International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 11s, 2025
https://theaspd.com/index.php

Cow's Milk-Related Symptom Score (Comiss) And Nutritional Status In Egyptian Infants With Non-Ige Cow's Milk Protein Allergy: A Single Center Experience

Ahmed Mohamed Ibrahem Nassef [1], Iman Ehssan Abdel Meguid[2], Hanna Mohamed Aboul-Ghar[3], Hala Hussien Mansour [4]

[1]**Assistance** lecturer of pediatrics, Armed Forces College Of Medicine, Egypt Ahmed.naasef@yahoo.com ORCID: 0009-0003-2508-4634

[2]Professor of pediatrics, faculty of Medicine, Cairo University, Egypt Iman.ehsan3@gmail.com

[3]Professor of pediatrics, faculty of Medicine, Cairo University, Egypt haboulghar@gmail.com, ORCID; 0000-0002-6527-3638

[4]Associate professor of pediatrics, faculty of Medicine, Cairo University, Egypt, hala.h.monsoor@kasralainy.edu.eg, ORCID: 0000-0002-6394-7694

[4]Hala Hussien Mansour: Associate professor of pediatrics, Faculty of Medicine, Cairo University, Egypt,halahusssienmansour@yahoo.com hala.h.monsoor@kasralainy.edu.eg

Abstract: *Background: Approximately 2% to 3% of children under four years old are affected by cow's milk allergy (CMA), which is the most difficult food allergy to identify since the clinical symptoms can vary widely in terms of kind and severity. CMA usually first appears in the first year of life. Along with allergies to eggs and peanuts, it is therefore one of the most common food allergies in children, and like other food allergies, its prevalence is predicted to rise. Between November 2021 and February 2023, a prospective cohort research was carried out at the Gastroenterology clinic at Cairo University's Children Hospital on a random sample of 300 children who had symptoms suggestive of non-Ig E CMPA. The purpose of the study was to evaluate the nutritional status and validate the change in Cow's Milk Related Symptom Score (CoMiSS) in Egyptian children with non-Ig E CMPA.*

Results: *The optimal cut-off point, according to our research, is a CoMiSS score of ≥12. CoMiSS by itself, however, is insufficient for a precise diagnosis of CMPA. The risk of non-Ig E mediated CMPA was protected by exclusive breastfeeding, but age ≤12 months, atopic eczema score >2, and CoMiSS≥12 were linked to positive OFC, whereas NICU admission and a positive family history of allergy were linked to andCoMiSS≥12. Patients with CoMiSS ≥ 12 had significantly reduced Weight-for-age z-score, weight-for-height Z-score, and mid upper arm circumference. The most common kind of malnutrition linked to positive Oral food challenge was moderate acute malnutrition.*

Conclusion: *CoMiSS is a useful method for identifying infants who exhibit non-Ig E-mediated CMPA symptoms. The optimal cut-off point, according to our research, is a CoMiSS score of ≥12. For a precise diagnosis of CMPA, CoMiSS by itself is insufficient. Infants exhibiting signs of CMPA should be managed with nutritional evaluation and the identification of various types of malnutrition.*

Keywords: *CMPA, CoMiSS, Oral food challenge, nutrition stat*

BACKGROUND

Cow's milk allergy (CMPA) is one of the most consistently observed dietary allergies among children and infants. The evaluation and therapy of CMPA is a multifaceted endeavor. CMPA is primarily characterized by various symptoms categorized according to the mediation type (non- IgE and/or IgE responses), the reaction time, and the affected organ systems [1]. Non-specific CMPA symptoms in infancy can delay proper diagnosis and lead to unfavorable clinical outcomes. Non-IgE-mediated CMPA presents significant diagnostic challenges, necessitating an oral food challenge (OFC) following an elimination diet that lasts for two to four weeks. The Cow's Milk-related Symptom Score (CoMiSS) is a clinical tool for primary care physicians designed to enhance recognition of CMPA symptoms and promote early diagnosis [2].The CoMiSS measure considers respiratory, gastrointestinal, and dermatological symptoms and general allergy signs (total score range from 0 to 33). However, it excludes numerous indications of allergy, including failure to prosper, vomiting, or rectal hemorrhage. Due to the potential recurrence of CMPA symptoms following a positive OFC,

parents frequently express reluctance to engage in a dietary challenge. According to Vandenplas et al. (2015), clinical practice would greatly benefit from an approved score that would eliminate or decrease the necessity for dietary challenges. Our work evaluated the nutritional status and validated CoMiSS in Egyptian newborns with non-IgE CMPA [3].

METHODOLOGY:

Between November 2021 and February 2023, a prospective cohort study was performed at the Gastroenterology Clinic of Cairo University's Children's Hospital on a random sample of 300 children presenting with symptoms suggestive of non-IgE CMPA. This study complies with the research regulations established by the Pediatric Department of Cairo University and was approved by Cairo University's Research Ethics Committee (MD-385-2021). All infants aged 1 to 24 months exhibiting symptoms of non-IgE CMPA were included. Suspected non-IgE CMPA was characterized by documented dietary exposure of infants, or breastfeeding infants through maternal intake, to cow's milk protein, along with pulmonary (chronic/recurrent lower and upper respiratory system diseases), gastrointestinal (vomiting, diarrhea, discharge of irregular and/or firm excrement), or dermatological (eczema, pruritus, erythema, papules, and vesicles) symptoms.Infants who had previously received AAF or EHF or experienced anaphylaxis due to a severe allergic reaction were excluded. Additional exclusion criteria included non-allergic comorbidities (such as cerebral palsy) that affect growth and food intake, inability to perform growth assessments, and secondary lactose intolerance or gastroenteritis.Allergy-focused medical history included mode of delivery, age of symptom onset, age at which whole cow's milk was introduced, gastrointestinal, respiratory, and dermatological symptoms, feeding refusal, infantile colic, and family history of allergies. Clinical evaluation included nutritional assessment using a 24-hour dietary recall based on the National Nutrition Institute (2006) Food Composition Tables for Egypt, 2nd Edition [4]. Caloric intake was assessed for adequacy using the 2004 FAO/WHO/UNI cutoffs. Evaluation based on the WHO 2009 Child Growth Standards included length-for-age, weight-for-length Z-score, weight-for-age Z-score, BMI-for-age, and head circumference-for-age. Percentiles and Z-scores were calculated electronically using WHO Anthro software version 3.2.2 [5].Evaluation of CoMiSS was conducted in individuals exhibiting symptoms indicative of non-IgE CMPA. Patients underwent a two-week elimination diet, during which they either received an amino acid-based formula or excluded dairy products from the maternal diet in the case of breastfed infants. A reassessment of manifestations was performed following the two-week elimination diet to evaluate its clinical efficacy, and the CoMiSS was re-evaluated. Study and outline of research was formulated in figure 1.

Oral food challenge (OFC):

Lips were treated with a single droplet of the formulation. If no reaction occurred within 15 minutes, the formula was administered orally. The dosage was progressively increased every 30 minutes (0.5, 1.0, 3.0, 10, 30, 50, and 100 mL). Infants were monitored for reactions for an additional two hours in the hospital following administering the final dose. Acute reactions occurred within two hours of the most recent administration of cow's milk protein during the challenge. If no acute reaction was observed, parents were instructed to administer at least 250 mL of standard cow's milk protein-based formula daily, beginning the following morning, for 14 days. Continuous monitoring of symptoms (including gastrointestinal, cutaneous, respiratory, or general manifestations) was conducted during this period. Delayed reactions may occur within up to two weeks following the OFC. A positive OFC was defined by the presence of at least one of the following symptoms: urticaria (more than three hives), vomiting, increased regurgitation, chronic diarrhea, worsening eczema, or irritability/chronic crying.

Interpretation of OFC:

Positive challenge: CMPA confirmed,If symptoms reappear, the diagnosis of CMPA is confirmed, and the infant should adhere to an elimination diet with either EHF or AAF, based on the severity of the condition, until the age of 9 to 12 months or for at least 6 months, whichever comes first. Supplementary feeding should be introduced with caution to prevent unintentional exposure to CMP. Nutritional management must ensure adequate intake of the prescribed formula (EHF or AAF) to maintain sufficient

calcium levels.

Negative challenge: Absence of CMPA

Children exhibiting no symptoms on the CM formula during the challenge and throughout the two- week follow-up period may resume their regular diet.

Reassessment of CoMiSS in patients with either a positive or negative challenge:

- If the initial score is > 12 and the OFC is positive, it is considered a true positive.
- If the initial score is < 12 and the OFC is positive, it is considered a false negative.
- If the initial score is > 12 and the OFC is negative, it is considered a false positive.
- If the initial score is < 12 and the OFC is negative, it is considered a true negative.

Confirmation of CMPA diagnosis requires an elimination diet followed by an OFC.

RESULTS

This cohort (longitudinal) study involved 300 infants recruited between October 2021 and February 2023 at the Gastroenterology Clinic of Cairo University Children's Hospital exhibiting signs of non-IgE CMPA. Of these, 155 were female (51.7%) and 145 were male (48.3%), with a median (IQR) age of 7 (4-10.75) months. Except for birth order, NICU admission, and family history of allergies, which exhibited significantly higher rates, no statistically significant differences were observed between individuals with CoMiSS < 12 and those with CoMiSS ≥ 12. Additionally, breastfeeding was significantly reduced among patients with CoMiSS ≥ 12.Moderate acute malnutrition was significantly more prevalent among patients with CoMiSS > 12 than in those with CoMiSS < 12. Moreover, a statistically significant decline in weight-for-age Z- score, weight-for-height Z-score, and MUAC was noted in patients with CoMiSS ≥ 12 compared to those with CoMiSS < 12. These parameters were significantly associated with CoMiSS ≥ 12, as demonstrated by univariate logistic regression. Multivariate logistic regression analysis further revealed that breastfeeding, a protective factor against increased CoMiSS, was the most significant factor associated with CoMiSS ≥ 12 (Table 1).A CoMiSS cutoff value ≥ 12 demonstrated a sensitivity of 91.3%, a specificity of 50%, and an area under the curve (AUC) of 0.833 (Figure 2). The demographic characteristics and clinical features of patients with positive and negative OFC outcomes did not differ significantly, except for a statistically significant reduction in the median age of patients with positive OFC. Patients with positive OFC exhibited significantly higher scores for regurgitation, atopic eczema, and pre- elimination CoMiSS than those with negative OFC. Furthermore, a significantly higher proportion of patients with positive OFC had pre-elimination CoMiSS scores ≥ 12, while post-elimination CoMiSS Scores were significantly reduced compared to those with negative OFC.A statistically significant increase in the proportion of positive OFC outcomes was found in patients with CoMiSS ≥ 12 compared to those with CoMiSS < 12. Additionally, weight, height/length, and MUAC were significantly lower in patients with positive OFC than those with negative OFC. A greater proportion of patients with positive OFC experienced moderate acute malnutrition than those with negative OFC. However, no significant differences were detected between the two groups regarding other evaluated parameters, including the proportion of individuals with potential nutritional deficiencies. According to univariate logistic regression analysis, factors significantly associated with positive OFC included age ≤ 12 months, atopic eczema score > 2, pre-elimination CoMiSS ≥ 12, breastfeeding, weight ≤ 5.9 kg, height/length ≤ 74.5 cm, MUAC ≤ 12 cm, and moderate acute malnutrition. Multivariate logistic regression analysis indicated that breastfeeding was significantly less prevalent among positive OFC patients, while pre-elimination CoMiSS > 12 was identified as the most significant predictor of a positive OFC outcome (Table 2).

Table 1: Comparison between patients with CoMiSS < 12 and patients with CoMiSS ≥ 12 regarding anthropometric measurements and nutritional assessment.

		CoMiSS < 12	CoMiSS ≥ 12	Test value	P-value	Sig.
		No. = 50	No. = 250			
Weight	Median (IQR)	7.3 (5.8 – 9)	6.45 (5.2 – 8)	-1.398≠	0.162	NS

	Range	3.85 – 14.6	3 – 15			
Height/length (cm)	Mean ± SD	68.05 ± 11.54	65.8 ± 8.54	1.594•	0.122	NS
	Range	52.5 – 101	52 – 100			
Weight/age Z- score	Median (IQR)	-0.88 (-1.9 – -0.4)	-1.55 (-2.51 – -0.58)	-2.265≠	0.023	S
	Range	-4 – 0.64	-6.62 – 1.69			
Height or length	Median (IQR)	-0.95 (-1.94 – -0.3)	-1.48 (-2 – -0.5)	-1.238≠	0.216	NS
Age Z-score	Range	-4 – 1.1	-5.21 – 1.41			
Weight/height Z- score	Median (IQR)	-0.29 (-1.11 – 0.04)	-0.77 (-1.6 – -0.18)	-2.311≠	0.021	S
	Range	-4.7 – 0.87	-6.75 – 1.49			
MUAC	Mean ± SD	12.26 ± 0.64	11.99 ± 0.58	2.907•	0.004	HS
	Range	11 – 13.5	11 – 13.5			
Moderately underweight		6 (12.0%)	52 (20.8%)	2.069*	0.150	NS
Severely underweight		5 (10.0%)	37 (14.8%)	0.797*	0.372	NS
Moderately stunted		8 (16.0%)	43 (17.2%)	0.043*	0.837	NS
Severely stunted		4 (8.0%)	17 (6.8%)	0.092*	0.761	NS
Moderate acute malnutrition		18 (36.0%)	150 (60.0%)	9.740*	0.002	HS
Severe acute malnutrition		7 (14.0%)	37 (14.8%)	0.021*	0.884	NS
Moderately wasted		2 (4.0%)	26 (10.4%)	2.017*	0.156	NS
Severely wasted		3 (6.0%)	21 (8.4%)	0.326*	0.568	NS
Overweight		0 (0.0%)	0 (0.0%)	0.000≠	1.000	NS

Table 2: Comparison between patients with negative and positive OFC regarding CoMiSS Assessment

		Negative OFC	Positive OFC	Test value	P-value	Sig.
		No. = 58	No. = 242			
Crying score	Median (IQR)	4 (2 – 5)	3.5 (2 – 4)	-0.554≠	0.580	NS
	Range	0 – 6	0 – 6			
	Yes	52 (89.7)	232 (95.8%)			
	No	6 (10.3%)	10 (4.1%)			
Regurgitation score	Median (IQR)	2.5 (0 – 4)	4 (2 – 4)	-3.783≠	0.000	HS
	Range	0 – 6	0 – 6			
	Yes	43 (74.1%)	235 (97.1%)			
	No	15 (25.9%)	7 (2.9%)			
Hematemesis	No	58 (100.0%)	238(98.3%)	0.972*	0.324	NS
	Yes	0 (0.0%)	4 (1.7%)			
Stools score	Median (IQR)	4 (4 – 4)	4 (4 – 4)	-1.247≠	0.212	NS
	Range	0 – 6	0 – 6			
	Yes	55 (95%)	232 (95.8%)			
	No	3 (5%)	10 (4.1%)			
Bloody stool	No	46 (79.3%)	198 (81.8%)	0.194*	0.660	NS
	Yes	12 (20.7%)	44 (18.2%)			
Constipation	No	52 (89.7%)	231 (95.5%)	2.944*	0.086	NS
	Yes	6 (10.3%)	11 (4.5%)			
	Median (IQR)	2 (1 – 3)	3 (2 – 3)			

Atopic eczema score	Range	0 – 4	0 – 5	-4.705≠	0.000	HS
	Yes	47 (81%)	238 (98.3%)			
	No	11 (19%)	4 (1.7%)			
Urticaria score	Median (IQR)	0 (0 – 0)	0 (0 – 0)	0.000≠	1.000	NS
	Range	0 – 0	0 – 0			
Respiratory score	Median (IQR)	1 (0 – 2)	1 (1 – 2)	-0.375≠	0.708	NS
	Range	0 – 3	0 – 3			
	Yes	40 (69%)	206 (85.1%)			
	No	18 (31%)	36 (14.9%)			
CoMiSS (pre-elimination)	Median (IQR)	11.5 (8 – 17)	15 (13 – 17)	-3.892≠	0.000	HS
	Range	5 – 21	6 – 21			
	CoMiSS < 12	29 (50.0%)	21 (8.7%)	57.521*	0.000	HS
	CoMiSS ≥ 12	29 (50.0%)	221 (91.3%)			
CoMiSS (post-elimination)	Median (IQR)	7 (4 – 11)	5 (4 – 6)	-4.788≠	0.000	HS
	Range	0 – 21	0 – 11			
	CoMiSS < 12	47 (81%)	237 (98.0%)	40.015≠	0.000	HS
	CoMiSS ≥ 12	11(19%)	5 (2.0%)			
CoMiSS % of reduction	Median (IQR)	33.3 (11.8 – 55.6)	68.6 (57.14 – 75.0)	7.735	0.000	HS
	Range	0 – 100	0 – 100			

*P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant; *: Chi-square test; ≠: Mann-Whitney test.*

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 11s, 2025
https://theaspd.com/index.php

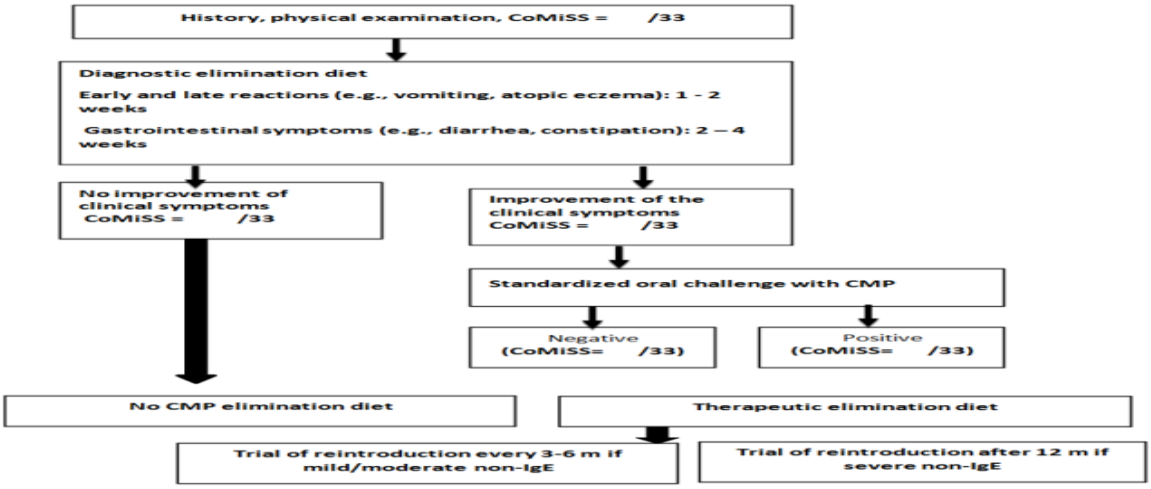
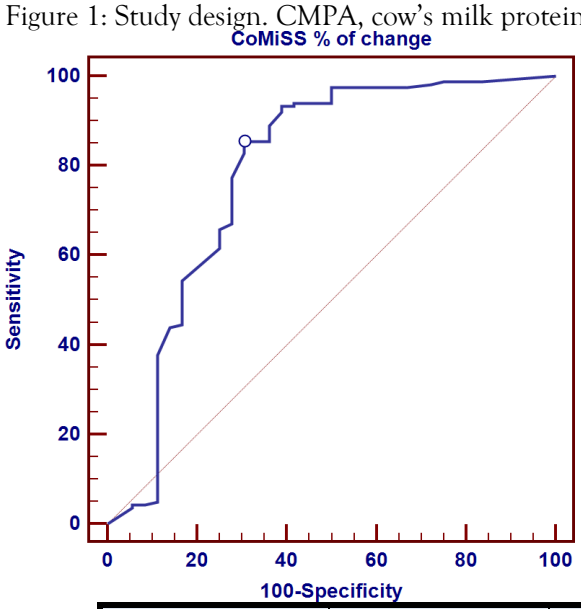


Figure 1: Study design. CMPA, cow's milk protein allergy; CoMiSS, Cow's Milk related Symptom Score.



Cut off point	AUC	Sensitivity	Specificity	+PV	-PV
≥ 12	0.833	91.3%	50.0%	88.4%	58.0%

Figure 2: Receiver operating characteristic curve (ROC) curve for CoMiSS % of change to detect patients with positive OFC results

DISCUSSION

CMPA is the most prevalent food allergy identified in infants and children. Its diagnosis and treatment are complex. CMPA is primarily characterized by various symptoms categorized by the type of mediation (IgE and/or non-IgE responses), the affected organ systems, and the reaction timing [1]. Diagnosing non-IgE CMPA requires a 2- to 4-week exclusion diet, followed by an OFC. The CoMiSS serves as a clinical tool for primary healthcare practitioners, designed to enhance the recognition of CMPA symptoms and promote early identification [2]. It evaluates general allergic manifestations, including dermatological, gastrointestinal, and respiratory symptoms, with a total score ranging from 0 to 33. Specific allergy symptoms, such as vomiting, rectal bleeding, or failure to thrive, are excluded from the score. Parents often hesitate to undertake a food challenge due to the potential recurrence of CMPA symptoms following a positive OFC [3]. The predominant nutritional issues include growth retardation, micronutrient deficiencies, and feeding difficulties. Growth faltering has been extensively studied and is recognized as a common presenting feature in pediatric food allergies [6].In our

randomized clinical trial, 300 patients with manifestations suggestive of non-IgE CMPA were recruited at the Gastroenterology Clinic, Children's Hospital, Cairo University, between November 2021 and February 2023.Among the 300 patients, 145 (48.3%) were male. The median age was 2 months [interquartile range (IQR) = 1-3 months], and the median age at presentation was 7 months (IQR = 4-10.75 months). The birth order distribution was as follows: 63 (21.0%) were first-born, 109 (36.3%) second-born, 88 (29.3%) third-born, 27 (9.0%) fourth-born, 10 (3.3%) fifth-born, 2 (0.7%) sixth- born, and 1 (0.3%) seventh-born. A total of 232 (77.3%) were offspring of consanguineous parents. Thirty-eight (12.7%) were delivered via normal vaginal delivery, and 262 (87.3%) via cesarean section. A history of NICU admission was reported in 62 (20.7%) patients. Eighty-nine (28.6%) were breastfed, of whom 16.3% received some supplemental formula, 189 (63.0%) were formula- fed, and 22 (7.3%) were on regular food. Deficient dietary intake was recorded in 76.7% of cases, based on the recommended daily intake for age by UNU/WHO/FAO, 2004 [7].Our study enrolled 300 Egyptian infants wIth manifestations suggestive of non-IgE CMPA, and a CoMiSS Score ≥ 12 was observed in 250 patients. This cutoff was highly significant concerning a positive OFC ($p = 0.000$). Similarly, El-Shafie et al. (2023), in a study of 100 Egyptian infants with non-IgE CMPA manifestations, identified a CoMiSS score of ≥ 12 as the optimal cutoff [8].Our receiver operating characteristic (ROC) curve analysis confirmed a CoMiSS Score ≥ 12 as the threshold, with a sensitivity of 91.3%, specificity of 50%, and overall accuracy of 83.3%. In contrast, Vandenplas et al. (2021), studying 250 Chinese infants (< 6 months old), reported a CoMiSS ≥ 12 with low sensitivity (20.3%) but high specificity (87.9%) [9]. However, El-Desouky et al. (2021) found the most accurate cutoff to be > 12 among 120 Egyptian infants, with a sensitivity of 86.4%, specificity of 93.4%, and overall accuracy of 90.8% [10].In our study, the median baseline CoMiSS was 15 (IQR 13-17) in patients with a positive OFC, compared to 11.5 (IQR 8-17) in those with a negative OFC. Similarly, Vandenplas et al. (2017) reported a mean CoMiSS of 13.65 ± 1.75 and a median of 13 (IQR 12-15) [11]. In contrast, Zeng et al. (2019) and Vandenplas et al. (2021) reported significantly lower scores, with a median of 8 (IQR 5-10) [9-12].In our study cohort of 300 infants exhibiting persistent symptoms indicative of CMPA, 242 (80.6%) were diagnosed with CMPA by positive OFC, with a median age of onset of 2 months. Similarly, El Shafie et al. (2023) found that the OFC diagnosed 84% of 100 Egyptian infants with persistent symptoms suggestive of CMPA and confirmed CMPA [8]. According to Stocklosa et al. (2020), CMPA typically occurs during the first year of life, with the average age at symptom onset being 2.3 months [13]. In our study, the majority of patients presented with stool changes according to the BSS (Bristol Stool Chart) 287/300 (95.6%), followed by atopic eczema 285/300 (95%), general manifestations (crying and irritability) 284/300 (94.6%), regurgitation 278/300 (92.6%), respiratory complaints 246/300 (82%), bloody diarrhea 56/300 (18.7%), constipation 17/300 (5.7%), and hematemesis 4/300 (1.3%).Among patients with positive OFC, 238/242 (98.3%) had atopic eczema, 235/242 (97.1%) had regurgitation, 232/242 (95.8%) had crying, 232/242 (95.8%) had stool changes, 206/242 (85.1%) had respiratory complaints, 44/242 (18.1%) had bloody diarrhea, 11/242 (4.5%) had constipation, and 4/242 (1.6%) had hematemesis. A statistically significant association was found between positive OFC and both regurgitation and skin scores.El-Shafie et al. (2023) reported statistically significant associations between positive OFC and stool and skin scores; 79/84 (94.05%) had stool changes, 77/84 (91.67%) had crying, 63/84 (75%) had regurgitation, 54/84 (64.29%) had skin manifestations, and 42/84 (50%) had respiratory complaints [8]. Similarly, Adriana et al. (2020) reported that the most frequent clinical manifestations in patients with positive OFC were rashes (87.5%), failure to thrive (82.5%), regurgitation (50%), and diarrhea (35%) [14].Univariate logistic regression showed statistically significant associations between a history of NICU admission ($p = 0.048$), positive family history of allergy ($p = 0.031$), MUAC ≤ 12 ($p = 0.002$), and moderate acute malnutrition ($p = 0.002$) with CoMiSS ≥ 12. Multivariate logistic regression identified exclusive breastfeeding as a protective factor ($p = 0.006$). El-Asheer et al. (2022) found that in a cohort of 40 Egyptian newborns, the method of feeding was significantly associated with CMPA, with 67.5% of cases being artificially fed and 12.5% breastfed ($p < 0.0001$) [15]. In our patients with positive OFC, 30 (12.4%) were exclusively breastfed. However, Saad et al. (2020), in a study of 317 Egyptian infants with manifestations of non-IgE CMPA, reported that parental food allergy and

cesarean section were independent risk factors for CMPA ($p < 0.01$) [16].Univariate logistic regression revealed statistically significant associations between age ≤ 12 months, atopic eczema score > 2, and CoMiSS ≥ 12 with positive OFC ($p = 0.000$ for all). Multivariate logistic regression identified CoMiSS ≥ 12 ($p = 0.000$) as a risk factor and breastfeeding ($p = 0.005$) as a protective factor.Doğan et al. (2021) demonstrated that among 83 infants exhibiting CMPA, 62.6% (n = 52) were detected with skin involvement as the initial manifestation [17]. Saad et al. (2020) concluded that exclusive breastfeeding ($p = 0.001$) was a protective factor for CMPA. The median anthropometric measurements among our patients were -1.45 (-2.51 – -0.51), -1.4 (-2 – -0.46), and -0.71 (-1.52 –-0.14) for WAZ, HAZ, and WHZ, respectively, with a mean MUAC of 12.03 ± 0.59 cm. A statistically significant association was found between low WAZ ($p = 0.023$) and WHZ ($p = 0.021$) and CoMiSS ≥ 12 points. MUAC was significantly lower among patients with CoMiSS ≥ 12 and positive OFC ($p = 0.004$). Taveira et al. (2023) concluded that WAZ and HAZ significantly reduced in infants with CMPA, with 15.3% and 6.4%, respectively, among the studied patients [18]. In contrast, Mailhot et al. (2016) found no significant difference in weight, height, and HAZ in CMPA children ($p = 0.83$, 0.76, and 0.24, respectively) [19].Our results indicated that among patients with positive OFC, 17.4% were moderately stunted, 7.4% severely stunted, 18.6% moderately underweight, 15% severely underweight, 10.3% moderately wasted, 7.9% severely wasted, 59% had moderate acute malnutrition, and 14.5% had severe acute malnutrition, while none of our patients were overweight. Moderate acute malnutrition was significantly higher in patients with CoMiSS ≥ 12 ($p = 0.002$). According to Assis et al. (2022), the frequency of short stature was 15.5%, and the frequency of underweight was 8.3% [20]. Thomassen et al. (2017) found that among 57 infants with non-IgE CMPA, the frequency of underweight and wasting was significant at 10.5%, while stunted development was seen in 5.3% of subjects [21]. Numerous studies have shown the association between different forms of malnutrition and CMPA [22-24]. However, Mailhot et al. (2016) found no significant difference in weight, height, and HAZ in CMPA children [19].

CONCLUSION

CoMiSS is an effective instrument for identifying newborns exhibiting signs of non-IgE- mediated CMPA. Our analysis identified a CoMiSS score of ≥ 12 as the optimal cutoff threshold. However, CoMiSS cannot be used independently to diagnose CMPA. NICU admission and a positive family history of allergy were associated with CoMiSS ≥ 12, while age ≤ 12 months, atopic eczema score > 2, and CoMiSS ≥ 12 were linked to positive OFC. Exclusive breastfeeding had a protective effect on the risk of non-IgE-mediated CMPA. WAZ, WHZ, and MUAC were significantly lower among patients with CoMiSS ≥ 12. Moderate acute malnutrition was the predominant form of malnutrition associated with positive OFC.

List of abbreviations:

AAF: Amino acid-based formula, BMI: Body mass index, CM: Cow's milk, CMPA: Cow's milk protein allergy, CoMiSS: Cow's Milk Related Symptom Score, EHFs: Extensively hydrolyzed formulas, HAZ: Height-for-age Z-score, HCA: Head circumference-for-age, LAZ: Length-for-age Z-score, LFA: Length-for age, MUAC: Mid upper arm circumference, NICU: neonatal intensive care unit, Non-Ig E CMPA: Non-Ig E-mediated cow's Milk Allergy, OFC: Oral food challenge, WAZ: Weight-for-age Z-score, WLZ: weight-for-length Z-score, WFA: Weight-for-age, WFL: Weight-for-length, WHZ: weight-for-height Z-score

Declarations:

- Ethical approval and consent to participate are available
- Funding: not applicable

REFERENCES

1. Barrera E, Ramirez-Farias C, Marriage BJ. Nutritional Management of Cow's Milk Allergy in Infants: A Comparison of DRACMA, ESPGHAN, and AAP Guidelines. The Open Nutrition Journal. 2021; 15(1).
2. Vandenplas Y, Mukherjee R, Dupont C, Eigenmann P, Høst A, Kuitunen M, Ribes-Koninkx C, Shah N, Szajewska H, von

Berg A, Heine RG. Protocol for the validation of sensitivity and specificity of the Cow's Milk-related Symptom Score (CoMiSS) against open food challenge in a single-blinded, prospective, multicentre trial in infants. BMJ open. 2018; 8(5): e019968.

3. Vandenplas Y, Dupont C, EigenmannP, Host A, Kuitunen M, Ribes- Koninckx C, Shah N, Shamir R, Staiano A, Szajewska H, Von Berg A. A workshop report on the development of the Cow's Milk- related Symptom Score awareness tool for young children. Acta Paediatrica. 2015; 104(4):334-9.
4. National Nutrition Institute. "Food composition tables for Egypt." 2006.
5. 2nd Edition WHO 2009 Child Growth Standard scale. Percentiles and z-scores will be electronically computed by using the WHO Anthro software V3.2.2.
6. Meyer R. Nutritional disorders resulting from food allergy in children. Pediatric Allergy and Immunology. 2018; 29 (7):689-704
7. United Nations University, World Health Organization. Human Energy Requirements: Report of a Joint FAO/WHO/UNU Expert Consultation: Rome, 17- 24 October 2001. Food & Agriculture Org.; 2004.
8. El-Shafie AM, Omar ZA, El Zefzaf HM, Basma EM, and Al Sabbagh NM, Bahbah WA. Evaluation of Cow's Milk Related Symptom Score [CoMiSS] accuracy in cow's milk allergy diagnosis. Pediatric Research. 2023; 1-9.
9. Vandenplas Y, Zhao ZY, Mukherjee R, Dupont C, Eigenmann P, Kuitunen M, Koninckx CR, Szajewska H, von Berg A, Bajerová K, Meyer R. Assessment of the Cow's Milk- related Symptom Score (CoMiSS) as a diagnostic tool for cow's milk protein allergy: a prospective, multicentre study in China (MOSAIC study). BMJ open. 2022 1; 12(2):e056641.
10. El Desouky AI, Anany HG, Mohammed IS. Assessment of CoMiSS among children with cow's milk allergy at zagazig university hospital. The Egyptian Journal of Hospital Medicine. 2021 Apr 1; 83(1):838-43.
11. Vandenplas Y, Steenhout P, Järvi A, Garreau AS, Mukherjee R. Pooled analysis of the Cow's Milk-related-Symptom-Score (CoMiSS™) as a predictor for cow's milk related symptoms. Pediatric gastroenterology, hepatology & nutrition. 2017; 20(1):22- 6
12. Zeng Y, Zhang J, Dong G, Liu P, Xiao F, Li W, Wang L, Wu Q. Assessment of Cow's milk-related symptom scores in early identification of cow's milk protein allergy in Chinese infants. BMC pediatrics. 2019; 19:1-7.
13. Stocklosa MI, Dijmarescu I, Lesanu G, Becheanu C, Pacurar D, Ulmeanu C. Food allergy in the first 6 months of life–clinical aspects. Romanian JouRnal of PediatRics. 2020; 69 (2):108.
14. Adriana B, Cristina M, Irina P, Tatiana C, Diana D, Adina U, Sergiu C, Larisia M. Assessment of IgE-mediated and non-IgE-mediated cow's milk protein allergy in children. ARS Medica Tomitana. 2020; 25(3):129-31.
15. El-Asheer OM, El-Gazzar AF, Zakaria CM, Hassanein FA, Mohamed KA. Frequency of gastrointestinal manifestations among infants with cow's milk protein allergy, Egypt. Egyptian Pediatric Association Gazette. 2022; 70(1):34.
16. Saad K, Ahmad AR, El-Tellawy MM, El-Ashry AH, Nagiub EM, Abdelsalam TA, Elhoufey A. Cow milk protein allergy: clinical phenotype and risk factors. Curr. Trend. Immunol. 2020; 21:129- 35.
17. Doğan E, Sevinc E, Gamsızkan Z, Korkut B, Sevinc N. The Frequency of Atopic Dermatitis and Other Skin Manifestations in Infants with Cow's Milk Protein Allergy in Karabük, Turkey. International Journal of Pediatrics. 2021; 9(3):13177- 84.
18. Taveira GR, Fernandes CD, Silva YF, de Aquino MC, da Silva AC, de Faria CP, Barbosa MC. Evolution of nutritional status and associated factors among formula-fed infants with cow's milk protein allergy in a government program. Archives of Public Health. 2023; 81(1):1-9.
19. Mailhot G, Perrone V, Alos N, Dubois J, Delvin E, Paradis L, Des Roches A. Cow's milk allergy and bone mineral density in prepubertal children. Pediatrics. 2016; 137(5).
20. Assis PP, Menezes JS, Diniz AD, Antunes MM, Cabral PC. Growth of infants with gastrointestinal manifestations of cow's milk protein allergy. Revista de Nutrição. 2022; 35: e210075.
21. Thomassen RA, Kvammen JA, Eskerud MB, Júlíusson PB, Henriksen C, Rugtveit J. Iodine status and growth in 0–2-year-old infants with cow's milk protein allergy. Journal of pediatric gastroenterology and nutrition. 2017; 64(5):806-11.
22. Meyer R, Venter C, Fox AT, Shah N. Practical dietary management of protein energy malnutrition in young children with cow's milk protein allergy. Pediatric allergy and immunology. 2012 Jun; 23(4):307-14.
23. Meyer R, De Koker C, Dziubak R, Godwin H, Dominguez-Ortega G, Chebar Lozinsky A, Skrapac AK, Gholmie Y, Reeve K, Shah N. The impact of the elimination diet on growth and nutrient intake in children with food protein induced gastrointestinal allergies. Clinical and translational allergy. 2016; 6:1- 7.
24. Pavić I, Kolaček S. Growth of children with food allergy. Hormone Research in Paediatrics. 2017; 88(1):91-100.