Risk Factors of Infantile Colic

Prof.Rehab Abdel Kader Mahmoud, Professor of Pediatrics, Ain Shams University

Prof.Ehab Mohamed Eid, Professor of Child Health, Ain Shams University

Prof.Ayman Mansour Abd El-Gawad, Professor of Child Health, National Research Center

Prof.Manal Abdel Moniem Mohsen, Professor of Child Health, National Research Center

Prof.Amira Abd El Monem Ali, Assistant Professor of Pediatrics, Faculty of Medicine, Ain Shams University

Dr.Sherin Ahmed el-Masry, Assistant Professor of Clinical Pathology, Faculty of Medicine- Ain Shams University

Sara Fawzy Sallam

Abstract

Background: Infantile colic is a common problem in first months of life. The etiology of infantile colic remains unknown, despite an abundance of research on the topic. A difference in gut micro flora as well as diet could play an important role in the pathogenesis of colic.

Aim: Assessment of infantile colic in relation to its predisposing factors including gut microlfora. To know impact of maternal diet on infantile colic.

Methods: Two hundred infants, aged 12.14±6.17 wk, free from episodes of gastroenteritis and without previous assumption of antibiotic and probiotic drugs, were enrolled in the study. They were divided into two groups: Colicky (100cases) and non colicky (100 controls), according to Wessel's criteria. Stool samples were collected, diluted and cultured on non selective and selective media to detect Gram negative anaerobe, Lactobacilli, Clostridium, Enterococci and Enterobacter. Statistical analysis was performed using Student's t-test,x2 test and a non- parametric test (Mann- Whitney U-test).

Results: Of 100 colicky infants, thirty seven infants were first in order of birth. Twenty two had positive family of atopy .Forty seven infants developed colic in the first week of life. Maternal exposure to smoke was positive in 52% p(0.007).Lactating mothers of colicky infants consume more dairy products than lactating mothers of non colicky infants p(0.003).Ninety eight percent of colicky infants had positive culture for Gram-ve anaerobe and Enterobacter, and only 7% have positive culture for Lactobacilli.

Conclusion: Type of food consumed by the lactating mother plays a role in development of infantile colic. It was also concluded that difference in the pattern of gut microflora between colicky and non colicky infants contributed in development of colic. Further studies are required to understand the causes of infantile colic and its consequences.

<div dir="rtl">

عوامل الخطورة للإصابة بمغص الرضع

مقدمة: يعتبر مغص الرضع من المشكلات الشائعة لدى الأطفال الرضع. ولا تزال الأسباب المرضية لمغص الرضع غير معروفة بالرغم من وفرة الأبحاث التى أجريت حول هذا الموضوع. ويلعب الاختلاف فى فلورا الأمعاء واختلاف النظام الغذائى دوراً هاماً فى التسبب فى مغص الرضع.

الهدف من الدراسة: تقييم مغص الرضع وعوامل الخطورة التى تتضمن فلورا الأمعاء؛ ومعرفة تأثير النظام الغذائى للأم على مغص الرضع.

طرق إجراء البحث: مائتى طفلاً فى الفئة العمرية ١٢,١٤ ± ٦,١٧ أسبوعاً ممن لا يعانون من نوبات التهاب المعدة والأمعاء وعدم خضوعهم للعلاج بالمضادات الحيوية أو البروبيوتيك. قسمت الحالات إلى: المجموعة الأولى وتشمل الأطفال المصابين بمغص الرضع (١٠٠) حالة فى حين تشمل المجموعة الثانية (١٠٠) طفلا من غير المصابين بمغص الرضع (المجموعة الضابطة)، وفقاً لمعايير ويسل. وقد تم عمل مزرعة على الوسائط المنتقاة وغير المنتقاة للكشف عن البكتيريا سالبة الجرام اللاهوائية واللاكتوباسلاى والكلوستريديوم إنتيروباكتر. وتم إجراء التحليل الإحصائى باستخدام اختبار تى ستودنت ومربع كاى والاختبار اللابارامترى (اختبار مان- ويتنى).

النتائج: أظهرت الدراسة أن ٣٧ من بين ١٠٠ طفلا مصابين بمغص الرضع كانوا فى الترتيب الولادى الأول وأن ٢٢ طفلا لديهم تاريخ عائلى للإصابة بالتأتب. كما أظهرت الدراسة أن ٤٧ طفلاً تعرضوا لمغص الرضع خلال الأسبوع الأول بعد الولادة. وكان تعرض الأمهات للتدخين بنسبة ٥٢%. وأوضحت نتائج الدراسة أن أمهات أطفال المجموعة الأولى يستهلكن قدراً أكبر من منتجات الألبان من أمهات أطفال المجموعة الثانية. وأوضحت الدراسة أن ٩٨% من الأطفال الذين يعانون من مغص الرضع قد أظهروا نتائج إيجابية بالمزرعة التى تم إجراؤها للكشف عن البكتيريا اللاهوائية والمكورات المعوية والأمعائية سالبة الجرام. إلا أن ٧% لمزرعة اللاكتوباسيلاى.

الخلاصة: يلعب نوع الطعام الذى تستهلكه الأمهات المرضعات دوراً هاماً فى تعرض الأطفال لمغص الرضع. وقد توصلت الدراسة إلى أن الإختلاف فى نمط فلورا الأمعاء بين الأطفال الذين يعانون من المغص وبين غيرهم يساهم فى تعرض الأطفال لمغص الرضع. وتوصى الدراسة بضرورة إجراء المزيد من الدراسات لفهم الأسباب الكامنة وراء مغص الرضع وعواقبه.

</div>

Introduction

Infantile colic is a common problem in first months of life; it remains enigmatic despite its long history and its relatively frequent occurrence.

Colic is characterized by excessive and inconsolable crying, hyper tonicity, and wakefulness that cluster in the evening. Consensus has not been reached regarding a definition for colic, but most research efforts have relied on modified Wessel criteria[1,2] in which the episodes of crying in an infant with colic last more than three hours per day and more than three days per week for at least three weeks.

Estimates of colic's prevalence range from5% to 40%, depending on the definition and methods used.C onsequently, there is contradictory evidence regarding colic's etiology[3,4].

Some hypothesis suggested organic or psychological disorder. However, infantile colic may be a result of synergistic interaction between biologic and behavioral factors. Abnormal gastrointestinal function and allergic problems such as protein intolerance has been suggested as a cause of infantile colic[5]. Other recent hypothesis such as dietary factors, maternal smoking and medicine during delivery are still to be confirmed[6].

This uncertainty, along with colic's frequent occurrence, colic's potential impact on the family, and the absence of an effective cure, underlines the importance of continued research.

The aim of the present study was to asses' infantile colic in relation to its predisposing factors including gut micro flora and to know impact of maternal diet on infantile colic.

Subject And Methods:

This study comprised 200 apparently healthy infants, 100 infants experienced infantile colic according to Wessel's criteria. They were selected from the in- patient and outpatient Clinic of Children's Hospital, Ain Shams university from November 2010 to May 2012. The control infants were taken from relatives and colleges of cases who experience no signs or symptoms of infantile colic. This is a case- control study that includes two groups.

1. Group1: It included 100 colicky infants with mean age of 12.88+/- 6.85 weeks and 22 weeks as range. Colicky breast fed infants were 56 infants with mean age 12.69± 7.06 weeks, while formula fed colicky infants were 44infants with mean age 12.11± 6.66 weeks. They were 60 male and 40 female.

2. Group 2 (Control): It included 100 non- colicky infants with mean age of 11.41+/- 5.5weeks and 20weeks as range. 50 infants were breastfed with mean 11.21± 5.49,and 50 were formula fed with mean age 11.30± 5.21 weeks. They were 41 male and 59 female.

   ¤ Inclusion criteria: Infants aged 6 months or less. Meets Wessel's criteria for colic, in which the episodes of crying last more than three hours per day and more than three days per week for at least three weeks.

   ¤ Exclusion criteria: Patients with the following conditions were excluded from the study: Acute infections. (e. g. O.M, meningitis...), Severe congenital anomalies, Inborn error of metabolism, Chromosomal abnormalities, Gastrointestinal malformation or surgery, on antimicrobial therapy.

Parents gave written consent to the inclusion of their infants in the study. The study was approved by the local ethical committee.

All patients and controls were subjected to the following.

1. Careful history taking: A questionnaire was planned to fulfill the following data:

   a. Infantile data: name, sex, age in weeks, order of birth, gestational age, history of NICU admission, weight (in Kilogram) at birth, weight (in Kilogram) and length (in centimeter) at time of sample taking.

   b. Maternal Data:

      ¤ Antenatal history: History of maternal infection in form of fever or bleeding, PROM, hypertension, gestational diabetes, chronic illness, vitamin intake during pregnancy, chronic exposure to smoking during pregnancy, family history allergy.

      ¤ Natal history including mode of delivery, type of anesthesia.

      ¤ Postnatal history including lactation in the first hour, nipple abnormality, lactation difficulty, postpartum infection or hemorrhage, drug intake with lactation.

   c. History of infantile colic: First developed, Frequency per day, Duration of each episode in minute's.P recipitating factors, Relieving methods.

   d. Infant feeding pattern: Type of feeding Breastfeed/ Formula feed, frequency of lactation on demand/ scheduled feds, herbal intake, lactose or sucrose consuming in the first 6 months, post feeding satisfaction. Introduction of any solid food

   e. Maternal Dietary pattern: Check list to obtain qualitative information about the different items of food and beverage consumed by the mother during lactation period.

2. Examination: Thorough clinical examination with particular emphasis on:

   a. Anthropometric measures; weight in kg and height in cm were plotted against percentiles for age and sex according to Egyptian growth charts.

   b. Head circumference and Fontanels examination.

   c. Chest And Heart Examination.

   d. Full abdominal examination, including hernia orifices and genitalia.

   e. Careful skin examination for signs of vitamin deficiency.

Results:

There was no significant difference between the two studied groups as regards age, birth weight and length but a significant difference was found in current weight being higher in non colicky infants (group 2).

A significant difference was also found in weight gain, with higher weight gain in non colicky infants.

Infantile colic was more prevalent among males and preterm infants; this was proved by statistically significant difference between the two groups as regards gender and gestational age.

We found statistically significant difference between colicky and non colicky infant as regards NICU admission as 21% of colicky infant had been admitted to NICU versus 7% in non colicky infants.

Table (1) Comparison between colicky and non colicky infants as regards gender, gestational age and history of NICU admission.

Variable		Group I	Group II	χ^2	P Value
Gender	Male	60	41	7.221	0.007
	Female	40	59		
NICU Admission	Yes	21	7	8.140	0.004
	No	79	93		
Gestational Age	Term	83	93	4.735	0.030
	Preterm	17	7		

P <0.05 (Significant), P >0.05 (Non- significant)

The range of birth orders was from (1- 7) with the most frequent one was the first order which comprised 37 colicky infants (37%).

Maternal exposure to smoke was significantly higher among mothers of colicky infants.

In this study, we observed a higher prevalence of colicky infants with a family history of atopy 22% in group I compared to 7% in group 2.

Table (2) Comparison between colicky and non colicky infants as regards prenatal maternal data

Variable	Group 1 (Yes)		Group 2 (Yes)		χ^2	P Value
	n	%	n	%		
Fever	5	5	3	3	0.521	0.47
Bleeding	2	2	2	2	0.000	1.00
PROM	5	5	4	4	0.116	0.733
Hypertension	9	9	13	13	0.817	0.366
Gestational Diabetes	5	5	6	6	0.096	0.756
Chronic Illness	15	15	4	4	7.037	0.008
Vitamin Intake	64	64	56	56	1.333	0.248
Exposure To Smoke	52	52	33	33	7.386	0.007
History Of Paternal Allergy	22	22	7	7	9.074	0.003

P <0.05 (Significant), P >0.05 (Non- significant)

No significant difference was found between two groups as regards mode of delivery. On the other hand this study detected significant difference between two groups as regards type of anesthesia.

Colicky and non colicky showed no significant difference as regards time of feeding as well as post feeding satisfaction. Colicky group in the current study displayed no significant difference as regards first hour lactation, nipple abnormality as well as lactation difficulty as post a postnatal risk factor proposed for colic.

As regards feeding pattern no statistically significant difference was detected between breast fed and formula fed infant with infantile colic.

Percentage of colicky infants was higher than non colicky infants as regards lactose/ sucrose intake as well as herbal intake

Vomiting and reflux was significantly higher in colicky infants compared with controls. This is a part of GIT symptoms associated with infantile colic.

Table (3) Comparison between colicky and non colicky infants as regards lactose/sucrose intake, herbal intake, post feeding satisfy and vomiting/reflux

Variables	Colicky (N= 100)		Non Colicky (N= 100)		χ^2	P Value
	n	%	n	%		
Lactose/Sucrose Intake	49	49	8	8	41.246	0.00
Herbal Intake	72	72	46	46	12	0.00
Post Feeding Satisfy	73	73	83	83	2.914	0.08
Vomiting/Reflux	15	15	Zero	Zero	16.216	0.00

P <0.05 (Significant), P >0.05 (Non- significant)

The percentage of formula fed infants that develop colic in the first week of life was (47.7%) and second week was (36.4%) which is higher than breastfed colicky infants whose percentages were (41.1%, 14.3% respectively) (p≤ 0.05). But no significant difference between breast fed colicky infants and formula fed colicky infants as regards frequency of colic per day or duration of each colic episode.

This study showed statistically significant relation between type of food consumed by mother and development of colic.

Table (4) Relation between colic and type of food consumed by mother among breast fed infants

Type Of Food	Colicky BF (N= 56)		Non Colicky Bf (N=5 0)		Or (Ci) 95%	P Value	χ^2
	No.	%	No.	%			
Tea	51	91	36	72	3.889 (1.499-10.092)	0.004	8.507
Coffee	8	14.2	2	4	4.54 (0.988-20.874)	0.036	4.412
Dairy Products	48	85	33	66	3.606 (1.524-8.531)	0.003	9.113
Garlic/Onion	47	84	10	20	21.143 (8.613-51.901)	0.000	54.986
Green Leaves	38	67.8	0	0	2.786 (2.071-3.747)	0.000	60.315
Banana, Strawberry, Jam	37	66	4	8	25.981 (8.497-79.442)	0.000	48.114
Cabbage/ Cauliflower	38	67.8	6	12	5.573 (2.152-14.434)	0.000	14.274
Tuna, Sardine, Mackerel	8	14.2	5	10	4.895 (1.761-13.604)	0.001	10.524
Processed Meat	33	59	5	10	13.00 (4.702-35.943)	0.000	31.694
Processed Food	44	78.5	8	16	19.066 (7.669-47.402)	0.000	50.351
Pickles	37	66	12	24	6.443 (2.934-14.148)	0.000	23.651

P <0.05 (Significant), P >0.05 (Non- significant)

Positive culture for gram negative anaerobe and Enterobacter was more among colicky infants than non colicky infants, this difference was statistically significant. Lactobacilli positive culture was higher among non colicky infants.
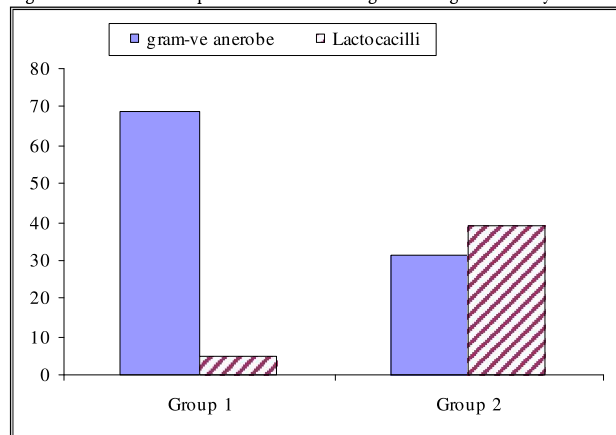

Figure (1) Percentage of gram- ve anaerobe and lactobacilli positive culture among the two groups

Discussion:

Regarding the demographic criteria of the studied groups, this study showed no significant difference between colicky and non colicky infants as regards age in weeks, length and birth weight. Results showed better weight gain in the non colicky group demonstrated by significant difference between two groups in weight for age percentile. In contrast to what was observed in a large cohort study done Denmark[7] associated low birth weight (<2.5 Kg) as well as low gestational age (<32 weeks) to elevated risk of infantile colic.

Our study recorded higher infantile colic percentage among males (60%) (p= 0.007). Lucassen[8] stated that male gender is not a risk factor for excessive crying.

As regards NICU admission this study revealed statistically significant

difference between colicky and non colicky infant as regards NICU admission as 21% of colicky infant had been admitted to NICU versus 7% in non colicky infants. In addition positive significant correlation was also found in this study between colic and NICU admission. This item was not studied in previous studies as separate risk factor.

The range of birth orders was from (1- 7) with the most frequent one was the first order which comprised 37 colicky infants (37%).T his agrees with an article on an Iranian prospective study[9] , that birth order is a risk factor, since the first born infant would suffer from excessive crying more often.

In this study exposure to smoke was significantly higher among colicky infants in agreement with what Hill, 2012 in recent epidemiologic evidence has suggested that exposure to cigarette smoke and its metabolites may be related to colic[10]. Maternal smoking and exposure to nicotine replacement therapy (NRT) during pregnancy may be associated with colic.

In this study, we observed a higher prevalence of colicky infants with a family history of atopy 22% in group I compared to 7% in group II, in agreement with what Jose et al.[11] reported that infants with infantile colic have a higher frequency of a family history of atopy and an increased risk of developing gastrointestinal and atopic diseases later in life.

Our study showed no significant difference between two groups as regards mode of delivery, Similar to Talachine et al study in which mode of delivery was not associated with colic[12].

On the other hand this study detected significant difference between two groups as regards type of anesthesia.

Colicky group in the current study displayed no significant difference as regards first hour lactation, nipple abnormality as well as lactation difficulty as post a postnatal risk factor proposed for colic.

As regards feeding pattern no statistically significant difference was detected between breast fed and formula fed infant with infantile colic. This appears different from what was published[13] from a community based study revealing that exclusive breast- feeding was protective against infantile colic, including infants of smoking mothers.

In this study no significant difference was revealed between breastfed and formula fed as regards colic. Despite observing some trend toward less colic in breast fed subgroup we were not able to reproduce the results of the latter study. Our smaller sample size might have caused the inability to detect meaningful differences.

In this study Vomiting and reflux was significantly higher in colicky infants compared with controls. As a part of GIT symptoms associated with infantile colic. In Italy, 7.1% of colicky infants had two or more episodes of regurgitation per day for 3 or more weeks. All had improved at 3- month follow- up. In another Italian study of 2879 infants in the first six months of life, 23.1% had regurgitation and 20.5% had colic[14].

In this study the percentage of formula fed infants that develop colic in the first week of life was (47.7%) and second week was (36.4%) which is higher than breastfed colicky infants whose percentages were (41.1%, 14.3% respectively) (p≤ 0.05). This goes with a prospective cohort study of 856 mother- infant dyads including exclusively breastfed, complementary fed, and exclusively formula fed in which Clifford et al. Concluded that Breastfeeding did not have a protective effect on the development of colic[15].

In our study significant association between type of food consumed by the mother and colic being higher with garlic and onion consumption (p= 0.000).

However, in an unblinded study, exclusion of cow's milk from the breastfeeding mother's diet resulted in the disappearance of colic in 13 of 18 infants. In a subsequent study, 66 breast- feeding mothers of colic infants were given a cow's milk- free diet. Colic disappeared in 35 infants, but reappeared in 23 following the reintroduction of cow's milk into the maternal diet.

The current study showed higher positive culture of gram negative anaerobe, enterococci and enterobacter in colicky infant than non colicky infants, this can be explained by the results of a Dutch study[16] that followed the temporal development of intestinal microbiota from birth to approximately 100 days in 24 infants suggested that early differences in the development and composition of gut flora may be at the root of infant colic At 2 weeks, Babies later diagnosed with colic had significantly less microbial diversity and stability than their healthy counterparts, as well as more than twice the abundance of proteobacteria and significantly reduced levels of Bacteroids. These differences were all seen in the first month of life, before the colic peak, and usually disappeared by (3- 4) months of age, when colic usually resolves.

On the other hand our study found higher percentage of Lactobacilli positive culture among control group this goes with what Bjorksten et al.[18] observed of lower counts of intestinal lactobacilli in colicky infants, in comparison with healthy infants.[17]

References:

1. Lucassen PL, Assendelft WJ, van Eijk JT, Gubbels JW, Douwes AC, van Geldrop WJ. Systematic review of the occurrence of infantile colic in the community. **Arch Dis Child**, 2001;84:398-403

2. Wessel MA, Cobb JC, Jackson EB, Harris GS, Detwiler AC. **Paroxysmal fussing in infancy,** sometimes called"colic"Tediatrics 1954;14:421-35

3. Maria A. L. Saaverdra, Juvenal S. Bias, Gilberto Garcias, Bernardo L. Horta, Elaine Tomasi, Rodrigo Mendonica. Infantile colic incidence and associated risk factors: A cohort study. **Pediatria** (Rio J) 2003; 79(2)115-22

4. Herman M, Le A. The crying infant. **Emerg Med Clin North Am**. 2007; 25 (4): 1137-59, vii.

5. Hill DJ, Hosking CS. Infantile colic and food hypersentivityj **Pediatr Gastroenterol Nut**. 2000; 30 (suppl): S67- S76.

6. Shenassa ED and Brown Mary- Jean. Maternal Smoking and Infantile Gastrointestinal Dysregulation: The Case of Colic. **Pediatr**. 2004; 114 (4): e497- e505.

7. Ioanna Milidou, Tine Henriksen, Morten Jensen, Jorn Olsen and Charlotte Sondergaard: Intrauterine Nicotine Exposure, Birth Weight, Gestational Age and the risk of infantile Colic. Does Central Nervous System Development Play a Role in Infantile Colic? **Neurology** 26, 2012; 78 (meeting Abstract 1): P07.137.

8. Lucassen PL, Assendelft WJ, van Eijk JT, Gubbels JW, Douswess AC, van Geldrop WJ. Systematic **review** of the occurrence of infantile colic in the community. **Arch Dis Child** 2001; 84:398-403.

9. Fazil M. prevalence and risk factors for infantile colic in district mansehra. **J Ayub Med** Coll Abbottabad 2011;23 (2)

10. Milidou I, Henriksen TB, Jensen MS, Olsen J, Sendergaard C. (2012): Nicotine replacement therapy during pregnancy and infantile colic in the offspring. **Pediatrics**. Mar 2012;129 (3): e652-8.

11. Jose A. Castro- Rodriguez, MD, Debra A. Stern, MS, Marilyn Halonen, PhD, AnneL. Wright, PhD, Catherine J. Holberg, PhD, Lynn M. Taussig, MD, Fernando D. Martinez, MD. Relation between infantile colic and

asthma/atopy: A prospective study in an unselected population. **Pediatrics** Vol. 108 No. 4 October 1, 2001. pp. 878-882

12. Talachian E, Bidari A, Rezaie MH. Incidence and risk factors for infantile colic in Iranian infants. World J. **Gastroenterol.**, 2008; 14: 4662-4666.

13. Canivet CA, Ostergren PO, JakobssonIL, Dejin- Karisson E, Hagander BM. Infantile colic, maternal smoking and infant feeding at 5 weeks of age. **Scand J Public Health**. 2008 May; 36 (3): 284-91.

14. Miele E, Simeone D, Marino A, Greco L, Auricchio R, Novek SJ, Staiano. Functional gastrointestinal disorders in children: an Italian prospective study. **Pediatrics**. 2004; ! 14:73-78. doi: 10.1542/peds. 114.1.73

15. Clifford TJ, Campbell MK, Speechley KN, Gorodzinsky F. Infant colic: empirical evidence of the absence of an association with source of early infant nutrition. **Arch Pediatr Adolesc Med**. 2002; 156:1123-1128.

16. Waknine Y. Colic preceded by gut flora differences. **Medscape Medical News**. Jan 14, 2013. Available at http://www.medscape.com/ viewarticle/ 777658.

17. Pokorna Kahvak D., Gwiazda E., Muszynska A., Steciwko A. Infant colic- diagnostics and therapeutic management in the family physician's practice. **Terapia**, 2010; 2: 40-43.

18. Bjorksten B, Sepp E, Julge K, Voor T, Mikelsaar M. Allergy development and the intestinal microflora during the first year of life. **J Allergy Clin Immunol** 2001; 108: 516-520.