Screening for Cow Milk Allergy among Young Egyptian Children

Thesis

Submitted for Partial Fulfillment
of Master Degree in ***Pediatrics***

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2020

سورة البقرة الآية: ٣٢

Acknowledgments

First and foremost, I feel always indebted to ***Allah*** *the Most Beneficent and Merciful.*

I wish to express my deepest thanks, gratitude and appreciation to ***Prof. Zeinab Awad****, Professor of Pediatrics, Ain Shams University, for her meticulous supervision, valuable instructions and generous help.*

Special thanks are due to ***Dr. Rasha Hassan****, Associate Professor of Pediatrics &* ***Dr. Hanan Abd El Lateef****, Lecturer of Pediatrics, Ain Shams University, for their sincere efforts, fruitful advice and encouragement.*

I am always indebted to my parents for their endless devotion, outstanding support, and sincere help and guidance.

Last but not least I express my gratitude to the patients and their families for their kind cooperation.

Ahmed Samir Ali Hammouda

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List of Abbreviations

Abb.	Full term
AAF	*Amino acid formula*
AD	*Atopic dermatitis*
AR	*Allergic rhinitis*
BA	*Bronchial asthma*
CAP-RAST	*Cow's milk allergy protein-Radio allegro sorbent test*
CMF	*Cow's Milk Formula*
CMPA	*Cow's Milk Protein Allergy*
CMPs	*Cow's Milk Proteins*
CoMiSS	*Cow's Milk related Symptom Score*
DBPCFC	*Double blind placebo-controlled oral food challenge*
DRACMA	*Diagnosis and Rationale for Action against Cow's Milk Allergy*
DSCG	*Oral sodium cromoglycate*
eHF	*Extensively Hydrolyzed (Milk) Formula*
EoE	*Allergic eosinophilic oesophagitis*
FNR	*False negative rate*
FPIAP	*Food protein-induced allergic proctocolitis*
FPIES	*Food protein –induced enterocolitis syndrome*
FPR	*False positive rate*
Ig E	*Immunoglobulin E*
IgG	*Immunoglobulin G*
LR-	*Negative likelihood ratio*

List of Abbreviations cont...

Abb.	Full term
LR+	*Positive likelihood ratio*
NICE	*National Institute of Health and Care Excellence*
NPV	*Negative predictive value*
OCT	*Oral challenge test*
OIT	*Oral immunotherapy*
pHF	*Partialy Hydrolyzed (Milk) Formula*
PPV	*Positive predictive value*
sIgE	*Specific IgE*
SPT	*Skin prick test*
UK	*United Kingdom*
WHO	*World Health Organization*

INTRODUCTION

Globally, the prevalence of food allergy and food intolerance is increasing and it is an important public health problem affecting children. Most patients with a food allergy that developed during infancy achieve resolution in childhood but food intolerance usually persists until adulthood ***(Wiparat and Pornthep, 2018).***

The cow's milk protein allergy (CMPA) is the most common form of food allergy in early childhood, and its prevalence has been on a steady rise over the years ***(Savage and Johns, 2015).*** Since infants are exposed to cow's milk protein in the maternal diet if breastfed and via infant formula, cow's milk is the most common cause of food allergy and food intolerance, especially in young children ***(Venkataraman et al., 2018).***

The CMPA is said to occur in about **0.5 %** of exclusively breast-fed infants and between **2.0 - 5.0 %** in CMP formula fed infants ***(Simons et al., 2015).***

Parents perceive CMPA in their children far more often than can be proven by oral food challenge; however, true CMPA does seem to peak in the first year of life, with a prevalence of approximately **2%** to **3%** in the infant population. This prevalence then falls to **<1%** in children **6** years of age and older ***(Koletzko et al., 2012).*** The highest rate

of initial onset food allergy is seen in infants less than one year; the rate decreases rapidly thereafter, and most food allergy cases in older age groups are a result of accidental ingestion ***(Ebisawa et al., 2017).*** A few exclusively breast-fed infants may also develop clinically significant CMPA via dairy protein transfer into human breast milk ***(Koletzko et al., 2012).***

In Egypt because of cultural and financial reasons, cow's milk and its products is introduced to the infants very early from the age of 2 months or even immediately after birth, owing to the low cost of these products and the wide availability that motivate their use ***(El-Zanaty, 2009)***.

There are insufficient published data on the prevalence of CMPA in Egypt. The frequency of CMPA in Damietta Governorate in infants in the first two years of life is **3.4%**, and the IgE-mediated CMPA was more common, as **67.6%** of cases had IgE-mediated CMPA and **32.3%** of cases had non-IgE-mediated CMPA ***(Maksoud et al., 2019).***

Aim of the work:

The aim of this study was to estimate the frequency of CMPA among young Egyptian children in a trial to delineate the magnitude of the problem in Egypt.

REVIEW OF LITERATURE

Cow's Milk Protein Allergy

Food allergy is defined as an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food, and usually involves the production of food-specific IgE antibodies, although other cells of the immune system can also be implicated ***(Sicherer and Sampson, 2014).*** On the basis of a large scale epidemiological survey in Japan, the prevalence of food allergy is estimated to be **5-10%** in infants, **5%** in young children, and **4.5%** in school children ***(Ebisawa et al., 2017).*** Food intolerance is a nonimmune reaction mediated by metabolic, toxic, pharmacologic or undefined mechanisms ***(Sicherer and Sampson, 2014).***

The CMPA is a hypersensitivity reaction initiated by specific immunologic mechanisms. In most children with cow's milk allergy, the condition can be immunoglobulin E (IgE)-mediated and is thought to manifest as a phenotypical expression of atopy, together with (or in the absence of) atopic eczema, allergic rhinitis and/or asthma. A subset of patients, however, have non-IgE mediated (probably cell-mediated) allergy and present mainly with gastrointestinal symptoms in reaction to the ingestion of cow's milk ***(Fiocchi et al., 2010).***

The symptoms of CMPA can be confused with other disorders that present similar clinical features, such as lactose intolerance, infectious gastroenteritis, celiac disease, non-celiac gluten sensitivity, inflammatory bowel disease, eosinophilic gastroenteritis, and pancreatic insufficiency ***(Heine et al., 2017).***

Lactose intolerance generally develops later in life, but can present in young patients in severe cases. It is due to an enzyme deficiency (lactase) and not allergy ***(Szilagyi and Ishayek, 2018).***

Celiac disease is caused by a permanent intolerance to gluten (present in wheat, rye, barley and oats), is neither an allergy nor simply intolerance, but a chronic, multiple-organ autoimmune disorder primarily affecting the small intestine ***(Szilagyi and Ishayek, 2018).***

It is important to not mix "CMPA" with "functional GI CM-related symptoms" because the middle to long term outcome of CMPA versus functional GI disorders differs substantially. Functional GI symptoms tend to improve much faster. Infantile colic and crying starts to decrease by the age of three to four months. The frequency of regurgitation drops sharp from the age of six months onwards. Functional constipation, on the contrary, does not tend to disappear spontaneously over time. Thus, prognosis and long-term outcome differ for allergy or a functional GI disorder. One

should not overlook that any of these manifestations can as well be caused by organic disease, different from allergy. A score, the Cow's Milk related Symptom Score (CoMiSS), was recently developed to raise awareness of health care professionals for this entity ***(Vandenplas et al., 2015).***

Cross-reactivity between milk proteins from different animal species:

Cross-reactivity between milk proteins (α-lactalbumins, ß-lactoglobulins, and caseins) from cow, buffalo, sheep, and goat is widespread ***(Spuergin et al., 1997).*** Thus, 92% of patients with allergy to cow's milk proteins showed a reaction to goat milk ***(Bellioni-Businco et al., 1999).*** In contrast, only 4% of children with allergy to cow's milk showed clinical reactivity to mare milk ***(Businco et al., 2000).*** Nevertheless, there have been reports of allergy to sheep and goat milk without allergy to cow's milk proteins ***(Ah-Leung et al., 2006).*** Camel milk is a safe and tolerable alternative for CMPA patients above the age of one year ***(Nagy et al., 2013).***

Etiology & Risk Factors:

The rate of allergic sensitization varies according to the month of birth. Subsequently, it was found that cord blood IgE concentration showed a significant cyclic trend, with a peak near the end of April and a trough in late October. Further, the risk of food sensitization was observed to peak among individuals born in winter, while it was the lowest among those