rate of celiac disease that varies between 0.43% to 0.94% which was a very minimal in comparison with this study [36]. However more or less the above mentioned percentage of prevalence rate of celiac disease was reported among the non-European countries that includes New Zealand [37], Australia³⁸, Brazil³⁹ and Argentina [40] which was entirely contradicting and quite fewer than the prevalence rate found in this present study. In comparison with the prevalence rate of celiac disease in Arab Countries outside Saudi Arabia a study conducted among the Turkish school [41] children reported only 0.47% of prevalence rate of celiac disease which was very small than the prevalence of celiac disease among children in the kingdom of Saudi Arabia. Similarly a study conducted in Tunisia among the school children reported a prevalence rate of 0.64% of celiac disease which was also lesser than this study results⁴². A study done in Italy by Catassi et al stated that the prevalence of celiac disease among the school children was 0.48% which was smaller than the prevalence rate in kingdom of Saudi Arabia⁴³. Similarly a study carried out among the Iranian school children [44] estimated the prevalence rate of celiac disease as 0.5% and another study done by Mäki et al [45] on Finnish school children found 1% of prevalence rate of celiac disease. However both the above mentioned study results were slighter in comparison with the present study. A study conducted by Alarida et al among the Libyan school children [46] described the prevalence rate of celiac disease as 1% and likewise a study by Karagiozoglou- Lampoudi et al [47] on Greek children reported a prevalence rate of celiac disease as 0.65% and a similar kind of study carried out by Nusier among the school children in Jordan found a prevalence rate of celiac disease as 0.8% [48]. Nevertheless the results of the above mentioned three studies were very minimal in contradiction of the results of the present study. The unique finding of

this study is the prevalence of celiac disease is quite higher in female children in comparison with the male children. The most common clinical symptoms reported in the current study are abdominal pain vomiting constipation and diarrhea which is more or less same in the studies that were conducted in the last few years about celiac disease among the school children [49-53].

CONCLUSION:

The study results proved that the prevalence of celiac disease among the children in the kingdom of Saudi Arabia ranges between 1.5 % to 18.5 % which is quite high. Type 1 diabetes, consanguinity and autoimmune thyroid disease were found to be the most common risk factors among the children with celiac disease. Abdominal pain, vomiting, constipation and diarrhea were the symptoms more often reported by the children with celiac disease. Thus there is a need for routine screening along with serological examination among the school children in the kingdom of Saudi Arabia for early diagnosis and enhanced prognosis.

Conflict of interest:

There is no conflict of interest.

Source of Support:

Nil

Acknowledgements:

None

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