# Assessment of Nutritional Status and Vitamin D Level in Infants with

# **Cow Milk Protein Allergy Before and After Treatment**

Waled Atef Shereif<sup>\*1</sup>, Mina AbdelMalak Zarea Ibrahim<sup>2</sup>

<sup>1</sup>Paediatric Department, AlKanater Central Hospital, Cairo, Egypt

<sup>2</sup>Paediatric Department, Al Galaa Teaching Hospital, Cairo, Egypt

\*Corresponding Author: Waled Atef Shereif, Email: Waled.Shereif@nhs.net, Mobile: +201150881028

## ABSTRACT

**Background:** Cow's milk allergy (CMA) is the predominant food allergy among babies, with an estimated frequency in developed nations between 0.5 percent and three percent.

**Aim:** This research aimed to evaluate the vitamin D level and nutritional status in babies with cow milk protein allergy before and after treatment.

**Patients and methods:** This observational study has been performed on a total of 30 infants diagnosed with cow's milk protein allergy (CMPA) and 40 healthy control infants to assess the nutritional status and vitamin D levels in infants diagnosed with CMPA before and after treatment.

**Results:** An insignificant variation has been observed among groups regarding family history of allergy, anthropometric assessment, maternal vitamin D supplementation throughout pregnancy, and EBF time p>0.05. Nonetheless, significant variation has been observed in antibiotic usage in the first triTrimester of life (p<0.05). Insignificant variations have been discovered in total energy, carbohydrates, proteins, lipids, calcium, 25(OH)D, and phosphate levels (p>0.05).

**Conclusion:** We found insignificant variances among groups in age, sex, gestational age, allergy history, anthropometric assessment, vitamin D supplementation, exclusive breastfeeding time, total energy, carbohydrate, protein, lipids, and calcium levels. However, significant differences were found in delivery type, antibiotic use during the first Trimester, and 25(OH)D and phosphate levels.

Keywords: Nutritional Status, Vitamin D Level, Infants, Cow Milk Protein Allergy

## INTRODUCTION

CMA is the predominant food allergy in babies, with a calculated occurrence in developed nations between 0.5 percent and three percent throughout the early years of life <sup>(1)</sup>. CMA has several clinical signs; its management necessitates the removal of goods containing CMP. This elimination diet could negatively impair the nutritional status of the kids involved <sup>(2)</sup>.

Certain factors may pose a risk for the progression of ACMP, including gender, genetics, early weaning, the timing of cow milk introduction, ethnicity, dietary changes (Fat type, vitamin D, obesity, antioxidants), the hygiene hypothesis (decreased exposure to parasites, intestinal colonization, and infectious agents), and exposure to food allergens (during pregnancy, breastfeeding, weaning, and through the skin) <sup>(3)</sup>.

The management of CMP allergy involves the elimination of allergenic protein and the formulation of a substitute regimen that adequately meets the case's nutritional requirements. The restriction must remain until the case establishes oral tolerance, typically occurring following the 1<sup>st</sup> or 2<sup>nd</sup> year of life <sup>(4)</sup>.

Cow's milk protein allergy negatively affects the health of newborns and young kids and imposes significant economic and emotional burdens on society and families. The only therapy is the removal of CMP from the regimen and the incorporation of extensively hydrolyzed milk protein as a dietary supplement <sup>(5)</sup>.

The taste of this heavily hydrolyzed formula is highly unpalatable to most kids, thus elevating the possibility of malnourishment. Appropriate and sufficient dietary support is essential for the growth and progress of kids with cow's milk protein allergies <sup>(6)</sup>.

A double-blind placebo-controlled food challenge is considered the gold standard for confirming the diagnosis of cow's milk allergy and the establishment of oral tolerance to cow's milk. This strategy can be difficult to execute, particularly when a reaction is postponed; an allergy may reappear for up to four weeks after re-exposure to the allergen <sup>(7)</sup>.

with cow's milk protein allergies who lack adequate dietary support are at an increased risk of diminished bone density and vitamin D deficiency, potentially resulting in rickets <sup>(8)</sup>.

Vit-D is a prohormone that has a role in both skeletal and extraskeletal functions, including tolerogenic, immunomodulatory, and anti-inflammatory activities, by diminishing the generation of proinflammatory cytokines, all associated with FA pathogenesis. Deficiency Vit-D comprises a significant public health concern, with raising rates globally, including in sunny regions, impacting all age demographics <sup>(9)</sup>. Multiple factors, including food, sun exposure, ethnicity, sex, and obesity, can influence vitamin D levels in kids <sup>(10)</sup>. This investigation aimed to evaluate the nutritional status and Vit-D concentrations in neonates with cow's milk protein allergy prior to and during therapy.

## PATIENTS AND METHODS

This observational research has been performed on a total of 30 infants diagnosed with CMPA and 40 healthy control infants to assess the dietary status and Vit-D concentrations in babies diagnosed with allergy of cow's milk protein prior to and following treatment.

**Inclusion criteria:** Infants aged 0–24 months have been involved in the research. The CMPA group consisted of babies with a confirmed CMPA diagnosis, while the control group included age- and sex-matched healthy infants without any known food allergies.

**Exclusion criteria:** Kids who are allergic to foods other than milk, cases who were breastfed, utilized corticosteroids in the 3 months before collecting information, and had disabsorptive disorders, including cystic fibrosis, celiac disease, and inflammatory bowel illnesses.

## **METHODS**

## All patients have been exposed to the following:

**Nutritional status assessment:** The height and weight of both groups have been measured and evaluated in accordance with the WHO, utilizing the anthropometric markers of height-for-age (ZH) and BMI-forage (ZBMI). Arm circumference and the tricipital and subscapular skinfolds have been assessed and categorized according to **Frisancho's criteria**<sup>(11)</sup>. Abdominal circumferences have been determined and categorized according to McCarthy and Ashwell, with an elevated ratio of waist-to-height defined as above half.

**Nutrient intakes:** The parents conducted a nonconsecutive 3-day nutritional record, comprising two weekdays and 1 weekend day, to assess nutritional intake. Parents were provided with explanatory materials that included guidelines and photographs of home measures to assist in completing the diary and measurements for estimation. The nutritional record has been reviewed and corrected by a qualified nutritionist in the presence of the parents at the time of birth. The dietary intake has been assessed utilizing the **DietWin® Plus version program**.

Vit-D and A status: For the cow's milk allergy group, only fifteen milliliter blood aliquots have been obtained via peripheral venipuncture in a dark environment by a qualified nurse. The samples were initially sent to UNIFESP's Inborn Errors of Metabolism Laboratory, where they underwent centrifugation at three thousand revolutions per minute for ten minutes. The sera collected post-centrifugation has been preserved at minus eightydegree Clusius and subsequently sent to the Clinical Laboratory Analysis for the assessment of betacarotene, retinol, and lycopene via high-performance liquid chromatography; 25(OH)D and parathyroid hormones through electrochemiluminescence immunoassays; and high sensitivity CRP utilizing immunoturbidimetric assay.

## **Ethical considerations:**

The investigation was executed following the acceptance of the protocol by the Local Research Committee, the Studies Committee, and the Research Ethics Committee of the Pediatric Department, AlKanater Central Hospital, Egypt. Informed written consent was gathered from all caregivers of cases, clearly outlining the research's objectives and methods. The Helsinki Declaration was followed throughout the study's conduct.

## Statistical analysis

The data have been examined utilizing SPSS software. Descriptive data have been expressed as mean  $\pm$  standard deviation. Group comparisons have been performed utilizing t-tests for continuous variables and chi-square testing for categorical parameters. A p-value of less than 0.05 has been deemed statistically significant.

## RESULTS

A statistically insignificant distinction has been observed among the examined group according to age, sex, and gestational age, while a statistically significant distinction has been observed among the examined group according to the type of delivery (Table 1).

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	CMPA group	Control group	P value		
	Number= Thirty	Number= Forty			
Age (months)					
<u>≤6</u>	10(33.4%)	10(24%)			
7–12	8(26.6%)	14(36%)			
13–18	6(20%)	7(18%)	0.8		
19–24	6(20%)	9(22%)			
Sex					
Male	17(56%)	19(47.5%)	0.4		
Female	13(44%)	21(52.5%)			
Type of delivery					
Transvaginal	3(10%)	12(30%)	0.04		
Cesarean section	27(90%)	28(70%)			
Gestational age					
Preterm	5(16.7%)	7(17.5%)	0.9		
Full-term/ post-term	25(83.3%)	33(82.5%)			

## Table (1) Distribution of baseline characteristics among the examined groups.

A statistically insignificant distinction has been observed among the examined groups according to family history of allergy, Anthropometric assessment (W/A), maternal supplementation with vitamin D during pregnancy and time of EBF (months), while a statistically significant variance has been observed among the examined groups according to usage of antibiotics in the 1<sup>st</sup> Trimester of life (Table 2).

#### Table (2): Distribution of characteristic data among the examined groups.

	CMPA group Number= Thirty	Control group Number= Forty	P value	
Family history of allergy	19 (63.33%)	30 (75%)	0.29	
Use of antibiotics in the 1 <sup>st</sup>	13 (43.33%)	6 (15%)	0.008*	
Trimester of life				
Anthropometric assessmen	nt (W/A)	-	-	
Low weight	2 (6.66%)	1 (2.5%)	0.39	
Normal weight	28 (93.33%)	39 (97.5%)		
Excess weight	0 (0%)	0 (0%)		
Maternal supplementation with vit-D throughout pregnancy				
yes	4 (13.33%)	2 (5%)		
no	26 (86.66%)	38 (95%)	0.22	
Time of EBF (months)				
≤1	8 (26.66%)	6 (15%)		
$1 \leq 3$	7 (23.33%)	10 (25%)	0.47	
$3 \leq 6$	15 (50%)	24 (60%)		

## EBF Exclusive Breastfeeding

A statistically significant distinction has been observed among the examined groups according to total energy while a statistically insignificant distinction has been observed among the examined groups according to carbohydrates, protein, and lipids (Table 3).

	CMPA group Number= Thirty	Control group Number= Forty	P value
Total energy	1050±120.3	1070±123.1	0.50
Carbohydrate	141.2±20.5	149±22.3	0.14
Protein	13.2±1.2	13.5±1.6	0.39
Lipids	33.2±3.5	34.6±3.1	0.08

#### Table (3): Distribution of dietary intake among the examined groups.

A statistically insignificant distinction has been observed among the examined group according to Calcium, while a statistically significant variance has been observed among the studied group regarding 25(OH)D and phosphate (Table 4 and figure 1).

#### Table (4): Distribution of markers between the studied groups.

	CMPA group	Control group	P value
	Number= Thirty	Number= Forty	
25(OH)D	$84.3 \pm 26.6$	$111.2 \pm 22.1$	0.002
Mean± SD			
Calcium	$2.7\pm0.08$	$3.0 \pm 0.08$	<0.001
Mean± SD			
Phosphate	$1.81 \pm 0.17$	$1.92 \pm 0.19$	0.01
Mean± SD			





## DISCUSSION

Vit-D is a hormone with pleiotropic effects, important for calcium balance and bone mineralization, as well as for controlling the immune system <sup>(9)</sup>. Numerous pediatric research organizations highlight an increased risk of vitamin D (serum 25(OH)D) deficiency in cases with cow's milk protein allergy and suggest supplementation during the CMP-elimination diet. Nonetheless, the concentrations of serum 25(OH)D that define deficiency in kids remain contentious <sup>(8)</sup>.

Our results indicated statistically insignificant variations among the examined group concerning sex, age, and gestational age; however, there was a statistically significant variance concerning the kind of delivery.

Consistent with our findings, **Che et al.** <sup>(10)</sup> aimed to identify variances in Vit-D and markers of bone metabolism among newborns with cow's milk protein allergy and healthy babies, involving forty-one kids diagnosed with CMPA and fifty healthy kids as a control group. Statistically insignificant variations have been discovered for sex, age, and gestational age among both groups, with p-values of 0.4, 0.648, and 0.388, correspondingly; nevertheless, a statistically significant difference has been detected for delivery mode among both groups.

Furthermore, **Silva** *et al.* <sup>(12)</sup> aimed to find out whether newborns with CMP allergy exhibit insufficient Vit-D levels, involving 120 kids categorized into two groups: the CMP allergy group and the control group. The analysis revealed statistically insignificant variations among both groups concerning gender, age, and gestational age, with p-values of 0.454, 0.093, and 0.612, correspondingly. Conversely, a statistically significant variation has been observed among the groups analyzed regarding type of delivery (P = 0.005).

**Boaventura** *et al.* <sup>(13)</sup> aimed to compare the anthropometric parameters and nutritional consumption of kids with cow's milk allergies to those of healthy controls, involving fifty-seven cases split into two groups: twenty-seven kids in the cow's milk allergy group and thirty in the control group. The research indicated statistically insignificant distinction among both groups concerning age and gender, with p-values of 0.958 and 0.776, correspondingly.

Our findings indicated a statistically insignificant distinction has been observed among the examined groups concerning family history of allergy, anthropometric assessment (W/A), maternal vitamin D supplementation throughout pregnancy, and duration of exclusive breastfeeding (months). However, a statistically significant distinction has been observed concerning the administration of antibiotics in the 1st Trimester of life. Consistent with our findings, **Silva** *et al.* <sup>(12)</sup> observed statistically significant differences among both groups concerning maternal vitamin D supplementation during pregnancy, duration of exclusive breastfeeding (months), and anthropometric assessment (weight-forage), with p-values of 0.15, 0.483, and 0.439, correspondingly.

**Che** *et al.* <sup>(10)</sup> indicated that there were statistically insignificant variations among both groups concerning vitamin D supplementation throughout pregnancy (P = 0.654). Additionally, there was no statistically significant variance regarding the father's history of allergic diseases (P= 0.399), whereas a statistically significant distinction has been observed concerning the mother's history of allergic illnesses (P= 0.035).

According to **Kalach** *et al.* <sup>(14)</sup> a larger positive correlation exists between having two or more allergic family members and the likelihood of their offspring developing food allergies.

Our findings indicated statistically insignificant variations among the examined groups concerning total energy, carbohydrates, proteins, and lipids.

According to our findings, **Boaventura** *et al.* <sup>(13)</sup> determined that there was statistically insignificant variation among the CMA group and the control group for total energy, carbohydrates, protein, and lipids, with p-values of 0.370, 0.326, 0.120, and 0.587, correspondingly.

Rowicka et al. (14) aimed to assess the dietary and nutritional condition of children with cow's milk protein allergy (CMPA), involving seventy-eight kids categorized into two groups: the CMPA group and the healthy control group. The result indicated a statistically significant distinction among the examined groups (CMA group and Control group) for protein [g] and total fat [g], with p-values of 0.8 and 0.2, correspondingly. In contrast to our findings, they identified a statistically significant distinction among the examined groups (CMA group and Control group) concerning energy [kcal] and total carbohydrate [g], with p-values of 0.003 and 0.0004, correspondingly.

Our findings indicated that a statistically insignificant variance has been observed in calcium levels among the examined groups; however, a statistically significant variance has been observed in 25(OH)D and phosphate levels.

Consistent with our findings, **Che** *et al.* <sup>(10)</sup> reported a statistically insignificant variance has been observed among the cow's milk protein allergy group and the control group concerning calcium (P = 0.112), whereas a statistically significant variance has been observed among both groups regarding 25(OH)D (P < 0.001) and phosphate (P = 0.015). Furthermore, **Rowicka** *et al.* <sup>(14)</sup> indicated a statistically insignificant variance has been observed among both groups (CMPA group and control group) for calcium [mmol/l] (P = 0.9).

In contrast to our results, **Boaventura** *et al.* <sup>(13)</sup> indicated statistically insignificant variations in phosphorus and vitamin D levels, with p-values of 0.678 and 0.598, correspondingly. Conversely, a statistically significant variation in calcium levels was observed among both groups (P = 0.003). **Rowicka** *et al.* <sup>(15)</sup> determined that there was a statistically insignificant distinction in phosphate [mmol/1] and 25(OH)D [ng/ml], with p-values of 0.9 and 0.1, correspondingly.

## CONCLUSION

In conclusion, we found statistically insignificant variances among the groups in terms of age, sex, gestational age, family history of allergy, anthropometric assessment (W/A), maternal supplementation with vitamin D during pregnancy, time of exclusive breastfeeding (EBF), total energy, carbohydrate, protein, lipids, and calcium levels. Nevertheless, there were statistically significant variances among the groups in relation to the type of delivery, utilization of antibiotics during the 1<sup>st</sup> Trimester of life, and levels of 25(OH)D and phosphate. Further studies are encouraged to validate these findings across diverse populations and clinical settings.

## DECLARATIONS

- **Consent for publication:** I certify that each author has granted permission for the work to be submitted.
- **Funding:** No fund
- Availability of data and material: Available
- Conflicts of interest: None
- Competing interests: None

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