

Cow's milk associated rectal bleeding: a population based prospective study

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Abstract

Background: Isolated rectal bleeding in infants is often attributed to the consumption of cow's milk. However, the prevalence of this condition has not been described, and its preferred diagnostic methods and management are controversial.

Methods: In a prospective population-based study following 13,019 children from birth, 21 infants with isolated rectal bleeding attributed to cow's milk protein consumption were identified. Following evaluation, parents were encouraged to resume cow's milk protein and infants were followed for reappearance of symptoms and thereafter for 6 yr. In addition, infants with rectal bleeding were compared to a control group of healthy infants.

Results: The prevalence of isolated rectal bleeding attributed to cow's milk consumption was 0.16%. All infants were asymptomatic within days of dietary modifications. Eleven of the 14 infants (78.5%) whose parents reintroduced cow's milk protein to their diet following our evaluation tolerated it with no adverse effects. Those 11 infants were significantly younger at initial consumption of cow's milk protein (6.7 ± 1.6 months) compared to those who continued elimination diet (17.7 ± 9.2 months), ($p = 0.002$) while their 1-yr hemoglobin levels were comparable ($p = 0.98$). No risk factors for rectal bleeding were identified.

Conclusions: The prevalence of isolated rectal bleeding attributed to cow's milk is low. The condition is generally benign and resolves quickly with elimination diet. Reintroduction of cow's milk following resolution of symptoms is often well tolerated and is recommended for confirming the diagnosis and avoiding prolonged unnecessary elimination diets.

Isolated rectal bleeding in infancy is a well-known phenomenon. While cases of iron deficiency anemia, hypoalbuminemia, and even massive bleeding have been reported, it generally has a benign course (1–7). However, it is often a cause for concern in parents and a subject for various investigations and treatments (1, 2). Potential etiologies for rectal bleeding include common (anal fissures and infection) and less common (Hirschsprung, inflammatory bowel disease) conditions (4, 5, 8).

Cow's milk allergy (CMA) comprises one of the most common, significant and potentially fatal food allergies. It is associated with several distinct entities such as IgE-mediated CMA, food protein-induced enterocolitis syndrome, and even constipation (9–11). Skin prick tests (SPT) assist in making the diagnosis of CMA, predicting its persistence (12, 13) and even in determining a starting dose for oral desensitization (14).

However, an oral food challenge (OFC) is the gold standard for diagnosis (15). Once the diagnosis is made an elimination diet is required, and alternative formulas are given (16, 17).

Although often implicated in this condition, the relative proportion of CMA as a cause for isolated rectal bleeding in infants is controversial (1, 4, 18). Several diagnostic methods, in addition to the infants' history, have been proposed, including the demonstration of improvement in symptoms with cow's milk elimination and recurrence upon provocation (1), elimination without provocation (3, 19) or the performance of colonoscopy with biopsies to demonstrate eosinophilic infiltration of the colonic mucosa (4, 5, 20). Still, given the invasiveness of performing biopsies and the fact that response to reprovocation may be delayed, a definitive diagnosis of CMA-induced allergic colitis is often not made.

In clinical practice, diagnosis and treatment include elimination of cow's milk protein (CMP) from the diet of the infant resulting in cessation of rectal bleeding within a few days (1–3, 5). Typically, rechallenge with the suspected offending food is not performed until the infant is 1 yr old (3, 4). However, given the transient nature of this condition, mislabeling of infants as having cow's milk-associated rectal bleeding may often occur and evidence regarding the need for such prolonged elimination diet is sparse. Recently, the role of CMP in the pathogenesis of rectal bleeding and the traditional approach of prolonged elimination diet have been questioned (1).

Although the natural course of rectal bleeding has been studied, no population-based studies providing information regarding its prevalence exist, to our knowledge. In this large-scale prospective study following a cohort of 13,234 newborns, we aimed to determine the prevalence and natural course of rectal bleeding attributed to CMP consumption, identify risk factors for its occurrence, and examine the effect of early reintroduction of CMP.

Methods

Study population

A cohort of 13,234 newborns, born between June 2004 and June 2006 at Assaf Harofeh Medical Center, Zerifin, Israel, was followed until the age of 6 yr, and 13,019 (98.38%) completed the study, as previously described (9). The research protocol was approved by the Helsinki Review Board of Assaf Harofeh Medical Center. Parents were asked to contact the allergy clinic immediately after any adverse reaction (cutaneous, respiratory, gastrointestinal, or systemic) suspected to be related to maternal or infants' consumption of CMP or, in the absence of any unusual event, 14–30 days after the initiation of CMP. All parents were contacted 3 months after birth, and infants' feeding pattern was recorded. Parents providing full breast-feeding were contacted bimonthly until the newborn consumed dairy products. Neonates with rectal bleeding observed in the nursery, who were evaluated and treated for more heterogeneous conditions, were excluded (21). Of the 381 infants with possible adverse events related to CMP, 25 infants were reported to have rectal bleeding. Infants diagnosed with other specific entities including CMP-induced enterocolitis syndrome, $n = 2$ (10); anal fissure, $n = 1$; and acute gastroenteritis, $n = 1$, were excluded. Overall, 21 infants with isolated rectal bleeding were followed.

Evaluation and follow-up

Initial management was done by the primary care physician or any other healthcare provider involved in the care of the infant. In all cases, labeling of infants as having rectal bleeding in relation to the consumption of cow's milk was based on symptom presentation and response to elimination diet. Evaluation in our clinic, performed at an average of 3 months following symptom presentation, included a detailed questionnaire, SPT and OFC when indicated. Parents were encouraged to resume the diet provided to the infant prior to the initiation

of rectal bleeding, and infants were subsequently followed for reappearance of symptoms. Hemoglobin levels were obtained from routine blood counts performed when infants were 1 yr old. Infants with rectal bleeding were compared to the entire group of infants who had no adverse effects related to CMP ($n = 12,638$). Using MATLAB's randperm function, 232 infants from this group were randomly chosen to serve as a control group for analyses of parameters that were not available for the entire cohort. Of those, 156 families were successfully recruited for evaluation.

Skin prick tests

SPT in infants were performed to CMP, soy, egg, and sesame by using the volar arm and reading the reaction after 20 min. A negative control and histamine (1 mg/ml; ALK-Abelló, Port Washington, NY, USA) were used. A 3-mm or larger wheal response was considered positive (9).

Oral challenge

OFC to cow's milk formula was performed using Materna (Maabarot Products Ltd, Maabarot, Israel) infant formula. Increasing doses were given, from a 1:10 diluted formula of 1.0 ml (2.7 mg of CMP) up to 120 ml (3.24 g of CMP) every 30 min. The challenge was terminated if a cutaneous, respiratory, gastrointestinal, or systemic response was observed. In case of a negative challenge result, the infants were observed for 3 h, and a subsequent contact was made 2 wk later to inquire about their feeding habits.

Statistical analysis

Statistical analyses were performed with SPSS software (version 16; SPSS, Inc, Chicago, IL, USA). Continuous variables were analyzed using the student's *t*-test or one-way ANOVA and are presented as mean \pm standard deviation. Fisher's exact test was used to analyze differences between groups in categorical variables. All analyses were 2-tailed, and a *p*-value of <0.05 was considered significant.

Results

Infants' characteristics at time of presentation

Twenty-one otherwise healthy infants (12 males) were diagnosed as having rectal bleeding attributed to CMP (0.16% of the study population), (Table 1). Most infants 20/21 (95.2%) were born full term with an average gestational age at birth of 39.5 ± 1.3 wk and one infant was born at 36 wk gestational age. Mean age at presentation was 52.9 ± 49.6 days (range, 10–210 days). Four infants were exclusively breast-fed at the time of presentation, and 17 infants were fed with CMP either exclusively ($n = 10$) or in addition to breast-feeding ($n = 7$). In those consuming CMP, the average time from introduction of CMP to the development of symptoms was 39.4 ± 47.4 days. Eleven infants had mild symptoms in addition to rectal bleeding (Table 1).

Table 1 Characteristics of infants with suspected CMP-related rectal bleeding

Characteristics	No. of patients (n = 21)*
Symptoms at presentation [†]	
Age (days)	52.9 ± 49.6
Exclusive breastfeeding	4 (19%)
CMP	10 (47.7%)
Breastfeeding + CMP	7 (33.3%)
Duration of CM exposure (days)	39.4 ± 47.4
Additional symptoms [‡]	11
Dietary intervention	
Breastfeeding + Maternal elimination diet	4 (19%)
Soy (±breast feeding and maternal elimination diet)	10 (47.7%)
Hydrolyzed formula	7 (33.3%)
Clinical evaluation	
Age (days)	158.3 ± 63.0
Positive SPT to CMP	2/20 (10%)
Positive SPT to non-related foods	3/20 (15%)
Reintroduction of CMP	
Successful	11 (52.4%)
Reappearance of symptoms	3 (14.3%)
No reintroduction	6 (28.6%)
Did not arrive for evaluation	1 (4.7%)
Age at reintroduction (days)	295.7 ± 155.1

CMP, cow's milk protein; CM, cow's milk; SPT, skin prick test.

Values represent mean ± s.d.

*Unless otherwise specified.

[†]Refers to time of initial symptom presentation.

[‡]Additional symptoms included other mild gastrointestinal symptoms (vomiting, n = 3 or non-bloody diarrhea, n = 1), and non-gastrointestinal symptoms (non allergic rash, n = 3; restlessness, n = 3; or cough, n = 1).

Nutritional adjustments

Initial diagnosis of CMP-related rectal bleeding was made by a primary care physician in the majority of infants (15/21), by our clinic in 2 infants, during hospitalization due to rectal bleeding in 1 infant, and by a nurse at the mother & child care center in 1 infant. Two families reported that the possibility that infants' symptoms were related to CMP exposure was raised by the parents themselves. Nutritional changes were made in all cases (Table 1). Those were recommended by the primary care physician in 18 cases (including cases where the diagnosis was suggested by the parents themselves), by a nurse at the mother & child care center in 1 case, and by the parents in 1 case, and in 1 case, the parents could not remember. All but one infant experienced resolution of symptoms after the nutritional change. This child was hospitalized, had a negative infectious work-up, and was fed with elemental formula until the age of 13 months when CMP was successfully reintroduced.

Clinical evaluation

Twenty infants were evaluated in our clinic, and one family refused evaluation and testing (Table 1). Infants were evaluated

at a mean age of 5.3 ± 2.1 months (2.9 ± 2.5 months following their initial presentation). SPT to CMP was negative in 18 infants. Of the two infants with positive SPT to CMP, one had a negative OFC followed by regular consumption of milk-based formula, and the other refused OFC, but his clinical presentation and delayed reaction were not consistent with IgE-mediated cow's milk allergy (12). An elimination diet was continued until he was incidentally exposed to CMP at the age of 32 months with no adverse effects. One infant had a positive SPT to soy but was consuming only CMP at the time of diagnosis; one had a positive SPT to egg and one to sesame. Following evaluation, all families were recommended to reintroduce CMP to the infants' diet along with an explanation that symptoms might recur. Fourteen of the evaluated families (70%) reintroduced CMP to the infants' diet either before or immediately after the clinic visit. Those parents who elected to postpone the reintroduction of CMP did so either because of their fear of reintroduction of CMP or based on their primary care physician's recommendation. In 11 of those who chose to reintroduce CMP (78.5%), no adverse effects were noted. Three children developed symptoms upon reintroduction of CMP (1 had rectal bleeding and 2 had non-bloody diarrhea) and resumed their previous formulas. If only those infants are considered to have actual CMP-related rectal bleeding, then the prevalence of this condition is only 0.023%. At the age of 24 months, all but one infant consumed CMP.

One-year hemoglobin levels in infants whose parents continued to eliminate CMP from their diet and in those who resumed CMP sooner were compared. While infants whose parents declined the reintroduction of CMP (n = 6) were at a mean age of 17.7 ± 9.2 months when CMP was finally reintroduced, those who successfully reintroduced CMP following clinic visit (n = 11) were significantly younger 6.8 ± 1.8 months, (p = 0.002). Despite the early reintroduction of CMP, 1-yr hemoglobin levels (available for 19 infants), did not differ between the 2 groups (12.26 mg/dl for those avoiding vs. 12.25 mg/dl for those consuming CMP, p = 0.98).

Risk factors for CMP-related rectal bleeding were not identified

We next compared the group of infants with rectal bleeding to the entire group of healthy infants who had no adverse effects related to CMP, n = 12,638 (Table 2). No significant demographic differences between the groups with rectal bleeding and the healthy controls were found. Birthweight was higher in infants with rectal bleeding with borderline significance. Parental allergy was reported in 6 families (28.6%) and was comparable to the reported parental allergy in the control group (33%), (p = 0.7) (Table 2).

Discussion

In this prospective population-based study unique in its size, we report that the prevalence of isolated rectal bleeding attributed to CMP is only 0.16% and that of actual CMP-related rectal bleeding is even lower. In addition, our findings emphasize the safety of early reintroduction of CMP following

Table 2 Comparison of infants with rectal bleeding and healthy controls

	Rectal Bleeding (n = 21)*	Healthy controls (n = 12,638)*	p value
Gender: male no.	12 (57.1%)	6409 (50.7%)	0.71
Ethnicity: jewish no.	17 (81%)	9789/12267 (78.9%)	0.89
Spontaneous delivery no.	17 (80.9%)	10,696 (84.6%)	0.86
Mean gestational age (wk)	39.5 ± 1.3	39.2 ± 1.9	0.37
Birth weight (kg)	3.4 ± 0.5	3.2 ± 0.5	0.05
Maternal age (yr)	30.4 ± 4	29.7 ± 5.2	0.52
Child order in family	2.0 ± 0.9	2.3 ± 1.5	0.36
Duration of breastfeeding (m)	6.3 ± 8.1	4.7 ± 5.9	0.28
Age at CMP introduction (d)	54.8 ± 85.7	61.6 ± 92.4	0.74
Parental academic education (yr)			
Mother	13.3 ± 3.3 (n = 19)	14.2 ± 3.7 (n = 154)	0.28
Father	13.5 ± 3.3 (n = 19)	14.4 ± 2.7 (n = 148)	0.26
Parental self-reported allergy no.	6 (28.6%)	51/156 (33.0%)	0.70

*Unless otherwise specified.

CMP, Cow's milk protein.

Values represent mean ± s.d.

symptom resolution and its importance in both diagnosis and management of these infants.

The prevalence of CMA-induced proctocolitis in infants with isolated rectal bleeding may be less common than previously estimated. Jenkins et al. (18) described 8 children who presented with rectal bleeding and all had food-associated allergic colitis. In contrast, Xanthakos et al. (4) found that only 64%, of 22 infants with rectal bleeding, had histologically defined allergic colitis, and Arvola et al. (1) found that the prevalence of CMP-related rectal bleeding was only 18% when the diagnosis was based on response to elimination and provocation diet with cow's milk. In our study, symptoms recurred in only 21.4% of infants upon reprovocation, suggesting that either CMP is less common as a cause for rectal bleeding, or that its course is shorter than previously estimated.

It is common practice to continue with elimination diet, even in exclusively breast-fed infants, until the infant is 1 yr old (3, 4, 22, 23). Poddar et al. (24) have shown a high rate of positive challenges to CMP, based on histological criteria, when it is reintroduced early (following 6 months of elimination diet). In contrast, Arvola et al. (1), using clinical symptoms to guide therapy, demonstrated that elimination diet was beneficial only in a sub-group of infants whose symptoms recurred after rechallenge with CMP. The low rate of symptoms in our patients upon reprovocation with CMP, and their significantly lower age at consumption of CMP compared to those whose parents elected to withhold CMP, supports the use of reprovocation to guide management. In addition, a risk of conversion to IgE-mediated CMA with prolonged elimination diet exists (9). Therefore, to prevent false-positive diagnoses of CMA and unnecessarily prolonged elimination diets, rechallenge should be performed shortly after the resolution of symptoms. Primary care physicians should be aware of these considerations as they have an important role in the family's behavior, both in raising the suspicion of CMP-related rectal bleeding and in recommending a dietary change.

Although the benign nature of rectal bleeding was previously demonstrated, iron deficiency anemia and hypoalbuminemia could be associated findings (18–20, 25–27). Arvola et al. have found hemoglobin levels <10.5 g/dl in 18% of their infants on admission and in only 3% at 1 yr of age, but this includes both infants who continued with elimination diet and those who resumed CMP. In our study, none of the infants had hemoglobin levels <10.5 g/dl, perhaps due to the routine iron supplementation given to all infants in Israel between the ages of 4 months and 1 yr, per AAP recommendations. Moreover, hemoglobin levels in infants who renewed the consumption of CMP and in those who continued to avoid it until the age of 1 yr and beyond were similar, emphasizing that there is no harm in earlier introduction of CMP.

Although a family history of atopy has been previously described as a risk factor for CMA (1, 4, 18, 28, 29), this is not supported by our finding of a lower prevalence of parental atopy in infants with rectal bleeding compared to controls. Birthweight was slightly higher in the infants with rectal bleeding, yet these results are not sufficient to identify birthweight as a risk factor. No other risk factors for CMP-associated rectal bleeding were identified.

In summary, we describe for the first time the low prevalence of isolated rectal bleeding attributed to CMP consumption using a large prospective population-based study. We demonstrate the benign nature of this condition and the importance of rechallenge with CMP upon resolution of symptoms to better establish the diagnosis and to avoid unnecessary elimination diets. These findings are primarily important for pediatricians who have a significant impact on the management of these infants.

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Conflict of interests

There are no reported conflicts of interest for any of the authors.

References

- Arvola T, Ruuska T, Keränen J, Hyöty H, Salminen S, Isolauri E. Rectal bleeding in infancy: clinical, allergological, and microbiological examination. *Pediatrics* 2006; **117**: e760–8.
- Maayan-Metzger M, Ghanem N, Mazkereth R, Kuint J. Characteristics of neonates with isolated rectal bleeding. *Arch Dis Child Fetal Neonatal Ed* 2004; **89**: F68–70.
- Lake AM. Food-induced eosinophilic proctocolitis. *J Pediatr Gastroenterol Nutr* 2000; **30**: S58–60.
- Xanthakos SA, Schwimmer JB, Melin-Aldana H, Rothenberg ME, Witte DP, Cohen MB. Prevalence and outcome of allergic colitis in healthy infants with rectal bleeding: a prospective cohort study. *J Pediatr Gastroenterol Nutr* 2005; **41**: 16–22.
- Machida HM, Catto Smith AG, Gall DG, Trevenen C, Scott RB. Allergic colitis in infancy: clinical and pathologic aspects. *J Pediatr Gastroenterol Nutr* 1994; **19**: 22–6.
- Hirose R, Yamada T, Hayashida Y. Massive bloody stools in two neonates caused by cow's milk allergy. *Pediatr Surg Int* 2006; **22**: 935–8.
- Wilson JF, Heiner DC, Lahey ME. Milk-Induced Gastrointestinal bleeding in infants with hypochloremic microcytic anemia. *JAMA* 1964; **189**: 568–72.
- Koop CE. Rectal bleeding in infants and children. *Pediatr Clin North Am* 1956; **3**: 207–14.
- Katz Y, Rajuan N, Goldberg MR, et al. Early exposure to cow's milk protein is protective against IgE-mediated cow's milk protein allergy. *J Allergy Clin Immunol* 2010; **126**: 77–82.e1.
- Katz Y, Goldberg MR, Rajuan N, Cohen A, Leshno M. The prevalence and natural course of food protein-induced enterocolitis syndrome to cow's milk: a large-scale, prospective population-based study. *J Allergy Clin Immunol* 2011; **127**: 647–53.e13.
- El-Hodhod MA, Younis NT, Zaitoun YA, Daoud SD. Cow's milk allergy related pediatric constipation: appropriate time of milk tolerance. *Pediatr Allergy Immunol* 2010; **21** (2 Pt 2): e407–12.
- Elizur A, Rajuan N, Goldberg MR, Leshno M, Cohen A, Katz Y. Natural course and risk factors for persistence of IgE-mediated cow's milk allergy. *J Pediatr* 2012; **161**: 482–7.e1. [Epub ahead of print].
- Santos A, Dias A, Pinheiro JA. Predictive factors for the persistence of cow's milk allergy. *Pediatr Allergy Immunol* 2010; **21**: 1127–34.
- Mori F, Pucci N, Rossi ME. Oral desensitization to milk: how to choose the starting dose! *Pediatr Allergy Immunol* 2010; **21**(2 Pt 2): e450–3.
- Costa AJ, Sarinho ES, Motta ME. Allergy to cow's milk proteins: what contribution does hypersensitivity in skin tests have to this diagnosis? *Pediatr Allergy Immunol* 2011; **22**(1 Pt 2): e133–8.
- Reche M, Pascual C, Fiandor A, et al. The effect of a partially hydrolysed formula based on rice protein in the treatment of infants with cow's milk protein allergy. *Pediatr Allergy Immunol* 2010; **21**(4 Pt 1): 577–85.
- Thompson-Chagoyan OC, Vieites JM, Maldonado J, Edwards C, Gil A. Changes in faecal microbiota of infants with cow's milk protein allergy – a Spanish prospective case–control 6-month follow-up study. *Pediatr Allergy Immunol* 2010; **21**(2 Pt 2): e394–400.
- Jenkins HR, Pincott JR, Soothill JF, Milla PJ, Harries JT. Food allergy: the major cause of infantile colitis. *Arch Dis Child* 1984; **59**: 326–9.
- Pumberger W, Pomberger G, Geissler W. Proctocolitis in breast fed infants: a contribution to differential diagnosis of hematochesia in early childhood. *Postgrad Med J* 2001; **77**: 252–4.
- Odze RD, Bines J, Leichtner AM, Goldman H, Antonioli DA. Allergic proctocolitis in infants: a prospective clinicopathologic biopsy study. *Human Pathol* 1993; **24**: 668–74.
- Thompson EC, Brown MF, Bowen EC, Smith LM, vander Griten D. Causes of gastrointestinal hemorrhage in neonates and children. *South Med J* 1996; **89**: 370–4.
- Maloney J, Nowak-Wegrzyn A. Educational clinical case series for pediatric allergy and immunology: allergic proctocolitis, food protein induced enterocolitis syndrome and allergic eosinophilic gastroenteritis with protein-losing gastroenteropathy as manifestations of non-IgE mediated cow's milk allergy. *Pediatr Allergy Immunol* 2007; **18**: 360–7.
- Anveden-Hertzberg L, Finkel Y, Sandstedt B, Karpe B. Proctocolitis in exclusively breast-fed infants. *Eur J Pediatr* 1996; **155**: 464–7.
- Poddar U, Yachha SK, Krishnani N, Srivastava A. Cow's milk protein allergy: an entity for recognition in developing countries. *J Gastroenterol Hepatol* 2010; **25**: 178–82.
- Goldman H, Proujansky R. Allergic proctitis and gastroenteritis in children. *Am J Surg Pathol* 1986; **10**: 75–86.
- Elian E, Bar-Shani S, Liberman A, Matoth Y. Intestinal blood loss: a factor in calculations of body iron in late infancy. *J Pediatr* 1966; **69**: 215–9.
- Rasch CA, Cotton EK, Harris JW, Griggs FC. Blood loss as a contributing factor in the etiology of iron-lack anemia in infancy. *Am J Dis Child* 1960; **100**: 627, (abstract).
- Crittenden RG, Bennett LE. Cow's milk allergy: a complex disorder. *J Am Coll Nutr* 2005; **6** (Suppl): 582S–91S.
- Sullivan PB. Cow's milk induced intestinal bleeding in infancy. *Arch Dis Child* 1993; **68**: 240–5.