

Cow's Milk Related Symptoms Score (COMISS) As a Predictor for Cow's Milk Allergy: An Interventional Study

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Abstract

Background: Primary health care physicians are insufficiently aware of symptoms caused by cow milk because there is no pathognomonic symptom and no reliable diagnostic test, which results in repeated consultations and inaccurate management. Due to the lack of other reliable diagnostic tests other than a food challenge with cow milk protein, infants suspected of suffering from cow's milk protein allergy (CMPA), developing an awareness tool to recognize cow's milk related symptoms in infants and young children for use. A Cow's Milk-related-Symptom-Score (CoMiSS), a score that considers general manifestations, dermatological, gastrointestinal and respiratory symptoms, was developed to be used as an awareness tool for cow's milk related symptoms. The study aimed to assess the value of Cow's milk related symptoms score (COMISS) in the prediction of cow's milk allergy in pediatrics. **Methods:** This study was conducted during at Pediatric Department, Faculty of Medicine, Zagazig University. This study was interventional one which included 120 infants (aged up to 18 month) presenting with one or more of the following CMPA symptoms: cutaneous (atopic dermatitis and urticaria), respiratory (cough and dyspnea, rhinitis), and gastrointestinal (digestive regurgitation, vomiting, rectal bleeding, constipation and diarrhea). A predesigned questionnaire, with informed consent obtained from parent/primary care giver of the infant, was used to collect information pertaining to the general characteristics and anthropometry, medical and feeding history and clinical examination via CoMiSS. **Results:** There was statistically significant lower in Albumin among Confirmed CMA than No CMA. There was statistically significant higher Total score of CoMiSS among Confirmed CMA than No CMA, and another one regarding each symptom of COMISS score. **Conclusion:** Accuracy of CoMiSS in diagnosis of CMA was 90.8%. the percentage of Sensitivity (86.4%), Specificity (93.4%), Positive predictive value % (88.3%) when the score is >12 Negative predictive value % (92.2%).

Key words: Cow's milk related symptoms score- cow's milk allergy in pediatrics- Evaluation

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I. Introduction:

Primary health care physicians are insufficiently aware of symptoms caused by cow milk because there is no pathognomonic symptom and no reliable diagnostic test, which results in repeated consultations and inaccurate management ⁽¹⁾.

The non-specific signs and symptoms of CMPA, ranging from colic and reflux to constipation, insomnia, eczema, diarrhea and crying, make diagnosis a real challenge. The symptoms involve many different organ systems, predominantly the skin and the gastrointestinal and respiratory tracts. The involvement of two or more organ systems increases the likelihood of CMPA ⁽²⁾.

Due to the lack of other reliable diagnostic tests other than a food challenge with cow milk protein, infants suspected of suffering from cow's milk protein allergy (CMPA), developing an awareness tool to recognize cow's milk related symptoms in infants and young children for use by primary healthcare providers may help, as its name implies, in increasing the awareness and the recognition of cow's milk related symptoms. Such a tool, helping in decision-making and correct management, would be appreciated by the parents because it will avoid both over and under-diagnosis, and also shorten the duration of distress of the infants and parental anxiety ⁽³⁾.

Delayed diagnosis of CMPA has a negative impact on the physical development of children ⁽⁴⁾.

A Cow's Milk-related-Symptom-Score (CoMiSS), a score that considers general manifestations, dermatological, gastrointestinal and respiratory symptoms, was developed to be used as an awareness tool for cow's milk related symptoms ⁽³⁾. The CoMiSS can also be used to evaluate and quantify the evolution of symptoms during a therapeutic intervention.

However, the CoMiSS does not diagnose CMPA and does not replace a food challenge. Its usefulness needs still to be evaluated by a prospective randomized study ⁽⁵⁾.

The study aimed to assess the value of Cow's milk related symptoms score (COMISS) in the prediction of cow's milk allergy in pediatrics.

II. Patients and Methods

This study was conducted during the period from December 2018 to May 2020 at Pediatric Department, Faculty of Medicine, Zagazig University.

Design of the study:

This study was interventional one which included 120 infants (aged up to 18 month) presenting with one or more of the following CMPA symptoms: cutaneous (atopic dermatitis and urticaria), respiratory (cough and dyspnea, rhinitis), and gastrointestinal (digestive regurgitation, vomiting, rectal bleeding, constipation and diarrhea).

Target population:

Infants up to 18 months of age at the time of enrolment who have signs and symptoms of cow's milk allergy

Inclusion criteria:

- Male or female infants aged up to 18 months.
- Infants suffered from CMPA symptoms.

Exclusion criteria:

- Infant or infant's parent unable to comply with trial procedures.
- Patients with a disease impairing normal gut transit, a known lactose intolerance, severe chronic diarrhea, failure to thrive and neurological disease, those that use antibiotics and those that have recently had surgical intervention or medical treatment.

(1) Operational design:

Type of the study: Interventional study

Steps of performance:

All infants were subjected to the following:

A- Full history taking (age and sex).type of Feeding

B- Full clinical examinations.

C- Investigations: -

- Complete blood count (CBC)
- Stool analysis (pH, reducing substance, WBC, Occult blood, Parasites).
- Serum albumin
- A predesigned questionnaire, with informed consent obtained from parent/primary care giver of the infant, was used to collect information pertaining to the general characteristics and anthropometry, medical and feeding history and clinical examination via CoMiSS.

• **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 and diagrammatic forms then interpreted.

Mean, standard deviation, range, frequency, and percentage were used as descriptive statistics.

The following test was done:

- **Chi-Square test X^2** was used to test the association variables for categorical data.

- **Student's t-test** was used to assess the statistical significance of the difference between two population means in a study involving independent samples.

- **Student's paired t-test** was used to assess the statistical significance of the difference between two population means in a study involving paired samples.

- **ROC curve** = receiver operator characteristic curve,

Sensitivity = ability of the test to detect the true +ve cases with minimal false negatives

Specificity = ability of the test to detect the true -ve cases with minimal false positives

PPV= positive predictive value= probability that an individual with +ve test result (\geq cut off value) has the condition.

NPV=negative predictive value = probability that an individual with -ve test result **don't have** the condition.

The accepted level of significance in this work was stated at 0.05 (P <0.05 was considered significant), P value >0.05 is non-significant (N-S)

III. Results:

- This **Table** shows that the percentage of the <12 was 77 (64.2%), \geq 12 was 43 (35.8%) (**Table 1**).

- There was no statistically significant difference between Confirmed CMA (positive challenge test) and No CMA (negative challenge test) regarding Age (Months), Weight Kg and sex. There was statistically significant decrease in birth weight among Confirmed CMA than No CMA (**Table 2**).

- There was statistically significant difference between Confirmed CMA (positive challenge test) and No CMA (negative challenge test) regarding Total score (**Table 3**).

- Accuracy of CoMiSS in diagnosis of CMA was 90.8%. The percentage of Sensitivity (86.4%), Specificity (93.4%), Positive predictive value % (88.3%) when the score is \geq 12, Negative predictive value % (92.2%) (**Table 4**).

- There was statistically significant lower Albumin among Confirmed CMA than No CMA (**Table 5**).

Table (1): Categories of total CoMiSS first visit

		No.	%
code	<12	77	64.2
	>12	43	35.8

Table (2): Comparison between Confirmed CMA (positive challenge test) and No CMA (negative challenge test) regarding demographic data

			Confirmed CMA (positive challenge test) (No.= 44)	No CMA (negative challenge test) (No.= 76)	t.test	P. value
Age (Months)	Mean ± SD		5.88 ± 3.64	7.48 ± 5.88	1.631	0.105
Weight Kg	Mean ± SD		6.28 ± 2.05	6.45 ± 1.57	0.498	0.619
birth weight	Mean ± SD		3.07 ± 0.33	3.19 ± 0.34	2.010	0.047
Sex	male	No.	19	38	X ² 0.282	0.595
		%	43.2%	50.0%		
	female	No.	25	38		
		%	56.8%	50.0%		

Table (3): Comparison between Confirmed CMA (positive challenge test) and No CMA (negative challenge test) regarding Categories of total CoMiSS

			Confirmed CMA (positive challenge test) (No.= 44)	No CMA (negative challenge test) (No.= 76)	X ²	P. value
Total score code	< 12	No.	6	71	77.148	.000
		%	13.6%	93.4%		
	>12	No.	38	5		
		%	86.4%	6.6%		

Table (4): Accuracy of CoMiSS in diagnosis of CMA

total CoMiSS	Sensitivity %	Specificity %	Positive predictive value %	Negative predictive value %	Accuracy%
cut off value 12	86.4%	93.4%	88.3%	92.2%	90.8%

Table (5): Comparison between Confirmed CMA (positive challenge test) and No CMA (negative challenge test) regarding Albumin

		Confirmed CMA (positive challenge test) (No.= 54)	No CMA (negative challenge test) (No.= 76)	t.test	P. value
Albumin	Mean ± SD	3.25 ± 0.48	3.482 ± 0.3616	-2.967-	.004

IV. Discussion

This study showed that, there was no statistically significant difference between Confirmed CMA (positive challenge test) and No CMA (negative challenge test) regarding age and sex.

These results agreed with **Zeng et al.,**⁽⁶⁾ who found that, there was no significant difference in gender, age, and weight between Infants with Confirmed CMPA (positive OFC) and those with No CMPA (negative OFC).

In our study, there was statistically significant lower in Albumin among Confirmed CMA than No CMA. In harmony with **AltinelAcoglu et al.,**⁽⁷⁾ who found that, hypoalbuminemia is associated with CMA.

Our study showed that, there were statistically significant higher Total score of CoMiSS among Confirmed CMA than No CMA, and another one regarding each symptom of COMISS score.

These results agreed with **Prasad et al.,**⁽⁸⁾ who found that, the mean CoMiSS of the children was 16.2 ± 6.8. The minimum CoMiSS was 2, and the maximum was 32. A score of above 12 was seen in 72% (60 of 83) of the children, warranting further evaluation and need for confirmatory diagnosis of CMPA. Overall, 84.3% (70 of 83) of the children were diagnosed with CMPA via oral food challenge/ImmunoCAP test. Fifty-five out of seventy of the confirmed cases of CMPA showed a CoMiSS > 12 while five out of thirteen cases did not show a confirmed diagnosis of CMPA even with CoMiSS > 12. This primarily suggested CoMiSS to be a particularly useful tool in diagnosing CMPA.

In harmony with a study by **Zeng et al.,**⁽⁶⁾ who found that the results of rank sum test showed that there was a significant difference in CoMiSS between two groups (F = 2.13, P < 0.05).

This study showed that, Accuracy of CoMiSS in diagnosis of CMA was 90.8%. the percentage of Sensitivity (86.4%), Specificity (93.4%), Positive predictive value % (88.3%) when the score is >12 Negative predictive value % (92.2%).

These results agreed with **Salvatore et al.,** ⁽⁹⁾ who aimed to assess the accuracy of the cow's milk-related symptom score (CoMiSS) in response found CoMiSS to be a useful tool to help identify infants with persisting gastrointestinal symptoms and suspected CMA that would benefit from CMFD.

Also, **Prasad et al.,** ⁽⁸⁾ who reported CoMiSS had a positive predictive value (PPV) of 93%, negative predictive value (NPV) of 33%, with sensitivity of 77%, and specificity of 66%. A receiver operating characteristics (ROC) curve area of 0.68 at a CoMiSS cutoff of 12 was observed.

As **Vandenplas et al.,** ⁽³⁾ said, CoMiSS is a simple score that will help clinicians to efficiently identify CMPA early, though it cannot be used as a diagnostic tool or a substitute for OFC test. The primary GI physician supervising the OFC is not absolutely blinded to the CoMiSS scores. It is easily to make the results to have bias. The application value of CoMiSS needs to be further confirmed by multi-center large sample studies.

V. Conclusion:

Accuracy of CoMiSS in diagnosis of CMA was 90.8%. The percentage of Sensitivity (86.4%), Specificity (93.4%), Positive predictive value % (88.3%) when the score is >12 Negative predictive value % (92.2%).

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