



## Hematological Changes Associated with Cow's Milk Allergy in Infants

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**Abstract**

Food safety is an important issue of public health in veterinary medicine due to its direct connection with human health. The aim of this study was to evaluate hematological changes and IgE levels in the blood of children with cow milk allergy (CMA) who showed clinical signs and compare them with healthy children. 200 children participants aged 6–12 months divided into two groups. Group I consisted of 100 children with history for CMA, children suspected of having CMA were diagnosed through the history of the child's health condition as well as the parents, in addition to clinical symptoms and an immunoglobulin test IgE to detect the presence of allergy. Healthy children were 100 in number selected for the control group who did not show any symptoms of food allergy. The current study showed that there were significant increases in the number of white blood cells ( $10.82 \pm 1.69$ - $8.10 \pm 2.77$ ,  $p < 0.0001$ ), platelets ( $348 \pm 79.73$ - $295 \pm 29.69$ ,  $p < 0.0001$ ), lymphocytes ( $41.09 \pm 11.90$ - $34.60 \pm 4.76$ ,  $p = 0.0006$ ), monocytes ( $3.36 \pm 0.454$ - $2.7 \pm 0.447$ ,  $p < 0.0001$ ), eosinophil's ( $4.58 \pm 0.982$ - $1.38 \pm 0.358$ ,  $p < 0.0001$ ) and the amount of hemoglobin ( $9.66 \pm 0.73$ - $10.9 \pm 0.27$ ,  $p < 0.0001$ ) between the CMA group and the control group, as well as examining the total IgE, a significant difference was found ( $26.8 \pm 11.07$ - $78.6 \pm 32.8$ ,  $p < 0.0001$ ). The study reveals that cow milk protein may cause food allergy in infants fed cow milk due to increases in the levels of allergy indicators, such as IgE and white blood cells.

**Key words:** Cow's milk protein; hematology; infants

**Introduction**

Nutrition has a substantial impact on a child's overall healthy growth due to the presence of nutrients and energy (1). Cow's milk allergy (CMA) may induce food allergy in infants. The diagnostic confirmation may involve history, physical examination, elimination diet technique, skin allergic tests, IgE serum tests, and food challenges (2). CMA is induced by the immune system to a proteinous compound in the milk. Casein and whey proteins are among these proteins; cow milk allergy (CMA) can be further subdivided into IgE and non-IgE (primarily cellular) mediated varieties. Despite the fact that IgE-mediated responses are readily identified by dependable diagnostic methods (3). From mild symptoms such as hives to severe symptoms such as anaphylaxis, milk allergy reactions can affect anyone. Children with elevated blood levels of cow's milk antibodies are more likely to continue to be allergic (4). Depending on the underlying cause, CMA symptoms and signs vary considerably. Early reactions can be recorded, such as anaphylaxis, acute angioedema, urticaria, and iron deficiency anemia. Late reactions can be manifested, such as atopic dermatitis, gastrointestinal pain, and diarrhea (5). Most children with CMA develop tolerance to the proteins in cow's milk, but in some cases the allergy symptoms persist for many years. Since they do not accurately reflect inflammatory processes, the established parameters for treating this condition are of limited utility. The aim of this study was to evaluate hematological changes and IgE levels in the blood of children with CMA who showed clinical signs and compare them with healthy children.

**Methods****Results****Ethical approval and Collection of Samples**

After obtaining ethical approvals from the General Administration of Samawah Governorate Health and informed consent from the patients, this retrospective case control study was conducted on 200 children participants aged 6–12 months divided into two groups. Group I consisted of 100 children with history for CMA, confirmed via the history of the child's health condition informed by the parents, in addition to previous clinical and laboratory diagnosis performed by medical specialists. Group II consisted of healthy children that were 100 in number selected for the control group who revealed no food allergy by utilizing the same diagnosis confirmation followed in the Group I. Each participant had 5 milliliters of venous blood drawn, which was divided as follows: Two milliliters (ml) were immediately placed in an EDTA tube for complete blood count, while the remaining three milliliters (ml) were placed in a plain tube, allowed to clot for 30 minutes at room temperature, and then centrifuged for 10 minutes at 4000 rpm to separate the serum. The separated serum was then divided into several aliquots and stored at  $80^{\circ}\text{C}$  until the time of assay.

**Assay techniques**

Using the Sysmex automatic blood counter (Japan). The immunoglobulin IgE was tested by an automatic test device from Hipro company (China).

**Statistic evaluation**

SPSS v20 (SPSS Inc. Chicago, IL, USA) was utilized to analyze the data. Mean  $\pm$  SD was employed. The  $p$  value for significance was determined as  $p < 0.05$ .



The results showed that there was a significant difference between the group infected with CMA and the control group in the numbers of white blood cells, and they were in higher quantities than the control group, as shown in Table (1). The affected group also recorded high statistically significant differences in the values of WBCs ( $10.82 \pm 1.69$ - $8.10 \pm 2.77$ ,  $p < 0.0001$ ), platelets ( $348 \pm 79.73$ - $295 \pm 29.69$ ,  $p < 0.0001$ ), lymphocytes ( $41.09 \pm 11.90$ - $34.60 \pm 4.76$ ,  $p = 0.0006$ ), monocytes ( $3.36 \pm 0.454$ - $2.7 \pm 0.447$ ,  $p < 0.0001$ ), and

eosinophil ( $3.36 \pm 0.454$ - $2.7 \pm 0.447$ ,  $p < 0.0001$ ). While the affected group recorded a slight statistically significant decrease in the value of RBC ( $4.54 \pm 0.311$ - $4.88 \pm 0.233$ ,  $p < 0.0001$ ). In addition, there was a significant decrease in the values of hemoglobin in the blood ( $9.66 \pm 0.73$ - $10.9 \pm 0.27$ ,  $p < 0.0001$ ) and neutrophils ( $59.2 \pm 10.76$ - $62.6 \pm 7.30$ ,  $p = 0.0674$ ), as shown in Table 1. There was a clear increase with a statistical difference in the values of total IgE in the blood in the group with CMA as shown in Table (2).

**Table 1:** Laboratory complete blood parameters of cow milk allergy group and healthy children.

Laboratory parameter	Clinically diagnosed cases (n=100)	Control (n=100)	P value
WBC ( $10^3/\mu\text{L}$ )	$10.82 \pm 1.69\text{A}$	$8.10 \pm 2.77\text{B}$	$<0.0001$
RBC ( $10^6/\mu\text{L}$ )	$4.54 \pm 0.311\text{B}$	$4.88 \pm 0.233\text{A}$	$<0.0001$
PLT ( $10^3/\mu\text{L}$ )	$348 \pm 79.73\text{A}$	$295 \pm 29.69\text{B}$	$<0.0001$
HGB g/dL	$9.66 \pm 0.73\text{B}$	$10.9 \pm 0.27\text{A}$	$<0.0001$
Neutrophils %	$59.2 \pm 10.76\text{A}$	$62.6 \pm 7.30\text{A}$	$0.0674$
Lymphocytes %	$41.09 \pm 11.90\text{A}$	$34.60 \pm 4.76\text{B}$	$0.0006$
Monocytes %	$3.36 \pm 0.454\text{A}$	$2.7 \pm 0.447\text{B}$	$<0.0001$
Eosinophil %	$4.58 \pm 0.982\text{A}$	$1.38 \pm 0.358\text{B}$	$<0.0001$
Basophils %	$0.54 \pm 0.164\text{A}$	$0.48 \pm 0.118\text{A}$	$0.0383$

Mean  $\pm$  SD

**Table 2:** Diagnostic validity of total IgE (IU/ml) in the CMA group and the control group

Groups	Total IgE levels (IU/ml)
Control (n=100)	$26.8 \pm 11.07\text{A}$
Clinically diagnosed cases (n=100)	$78.6 \pm 32.84\text{B}$
Test of significance	$t = 11.3889$
P value	$<0.0001$

## Discussion

The current study worked to prove the presence of statistically significant changes in the values of blood analysis for children with CMA compared to a control group that did not show clinical signs. Infants may experience a wide variety of symptoms from CMA, all of varying severity [7-11]. The results of the current study showed a statistically significant increase in the percentage of WBCs and eosinophil's. This is consistent with results of Sommanus *et al.*, (12) and Beşer *et al.*, (13). The clinical relevance of eosinophilia in infants with milk allergy is not clear because the role of eosinophilia in infants is not fully known (14). The results also indicated a statistically significant decrease in the percentage of red blood cells and the percentage of hemoglobin. This agreed with the results of (15,16). When severe iron deficiency anemia (IDA) occurs in children, it is linked to hypoalbuminemia and may be brought on by consuming too much cow's milk. Although the exact mechanism of this illness is not known, it appears to develop separately from CMA. The differential diagnosis for kids who have edema and iron deficiency anemia symptoms should include enteropathy with protein loss linked to excessive cow's

milk consumption (17). The results also indicated a statistically significant increase in the IgE test in average  $78.6 \pm 32.84$ , which is characteristic of allergy, in the milk allergy group, compared to the control group  $26.8 \pm 11.07$ , whose values were within the normal limits. In the current research, a positive association was found between total serum IgE and milk allergy, this agreed with the results of (18,19). The assessment of total IgE is now only regarded as an additional diagnostic tool for allergic disorders due to its limited sensitivity and specificity and cost (20).

## Conclusion

The study reveals that cow milk protein may cause food allergy in infants fed cow milk due to increases in the levels of allergy indicators, such as IgE and white blood cells.

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## Conflict of interest

No conflict of interest was detected



## References

- <http://www.mmj.eg.net/text.asp?2014/27/3/524/145500> .
- 12 .Sommanus S, Kerddonfak S, Kamchaisatian W, Vilaiyuk S, Sasisakulporn C, Teawsomboonkit W, et al. Cow's milk protein allergy: immunological response in children with cow's milk protein tolerance. *Asian Pac J Allergy Immunol*. 2014;32(2):171-7. <https://doi.org/10.12932/AP0319.32.2.2013> .
  - 13 .Beşer OF, Sancak S, Erkan T, Kutlu T, Cokuğraş H, Cokuğraş FÇ. Can fecal calprotectin level be used as a marker of inflammation in the diagnosis and follow-up of cow's milk protein allergy? *Allergy Asthma Immunol Res*. 2014;6(1):33-8. <https://doi.org/10.4168/aa.2014.6.1.33> .
  - 14 .Imamura T, Watanabe M, Kaneko M, Shibukawa Y, Fukuda Y, Nagasawa K. Cow's milk allergy with severe eosinophilia. *Pediatr Neonatol*. 2016;57(1):69-71. <https://doi.org/10.1016/j.pedneo.2013.06.008> .
  - 15 .Lai FP, Yang YJ. The prevalence and characteristics of cow's milk protein allergy in infants and young children with iron deficiency anemia. *Pediatr Neonatol*. 2018;59(1):48-52. <https://doi.org/10.1016/j.pedneo.2017.01.004> .
  - 16 .Graczykowska K, Kaczmarek J, Wilczyńska D, Łoś-Rycharska E, Krogulska A. The consequence of excessive consumption of cow's milk: protein-losing enteropathy with anasarca in the course of iron deficiency anemia—case reports and a literature review. *Nutrients*. 2021;13(3):828. <https://doi.org/10.3390/nu13030828> .
  - 17 .Graczykowska K, Kaczmarek J, Wilczyńska D, Łoś-Rycharska E, Krogulska A. The consequence of excessive consumption of cow's milk: protein-losing enteropathy with anasarca in the course of iron deficiency anemia—case reports and a literature review. *Nutrients*. 2021;13(3):828. <https://doi.org/10.3390/nu13030828> .
  - 18 .Ayats-Vidal R, Valdesoiro-Navarrete L, García-González M, Asensio-De la Cruz O, Larramona-Carrera H, Bosque-García M. Predictors of a positive oral food challenge to cow's milk in children sensitized to cow's milk. *Allergol Immunopathol (Madr)*. 2020;48(6):568-75. <https://doi.org/10.1016/j.aller.2020.03.007> .
  - 19 .Dodi G, Di Filippo P, Di Pillo S, Chiarelli F, Attanasi M. Total serum IgE levels as predictor of the acquisition of tolerance in children with food allergy: findings from a pilot study. *Front Pediatr*. 2022;10:1013807. <https://doi.org/10.3389/fped.2022.1013807> .
  - 1 .El-Nmer F, Salama AA, Elhawary D. Nutritional knowledge, attitude, and practice of parents and its impact on growth of their children. *Menoufia Med J*. 2014;27:612-6. Available from: <https://www.mmj.eg.net/text.asp?2014/27/3/612/145529> .
  - 2 .Lifschitz C, Szajewska H. Cow's milk allergy: evidence-based diagnosis and management for the practitioner. *Eur J Pediatr*. 2015;174(2):141-50. <https://doi.org/10.1007/s00431-014-2422-3> .
  - 3 .Martorell-Aragónés A, Echeverría-Zudaire L, Alonso-Lebrero E, Boné-Calvo J, Martín-Muñoz MF, Nevot-Falcó S, et al. Position document: IgE-mediated cow's milk allergy. *Allergol Immunopathol (Madr)*. 2015;43(5):507-26. <https://doi.org/10.1016/j.aller.2015.01.003> .
  - 4 .El-Sebay HM, Badr EA, El-Ghobashi Y, Khalil MM, El-Mashad GM. The role of specific IgE antibodies in infants with cow milk protein allergy. *Menoufia Med J*. 2016;29:874-80 .
  - 5 .Caffarelli C, Baldi F, Bendandi B, Calzone L, Marani M, Pasquinelli P, et al. Cow's milk protein allergy in children: a practical guide. *Ital J Pediatr*. 2010;36:5. <https://doi.org/10.1186/1824-7288-36-5> .
  - 6 .D'Auria E, Venter C. Precision medicine in cow's milk allergy. *Curr Opin Allergy Clin Immunol*. 2020;20(3):233-41. <https://doi.org/10.1097/ACI.0000000000000640> .
  - 7 .Høst A. Frequency of cow's milk allergy in childhood. *Ann Allergy Asthma Immunol*. 2002;89(6 Suppl 1):33-7 .
  - 8 .Caffarelli C, Baldi F, Bendandi B, Calzone L, Marani M, Pasquinelli P, et al. Cow's milk protein allergy in children: a practical guide. *Ital J Pediatr*. 2010;36:5. <https://doi.org/10.1186/1824-7288-36-5> .
  - 9 .Lifschitz C, Szajewska H. Cow's milk allergy: evidence-based diagnosis and management for the practitioner. *Eur J Pediatr*. 2015;174(2):141-50. <https://doi.org/10.1007/s00431-014-2422-3> .
  - 10 .Sicherer SH, Sampson HA. Food allergy: A review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. *J Allergy Clin Immunol*. 2018;141(1):41-58. <https://doi.org/10.1016/j.jaci.2017.11.003> .
  - 11 .Ragab S, Hegran H, Kassem S. The effect of zinc supplementation on growth and development in preterm neonates. *Menoufia Med J*. 2014;27:524-8. Available from:



20. Muraro A, Fernandez-Rivas M, Beyer K, Cardona V, Clark A, Eller E, et al. The urgent need for a harmonized severity scoring system for acute allergic reactions. *Allergy*. 2018;73(9):1792-800.  
<https://doi.org/10.1111/all.13408>.