COW'S MILK SENSITIVITY IN INFANTS AND CHILDREN WITH ATOPIC DERMATITIS AND URTICARIA

Thesis

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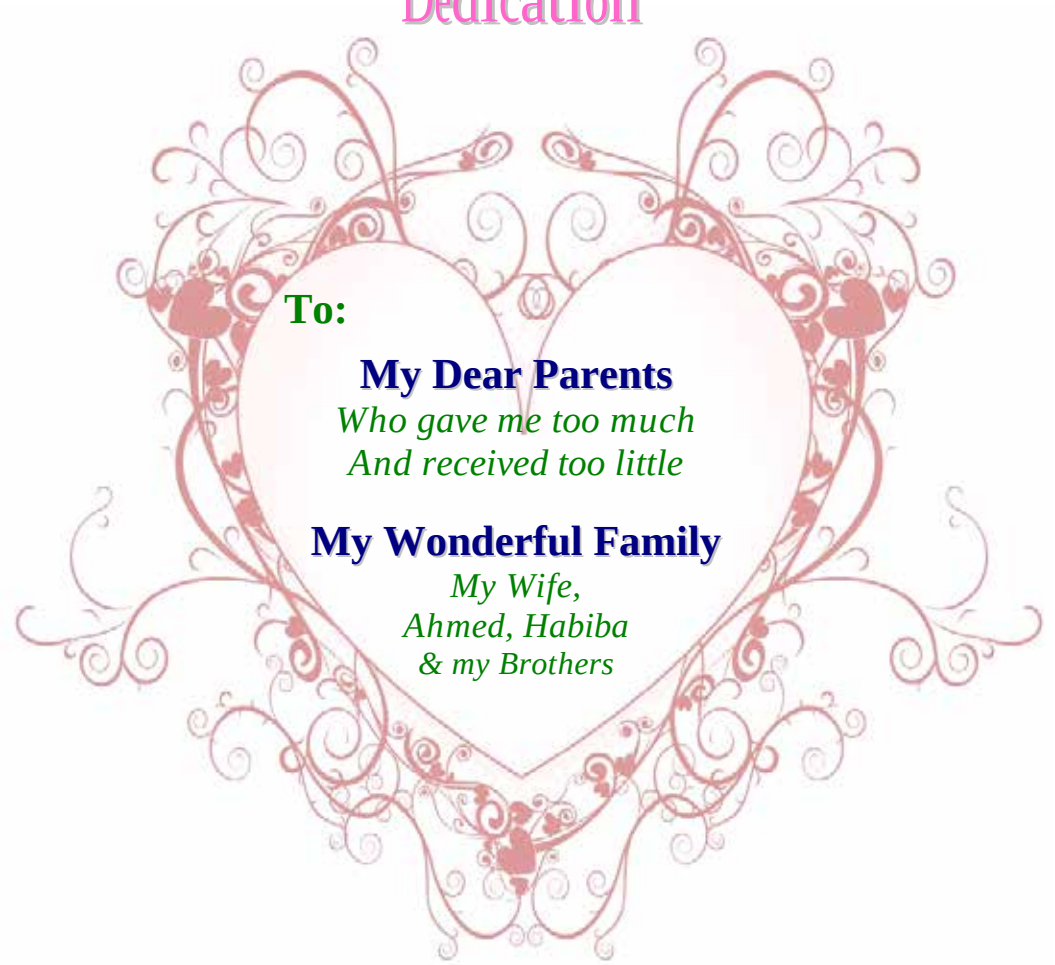
Dedication



To:

My Dear Parents

Who gave me too much
And received too little

My Wonderful Family

My Wife,
Ahmed, Habiba
& my Brothers

First, thanks to **ALLAH** *to whom I relate any success in achieving any work in my life.*

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Mohammad Borick

بسم الله الرحمن الرحيم

(رَبِّ أَوْزِعْنِي أَنْ أَشْكُرَ نِعْمَتَكَ الَّتِي
أَنْعَمْتَ عَلَيَّ وَعَلَى وَالِدَيَّ وَأَنْ أَعْمَلَ
صَالِحًا تَرْضَاهُ وَأَصْلِحْ لِي فِي ذُرِّيَّتِي
إِنِّي تُبْتُ إِلَيْكَ وَإِنِّي مِنَ الْمُسْلِمِينَ)

صدق الله العظيم

سورة الأحقاف الآية (١٥)

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List of Abbreviations

AD	*Atopic dermatitis*
APC	*Antigen presenting cells*
APT	*Atopic patch test*
BA	*Bronchial asthma*
BMC	*Bone mineral content*
BMD	*Bone mineral density*
CM	*Cow's milk*
CMA	*Cow's milk allergy*
CMH	*Cow's milk hypersensitivity*
CMI	*Cow's milk intolerance*
CMPA	*Cow's milk protein allergy*
CMS IgE	*Cow's milk specific IgE*
DBPC FCs	*Double blind placebo controlled food challenges*
EHF	*Extensively hydrolyzed formulas*
FN	*False negative*
FP	*False positive*
GALT	*Gut associated lymphoid system*
GER	*Gastroeosphageal refulx*
GIT	*Gastrointestinal tract*
IFN-γ	*Interferon-gamma*
IL-4	*Interleukin -4*
IQR	*Interquartile range*
NPV	*Negative predictive value*

OCT	*Open challenge test*
pHF	*Partially hydrolyzed formulas*
PPV	*Positive predictive values*
RAST	*Radio-allegrosorbent test*
SD	*Standard deviation*
SECP	*Serum level of eosinophil cationic protein*
S-IgE	*Specific IgE*
SIT	*Specific Immunotherapy*
SPTs	*Skin prick tests*
T reg	*Regulatory T cells*
TGF-β	*Transforming growth factor-beta*
TH	*T helper*
TN	*True negative*
TNF-α	*Tumour necrosis factor alpha*
TP	*True positive*
USA	*United States of America*

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INTRODUCTION

Food allergy affects between, 5-7% of children *(Arora and Kumar, 2003).* Cow's milk allergy (CMA) is the most common food allergy in young children; its prevalence is between 2-5%. About 3% of all newborns will suffer from CMA within first year of life. Although breast milk is the best to provide, up to 1.5% of breast fed will still develop CMA *(Suzanne et al., 2003).*

The symptoms of cow milk allergy may begin quickly after ingestion of cow milk as eczema, skin rash and abdominal cramps. Several hours later vomiting, diarrhea and abdominal cramps may develop. Constipation, failure to gain weight and gastro-esophageal reflux may appear later *(Yimyaem et al., 2003).*

Atopic eczema affects about 18% of infants in the first 2 years of life and the main cause is allergy to multiple foods *(Turjanmaa, 2002).* CMA and atopic eczema are predictors of allergic airway disease however its incidence as a cause for bronchial asthma is low *(Halken, 2003).*

Studies have shown that among different kinds of food allergens cow milk has almost always been one of the most common *(Pourpak et al., 2004).*

AIM OF THE WORK

The aim of this study was to estimate the frequency of CMA in infants and children with atopic dermatitis and urticaria in a trial to delineate the magnitude of the problem in Egypt.

COW'S MILK PROTEIN ALLERGY

Although cow's milk allergy (CMA) and cow's milk intolerance (CMI) are two different terms, they are often used interchangeably, resulting in confusion both in clinical practice and in research reports. CMA, also known as cow milk protein-allergy (CMPA) is an immunologically mediated reaction to cow's milk proteins that may involve the gastrointestinal tract (GIT), skin, respiratory tract, or multiple systems, i.e. systemic anaphylaxis. Even though it can cause severe morbidity and even fatality, dietary elimination is associated with a good prognosis. CMI refer to non immunologic reactions to cow's milk (CM), such as disorders of digestion, absorption, or metabolism of certain CM components. The most common cause of CMI is lactase deficiency *(Bahna, 2002).*

INCIDENCE:

The prevalence of atopic diseases is increasing worldwide. In developed countries they are about the commonest, chronic diseases, reaching between 15-30% of the population *(Ayuso et al., 2000).* Sensitization to food allergens has been implicated in pathogenesis of atopic diseases *(Wolkerstorfer, 2002).* Between 5% and 15% of infants show symptoms suggesting adverse reactions to cow's milk protein (CMP) at some time.

Differences in diagnostic criteria and study design contribute to the wide range of prevalence estimates and underline the importance of an accurate diagnosis, which will reduce the number of infants on inappropriate elimination diets. CMA is easily missed in primary care settings and needs to be considered as a cause of infant distress and diverse clinical symptoms *(Ewing and Allen, 2005)*.

CMPA can develop in exclusively and partially breast-fed infants, and when CMP is introduced into the feeding regimen. Early diagnosis and adequate treatment decrease the risk of impaired growth *(De Boissieu and Dupont, 2002)*. In a wide base study (5356 live birth), *Garcia et al. (2003)* estimated that the incidence of CMPA in the first year of life is at least 1.9%. Another wide base, long term study denoted 2.2% in the same age group *(Host et al., 2002).* It is clear that CMA is most prevalent in early childhood, with figures generally reported between 2 and 6% *(Garcia-Ara et al., 2004)*, and decreases into adulthood to an incidence of 0.1-0.5% *(Järvinen and Suomalainen, 2001)*.

CMA causes symptoms before 1 month of age, often within 1 week after introduction of CMP-based formula *(Host, 2002)*. CMPI is mostly acquired during late childhood or adulthood. It has high racial

predilection, being highest in dark skinned populations and lowest in northern Europeans *(Bahna, 2002).*

ETIOLOGY AND RISK FACTORS:

The type of immune reaction to food allergen depends on the quantity and frequency of doses and the age at introduction, and is also being influenced by genetic factors *(Saarien and Savilahti, 2000)*.

In an attempt to determine the quantity of food that elicits reactions during double blind placebo controlled food challenges (DBPCFCs) and to evaluate parameters that may predict the provocative dose and severity of reaction, *Jenmalm and his colleagues (2000)* found that food-allergic patients may react to as little as 100 mg of food, possibly less, and the dose causing a reaction and the severity of reaction is not predicted by the radio-allegro-sorbent test (RAST) for specific IgE detection.

A family history of atopy is a significant predictor for allergy *(Bjorksten, 2005)*. According to the literature, incidence of CMA without atopy in the family is about 12%. Incidence rises to 20% if both parents are atopic, and up to 72% if the parents have matching types of atopic disease (for example, both have eczema or hives) *(Salvatore and Vandenplas, 2002)*.

It was found that 41 - 73% of children with CMPA have a family history of atopy *(Korol and Kaczmarski, 2001).* In infants with two first-degree family members with atopic disease, the probability of developing allergy to cow's milk proteins during the first year of life was found to be 3.8% *(Sanz Ortega et al, 2001).*

In families with known allergies, it was suggested to counsel the mother if she intends to breast-feed to avoid the most highly allergic foods (milk, eggs, peanuts, and occasionally fish) in her own diet during the third trimester and while breast-feeding *(Nocerino and Guandalini, 2003)*. Regardless of whether breast-fed or formula-fed, in these families, introduction of solids should wait until the child is six months of age with a slow progression of new foods.

On the other hand, significant risk factors for the presence of cow's milk IgE antibodies in allergic infants may include long breast feeding, exposure to cow's milk at the maternity hospital and breast feeding during the first 2 months at home either exclusive or combined with infrequent exposure to small amounts of cow's milk *(Saarinen et al., 2002).*

A large study on 6209 subjects *(Saarinen and Savilahti, 2000)* found that prolonged breast-feeding may increase the risk of IgE-sensitization. Allergic IgE sensitization can occur as early as during the fetal