

## Comparison between General Pediatricians and Other Sub-Specialty of Pediatrics Regarding Knowledge of CMPA

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### ABSTRACT

**Background:** Food allergy is an adverse health effect arising from a specific immune response that occurs reproducibly following exposure to a given food. The main cause of food allergies in children under three years old is Cow's Milk Protein (CMP). The estimated prevalence of Cow's Milk Protein Allergy (CMPA) is 2% to 3% in the first year of life. An observational study conducted in pediatricians' offices revealed a gastroenterologist-diagnosed prevalence of 5% in the group of patients.

**Objective:** to compare between general pediatricians and other sub-specialty of pediatrician regarding awareness of cow's milk protein allergy.

**Patients and Methods:** This study was conducted in El-Sharkia Governorate, Egypt. Pediatricians of both sexes of different subspecialties work in government facility with or without private facility and work in El-Sharkia Governorate. The sample size calculated using open Epi was 256 physicians.

**Results:** This study showed that general pediatricians were 78.1%, gastroenterologists were 3.2%, immunologists were 2.7% and pulmonologists were 3.9%. There was a low level of knowledge about CMA among the studied group.

**Conclusion:** Our findings revealed that there was a low knowledge about Cow's Milk Protein Allergy among pediatricians. We found a huge variability in general pediatricians and other sub-specialty of pediatrics regarding CMPA.

**Keywords:** General pediatricians, Sub-specialty of pediatrics, CMPA.

### INTRODUCTION

Food allergy is an adverse health effect arising from a specific immune response that occurs reproducibly following exposure to a given food. The main cause of food allergies in children under three years old is cow's milk protein (CMP). The estimated prevalence of cow's milk protein allergy (CMPA) is 2% to 3% in the first year of life. An observational study conducted in pediatricians' offices revealed a gastroenterologist-diagnosed prevalence of 5% in the group of patients <sup>(1)</sup>.

The immune mechanisms involved in CMPA may be immunoglobulin (Ig) E-mediated (with production of Ig E-specific antibodies), which presents immediate symptoms such as urticaria and angioedema, or the non Ig E-mediated (T-cell mediated), which manifests through later reactions, such as vomiting, diarrhea, colic and intestinal constipation. Mixed reactions (immediate and late) can also occur, such as eosinophilic esophagitis, eosinophilic gastroenteropathy, atopic dermatitis and asthma. The diagnosis and treatment of CMPA is based on the exclusion of CMP from the diet. Cow's milk elimination without adequate replacement may impair the normal growth and development of the child <sup>(2)</sup>.

During the period of exclusion of CMP, a nutritional status assessment should be performed by the health professional to establish the adequacy of food consumption for the child's nutritional needs <sup>(3)</sup> and family members must be oriented to perform a thorough reading of the labels of industrialized foods offered to their children <sup>(2)</sup>.

The present work aimed to compare between general pediatricians and other sub-specialty of pediatrician regarding awareness of cow's milk protein allergy.

### PATIENTS AND METHODS

This descriptive cross-sectional study was conducted in El-Sharkia Governorate, Egypt during the period from February 2020 to August 2020. 256 pediatric physicians participated in this study (questionnaire-survey).

**Sample size:** The sample size was calculated using open Epi according to the following awareness of physicians about allergy symptoms was 88% <sup>(4)</sup>, and total number of pediatric physicians in El-Sharkia Governorate was 592 so at CI 95% the sample was calculated to be 256 physicians with design effect = 2.

**Inclusion criteria:** Pediatricians of both sexes of different subspecialties that were working in government facility with or without private facility at El-Sharkia Governorate.

### Operational design:

1. Pediatricians were subjected to voluntary participation to answer the prepared questionnaire and no patient-specific information was collected.
2. The questionnaire was applied via face-to-face method.
3. The prepared questionnaire included two parts:



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- a) The first part included questions about pediatricians themselves such as gender, age, subspecialty, scientific degree, years of experience, workplace and living place.
- b) The second one included questions about pediatricians' awareness and practice of cow's milk protein allergy such as:
  - Diagnostic symptoms and signs.
  - Knowing cow's milk-related symptoms score (CoMiSS) and its practice.
  - Knowing the difference between practice of cow's milk protein allergy and lactose intolerance.
  - Diagnostic tests.
  - Diagnostic elimination and use of therapeutic formulas [partially hydrolyzed formula (pHF), extensively hydrolyzed formula (eHF) and amino acid- based formula (AAF) with respect to clinical presentation, ongoing feeding patterns and optimal timing for rechallenge.
  - Knowing diagnosis and rational for action against cow's milk allergy (DRACMA) and National Institute of Allergy and Infectious Diseases (NIAID).
  - Knowing oral food rechallenge test and its practice.

**Ethical approval and written informed consent:**

Approval was obtained from Zagazig University Institutional Review Board (IRB). Informed consent from each pediatric physician that participated in this research was taken.

**Statistical analysis**

The data were coded, entered and processed on computer using statistical package for social science (SPSS) version 24. The results were represented in tabular forms then interpreted. Frequency and percentage were used as descriptive statistics. Categorical variables were described using their absolute frequencies and were compared using Chi square test and Fisher exact test when appropriate. The level of statistical significance was set at 5% ( $P \leq 0.05$ ).

**RESULTS**

Regarding gender, table (1) showed that females were 129 (50.4%) and male were 127 (49.6%). Regarding age group, 82 (32%) were 50-60, 26 (10.2%) were 40-50, less than 40 years were 147 (57.4%) and more than 60 were 1 (0.4%). Regarding

sub-specialty, general pediatricians were 78.1%, gastroenterologist were 3.2%, immunologists were 2.7% and pulmonologists were 3.9%.

There was statistically significant difference between sub-specialty and knowledge of Cow's Milk-related Symptoms Score. Regarding knowledge of Cow's Milk Symptoms Score, having a copy of CoMiSS, use of CoMiSS score in diagnosis of CMPA and use of CoMiSS score in evaluation of results of therapeutic intervention and confirmation of CMPA diagnosis if final CoMiSS score was  $> 12$  (Table 2).

There was statistically significant difference between sub-specialty and diagnostic tests recommended for diagnosis of CMPA regarding occult blood in stool, pH in stool, detection of amoebic antigens in stool, stool culture and skin prick test. While there was no statistically significant difference between sub-specialty and diagnostic tests recommended for diagnosis of CMPA regarding complete blood count, blood test (detection of IgE) in blood and colonoscopy (Table 3).

There was statistically significant difference between sub-specialty and knowledge of oral food challenge test regarding oral food challenge test knowledge, oral food challenge test is a best diagnostic method, use of protocol and oral food challenge test that can be done after an elimination diet by (Table 4).

There was statistically significant difference between sub-specialty and formula recommended for infants with family history of severe allergy and no chance of exclusively breast-feeding (Table 5).

**Table (1):** Demographic data among the studied group

		No.	%
<b>Gender</b>	<b>Female</b>	129	50.4
	<b>Male</b>	127	49.6
<b>Age group</b>	<b>40-50</b>	82	32.0
	<b>50-60</b>	26	10.2
	<b>Less than 40 years</b>	147	57.4
	<b>More than 60</b>	1	0.4
<b>Sub-specialty</b>	<b>Gastroenterologist</b>	8	3.2
	<b>General pediatrician</b>	231	78.1
	<b>Immunologist</b>	7	2.7
	<b>Pulmonologist</b>	10	3.9

**Table (2):** Relation between sub-specialty and knowledge of Cow’s Milk-related symptoms score

			Gastroenterologist	General pediatrician	Immunologist	Pulmonologist	Total	X <sup>2</sup>	P. value
<b>Knowledge of Cow’s Milk Symptoms Score</b>	<b>No</b>	<b>No.</b>	2	154	1	1	158	24.946	0.000
		<b>%</b>	25.0%	66.7%	14.3%	10.0%	61.7%		
	<b>Yes</b>	<b>No.</b>	6	77	6	9	98		
		<b>%</b>	75.0%	33.3%	85.7%	90.0%	38.3%		
<b>Having a copy of CoMiSS</b>	-*	<b>No.</b>	2	154	1	1	158	36.496	0.000
		<b>%</b>	25.0%	66.7%	14.3%	10.0%	61.7%		
	<b>No</b>	<b>No.</b>	0	18	0	0	18		
		<b>%</b>	.0%	7.8%	.0%	.0%	7.0%		
	<b>Yes</b>	<b>No.</b>	6	59	6	9	80		
		<b>%</b>	75.0%	25.5%	85.7%	90.0%	31.3%		
<b>Use of CoMiSS score in diagnosis of CMPA</b>	-	<b>No.</b>	2	157	1	1	161	75.060	0.000
		<b>%</b>	25.0%	68.0%	14.3%	10.0%	62.9%		
	<b>No</b>	<b>No.</b>	0	53	0	7	60		
		<b>%</b>	.0%	22.9%	.0%	70.0%	23.4%		
	<b>Yes</b>	<b>No.</b>	6	21	6	2	35		
		<b>%</b>	75.0%	9.1%	85.7%	20.0%	13.7%		
<b>Use of CoMiSS score in evaluation of results of therapeutic intervention</b>	-	<b>No.</b>	2	157	1	1	161	58.326	0.000
		<b>%</b>	25.0%	68.0%	14.3%	10.0%	62.9%		
	<b>No</b>	<b>No.</b>	1	59	2	7	69		
		<b>%</b>	12.5%	25.5%	28.6%	70.0%	27.0%		
	<b>Yes</b>	<b>No.</b>	5	15	4	2	26		
		<b>%</b>	62.5%	6.5%	57.1%	20.0%	10.2%		
<b>Confirmation of CMPA diagnosis if final COMiSS score is &gt;12</b>	-	<b>No.</b>	2	157	1	1	161	33.774	0.000
		<b>%</b>	25.0%	68.0%	14.3%	10.0%	62.9%		
	<b>No</b>	<b>No.</b>	2	46	3	7	58		
		<b>%</b>	25.0%	19.9%	42.9%	70.0%	22.7%		
	<b>Yes</b>	<b>No.</b>	4	28	3	2	37		
		<b>%</b>	50.0%	12.1%	42.9%	20.0%	14.5%		

\*(-) refers to pediatricians who skip this question.

**Table (3):** Relation between sub-specialty and diagnostic tests recommended for diagnosis of CMPA

			Gastroenterologist	General pediatrician	Immunologist	Pulmonologist	Total	X <sup>2</sup>	P. value
Occult blood in stool	No	No.	0	28	0	8	36	39.151	0.000
		%	0.0%	12.1%	0.0%	80.0%	14.1%		
	Yes	No.	8	203	7	2	220		
		%	100.0%	87.9%	100.0%	20.0%	85.9%		
Ph in stool	No	No.	8	121	7	10	146	20.874	0.000
		%	100.0%	52.4%	100.0%	100.0%	57.0%		
	Yes	No.	0	110	0	0	110		
		%	0.0%	47.6%	0.0%	0.0%	43.0%		
Detection of amoebic antigens in stool	No	No.	8	173	7	10	198	8.116	0.044
		%	100.0%	74.9%	100.0%	100.0%	77.3%		
	Yes	No.	0	58	0	0	58		
		%	0.0%	25.1%	0.0%	0.0%	22.7%		
Stool culture	No	No.	7	155	7	10	179	9.363	0.025
		%	87.5%	67.1%	100.0%	100.0%	69.9%		
	Yes	No.	1	76	0	0	77		
		%	12.5%	32.9%	0.0%	0.0%	30.1%		
Complete blood count (eosinophilia)	No	No.	2	41	3	0	46	5.408	0.144
		%	25.0%	17.7%	42.9%	0.0%	18.0%		
	Yes	No.	6	190	4	10	210		
		%	75.0%	82.3%	57.1%	100.0%	82.0%		
Skin prick test	No	No.	2	78	6	7	93	13.382	0.004
		%	25.0%	33.8%	85.7%	70.0%	36.3%		
	Yes	No.	6	153	1	3	163		
		%	75.0%	66.2%	14.3%	30.0%	63.7%		
Blood test (detection of IgE in blood)	No	No.	2	11	0	0	13	7.544	0.056
		%	25.0%	4.8%	0.0%	0.0%	5.1%		
	Yes	No.	6	220	7	10	243		
		%	75.0%	95.2%	100.0%	100.0%	94.9%		
Colonoscopy	No	No.	6	127	7	7	147	7.413	0.060
		%	75.0%	55.0%	100.0%	70.0%	57.4%		
	yes	No.	2	104	0	3	109		
		%	25.0%	45.0%	0.0%	30.0%	42.6%		

**Table (4):** Relation between sub-specialty and knowledge of oral food challenge test

			Gastroenterologist	General pediatrician	Immunologist	Pulmonologist	Total	X <sup>2</sup>	P. value
Knowledge of oral food challenge test	No	No.	0	105	0	0	105	19.266	0.000
		%	0.0%	45.5%	0.0%	0.0%	41.0%		
	Yes	No.	8	126	7	10	151		
		%	100.0%	54.5%	100.0%	100.0%	59.0%		
Oral food challenge test is a best diagnostic method	-*	No.	0	99	0	0	99	28.585	0.000
		%	0.0%	42.9%	0.0%	0.0%	38.7%		
	No	No.	0	31	0	0	31		
		%	0.0%	13.4%	0.0%	0.0%	12.1%		
	Yes	No.	8	101	7	10	126		
		%	100.0%	43.7%	100.0%	100.0%	49.2%		
Used Protocol	-	No.	0	130	0	0	130	49.382	0.000
		%	0.0%	56.3%	0.0%	0.0%	50.8%		
	Open	No.	7	62	7	10	86		
		%	87.5%	26.8%	100.0%	100.0%	33.6%		
	Single	No.	1	39	0	0	40		
		%	12.5%	16.9%	0.0%	0.0%	15.6%		
Oral food challenge test can be done after an elimination diet by	-	No.	0	99	0	0	99	49.704	0.000
		%	0.0%	42.9%	0.0%	0.0%	38.7%		
	2-4 weeks	No.	6	53	3	10	72		
		%	75.0%	22.9%	42.9%	100.0%	28.1%		
	5-7 weeks	No.	0	60	4	0	64		
		%	0.0%	26.0%	57.1%	0.0%	25.0%		
	8-10 weeks	No.	2	19	0	0	21		
		%	25.0%	8.2%	0.0%	0.0%	8.2%		

\*(-) refers to pediatricians who skip this question.

**Table (5):** Relation between sub-specialty and formula recommended for infants with family history of sever allergy and no chance of exclusively breast feeding

			Gastroenterologist	General pediatrician	Immunologist	Pulmonologist	Total	X <sup>2</sup>	P. value
Formula recommended for infants with family history of sever allergy and no chance of exclusively breast feeding	Amino acid formula	No.	2	72	0	0	74	63.133	0.000
		%	25.0%	31.2%	0.0%	0.0%	28.9%		
	Extensively hydrolyzed formula	No.	0	73	3	0	76		
		%	0.0%	31.6%	42.9%	0.0%	29.7%		
	Partially hydrolyzed formula	No.	6	37	4	0	47		
		%	75.0%	16.0%	57.1%	0.0%	18.4%		
	Age appropriate standard formula	No.	0	49	0	10	59		
		%	0.0%	21.2%	0.0%	100.0%	23.0%		

## DISCUSSION

This study showed that, most of pediatricians were general pediatricians (78.1%). This agrees with **Yüce et al.** <sup>(4)</sup> who made cross-sectional questionnaire-survey that was designed to evaluate CMPA awareness and practice among Turkish pediatricians. A total of 410 pediatricians were included based on their voluntary participation. They found that most of pediatricians were general pediatricians (56.3%)

This study showed that there was low level of knowledge about CMA among the studied group. In 2017, **Vandenplas et al.** <sup>(5)</sup> reported similar finding when they evaluated the adherence of 1,481 physicians (66.1% pediatricians and 7,1% pediatric gastroenterologists) from Middle Eastern and North African countries regarding primary prevention of food allergy, and 60% recommended delayed introduction of potentially allergenic foods.

Guideline adherence has been discussed by many authors worldwide in the past decades. **Cabana et al.** <sup>(6)</sup> identified a wide spectrum of barriers to guideline adherence such as lack of awareness, lack of familiarity, lack of agreement, lack of self-efficacy, lack of outcome expectancy, inertia of previous practice and external barriers that impact guideline implementation.

Intentional non-compliance may be motivated by valid reasons, mainly related to contraindications and patient preferences, that must be considered when developing a guideline <sup>(7)</sup>, but lack of awareness seems to be an important barrier in our study. A large study that was conducted in the USA showed that only 55% of patients are cared for according to the recommendations described in guidelines <sup>(8)</sup>.

This study showed that, majority of pediatricians in this study considered CMPA to be able to develop in an exclusively breast-fed infant and indicated continuation of breast feeding via elimination of CMP containing products from maternal diet as the treatment of choice for diagnostic elimination in this group. This seems consistent with the diagnostic elimination recommended in exclusively breast-fed infants that is elimination of the cow's milk-containing products from the maternal diet <sup>(9)</sup>.

This study showed that, regarding diagnostic tests for diagnosis of CMPA, blood test (detection of IgE in blood (94.9%), occult blood in stool (85.9%), skin prick test (63.7%), elimination diet followed by an oral food challenge test (57%), oral food challenge test (49.2%) and colonoscopy (42.6%). This is in agreement with **Johannes et al.** <sup>(10)</sup> who reported that owing to diagnostic burdens, as the diagnosis needs elimination of cow's milk followed by challenge, children should undergo tests to prove diagnosis.

Food elimination and challenge test is the only method to confirm CMPA diagnosis <sup>(11)</sup>. Oral food challenge (OFC) is the 'gold standard' to confirm children suspected of food hypersensitivity <sup>(12)</sup>.

**Yüce et al.** <sup>(4)</sup> found accordingly, majority of their pediatricians considered atopic dermatitis, diarrhea, blood in stool and colic to be suggestive of CMPA. Overall, colonoscopy was the most common diagnostic test considered by pediatricians (85.5%) to be not the first priority in evaluation of a well-developed infant presenting with flecks or streaks of blood in stool.

This seems consistent with consideration of upper and/or lower endoscopies with multiple biopsies to be appropriate in patients with otherwise unexplained significant and persistent gastrointestinal symptoms, failure to thrive, or iron deficiency anemia, and the fact that macroscopic lesions and histological findings are neither sensitive nor specific for CMPA <sup>(13)</sup>.

The initial step to diagnose CMPA is a thorough medical history and physical examination. If any of the features occur in an infant or a child and cannot be explained by another cause, CMPA may be considered a potential diagnosis. In most cases with suspected CMPA, the diagnosis needs to be confirmed or excluded by an elimination and challenge procedure. This can be performed as an open, single blind or double blind challenge, depending on clinical findings, history, and age of the child. However, there are conditions under which physicians may cancel a challenge procedure because either the diagnosis of CMPA is extremely high or the challenge procedure would be very risky if there is a history of anaphylaxis in a sensitized child <sup>(14)</sup>.

For clinical practice, the determination of specific immunoglobulin E (IgE) in a blood sample and the skin prick test (SPT) are useful diagnostic tests at any age, but it is not necessary to do the two tests for the diagnostic workup. The presence of CMP-specific IgE and/or a positive SPT to cow's milk means sensitization to CMP and presence of IgE-mediated immunological process. However, physicians must decipher these results through medical history and food challenge procedure <sup>(3)</sup>.

**Pascual Pérez et al.** <sup>(15)</sup> who aimed to analyze the variability in cow's milk protein allergy (CMPA) management in Spain. They found that 33% considered oral challenge necessary for the diagnosis of CMPA and 52% considered that symptom improvement after cow's milk removal was enough for the diagnosis. Oral challenge was performed at home by 83.5% in non-IgE mediated cases. Extensively hydrolyzed casein formulas were the treatment of choice for 69.9%.

**Boonyaviwat *et al.*** <sup>(16)</sup> reported that 76% of the respondents thought that non-IgE mediated CMPA diagnosis should not be made exclusively based on its results.

This study showed that regarding Cow Milk Symptoms Score among the studied group, 38.3% had knowledge of COMSS. This is in disagreement with **Can *et al.*** <sup>(17)</sup> who evaluated Knowledge of Cow's Milk Allergy among Pediatricians. The results of their study indicated that occupational education significantly increased the level of knowledge about CMA in pediatricians.

We found a huge variability general pediatricians and other sub-specialty of pediatrics regarding CMPA. This is the first survey conducted among pediatric in Egypt on this topic.

## CONCLUSION

Our findings revealed low knowledge of Cow's Milk Protein Allergy among pediatricians. Educational strategies should be proposed and performed to enable these professionals to act in an adequate manner in the establishment of the diagnosis and treatment of CMPA in infants. Thus, it is possible for these professionals to review their therapeutic behaviors for guarantee of the quality of life of the infant that is the faster reversal of clinical manifestations and nutritional recovery. Furthermore, avoiding the use of dietary elimination based on inadequate behaviors and that can lead to nutritional deficits, besides to rationalizing the use of resources in the treatment of patients with CMPA.

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