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Human milk antibiotic residue levels and their relationship with delivery mode, maternal antibiotic use and maternal dietary habits

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Abstract. – OBJECTIVE: It is important to identify undesirable toxins and metabolites present in human milk that may be passed on to nursing infants. Such residues may derive from the antibiotics that are widely used to treat infectious diseases in both humans and food-producing animals. To the best of our knowledge, there are no reports in the literature on human milk antibiotic residue levels.

PATIENT AND METHODS: As a part of the Human Milk Artificial Pollutants (HUMAP) study, we aimed to evaluate human milk antibiotic residues among mothers with 7 to 90-day-old babies. Pregnant women who had received antibiotic treatment during pregnancy were excluded. The use of antibiotic prophylaxis with cefazoline sodium during labor was noted among the study subjects. Human milk antibiotic residues were evaluated with the InfiniPlex for Milk Array (Randox Laboratories, London, United Kingdom), a semi-automated system with a multi-array biochip designed to detect antibiotic residues and toxins.

RESULTS: The HUMAP study included 83 mothers, ranging in age from 17 to 41 years (mean 29.7 ± 6.2 years). Of these, 59% received cefazoline sodium shortly after birth, while 41% did not receive any antibiotics during the pregnancy, delivery or lactational periods. Testing revealed that 71/83 (85.5%) human milk samples were positive for beta-lactams and 12 (14.5%) samples were positive for quinolones. There was no difference in maternal age, gestational week, delivery type, sampling time, maternal dietary habits between the mothers with quinolones or beta-lactam residues in their milk and those without ($p > 0.05$ for both). Beta-lactam and quinolone residues were detected in 85.7% and 23.5%, respectively, of the human milk samples of mothers who did not receive antibiotics at birth and/or during the first seven days after birth.

CONCLUSIONS: We found that the majority of human milk samples included beta-lactams or quinolones, even though the mothers did not receive these antibiotics during pregnancy and lactation. Antibiotic residues in human milk may affect early maintenance of the intestinal microbiota. Previous studies have shown that antimicrobials in food might increase the risks of allergies and could lead to the development of antibiotic-resistant bacterial strains. Effective policies on food safety and appropriate antibiotic use during pregnancy and lactation are needed.

Key Words:
Human milk, Antibiotic, Antibiotic residue, Beta-lactam, Quinolone.

Introduction

Health organizations and scientific societies recommended that all infants should breastfeed for the first six months of life and then continue breastfeeding with supplementary foods until they reach 24 months[1]. Breastfeeding is thought to play an important role in maternal-infant interactions as well as to have a positive impact on the baby's gastrointestinal system, immunological functions and overall development[2,3]. Breastfeeding has been also shown to be a determining factor in the successful development of the intestinal microbiota[4]. Human milk is an important and unique nutrient source; however, nursing mothers may

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be exposed to natural and artificial pollutants, or they may consume foodstuffs contaminated with toxins during the breastfeeding period. Therefore, it is important to identify undesirable toxins and metabolites that are present in human milk and that may be passed on to breastfeeding infants[5,6]. Antibiotics are the primary treatment for bacterial infections in outpatient and hospital settings, making them some of the most commonly prescribed/used drugs worldwide. Antibiotics are critical for eliminating certain bacterial infections, but they can be inappropriately used in routine daily practice[7]. Antibiotics are also commonly used for therapeutic and prophylactic purposes in veterinary practice and trace quantities of the antibiotics may be present as residues in animal and dairy products[8]. Antibiotic residues in food of animal origin may cause adverse effects on human health and should not be permitted in food intended for human consumption[9,10]. Antibiotic residues are potentially toxic and may lead to the development of antibiotic resistance[10]. In addition, continuous exposure to antibiotics may alter the microbiota composition[11]. If antibiotics are necessary to treat animal diseases, a withholding period must be observed until the residues are no longer detected[10].

Antibiotic administration is generally limited during pregnancy except for patients with severe infections. Antibiotics are often used during the delivery and postpartum periods, especially with mothers who give birth with a Caesarean section[12,13]. Some antibiotics are classified as safe to use during pregnancy and lactation and have been appropriately prescribed[13]. It is thought that antibiotics may pass from the mother to the baby in the form of residual circulation, but no research has been conducted on antibiotic exposure from maternal dietary components or antibiotic residues in maternal circulation during pregnancy and lactation. Therefore, the analysis of the antibiotic residues in food products is very important for human health. To the best of our knowledge, there are no reports in the literature on antibiotic residues in human milk. This study evaluated the levels of antibiotic residues in human milk samples obtained from lactating mothers.

Materials and Methods

The Human Milk Artificial Pollutants (HUMAP) study is a cross-sectional study designed to evaluate the presence of mycotoxins, bisphenol A, phthalate and antibiotic residues in human milk samples in Turkey. In this part of the HUMAP study, we evaluated the presence of antibiotic residues in human milk. The study protocol was evaluated and approved by the Eskisehir Osmangazi University Local Ethics Committee. The study was supported by the Eskisehir Osmangazi University Scientific Research Grant.

We evaluated all lactating mothers with 7 to 90-day-old babies at the Eskisehir Osmangazi University and Eskisehir Maternity and Children Hospital (Eskisehir, Turkey). Mothers who had taken antibiotics during pregnancy were excluded from the study. Maternal age, the number of pregnancies, gestational age and the number of breastfeeding days were noted for each study participant. The use of cefazoline sodium (a routinely used antibiotic before and after surgical intervention in our hospital) during and after the delivery was determined from the patients' medical records. The following exclusions were applied: mothers who received antibiotics other than cefazoline sodium or who received a combination of antibiotics; mothers who required more than seven days of antibiotics; and mothers who required antibiotic treatment during the lactational period for any reason. Maternal dietary habits during the pregnancy and lactation periods were evaluated with a questionnaire. The dietary questionnaire included questions about the consumption of different food groups including poultry, fish, milk products (milk, yoghurt and cheese), dried fruits (dried fig and dried apricot), honey, sea foods, flaked red pepper and spice. The maternal demographic factors, delivery characteristics and dietary habits are summarized in Table I. Within the scope of the study and after receiving informed consent, 3-5 cc of human milk was obtained from each participant under sterilized conditions and stored at -20°C until the end of the study period. The human milk was tested for residues of 45 antibiotics and other drugs using the InfiniPlex for Milk Array (Randox Laboratories, London, United Kingdom). Table II contains a list of the antibiotics and other drugs that were studied. The standardized kit allowed all these compounds to be tested with a single sample. The kit was developed with biochip technology for use as an *in-vitro* qualitative diagnostic marker. All the evaluation steps have been performed according to manufacturer's instructions. Study protocol includes tests which have been established for each detectable drug residue, as ppb levels for each drug

Table I. Demographic and antenatal factors, antibiotic use and the dietary habits of the mothers included in the study.

	Mothers not-receiving antibiotic at birth or after (N=34)	Mothers receiving antibiotic during 3 to 7 days after birth (N=49)	Total (N=83)
Age (years)	28.0 ± 6.7 years (17-41 years)	31.0 ± 5.6 years (18-40 years)	29.7 ± 6.2 years (17-41 years)
Caesarean section	18 (52.9%)	29 (59.2%)	47 (56.6%)
Gestational week (weeks)	37.8 ± 1.6 (34-41)	37.7 ± 2.85 (26-40)	37.7 ± 2.41 (26-42)
Exclusive breast feeding	24/34 (70.6%)	35/49 (71.4%)	59/83 (71.1%)
Sampling time (days)	26.9 ± 16.1	42.2 ± 22.7	35.9 ± 21.6
Maternal Dietary Habits (3-5 days / Everyday, per week)			
Chicken	8.8% - 2.9%	0% - 0%	8.4% - 2.4%
Fish	0% - 0%	6.1% - 2.0%	8.4% - 32.5%
Meat	11.7% - 2.9%	2% - 42.8%	18.0% - 20.4%
Honey	17.6% - 17.6%	20.4% - 24.4%	19.2% - 18.0%
Dry fig	14.7% - 14.7%	20.4% - 20.4%	13.2% - 36.1%
Dry apricots	17.6% - 14.7%	12.2% - 28.5%	3.6% - 34.9%
Milk products	14.7% - 47.0%	2% - 38.8%	4.8% - 56.6%
Flaked red pepper	5.8% - 29.4%	6.1% - 65.3%	4.0% - 2.0%
Spice	2.9% - 44.1%	6.0% - 2.4%	0% - 0%

U6: small nuclear RNA, snRNA; KIF23: Kinesin family member 23; GAPDH: glyceraldehyde-3-phosphate dehydrogenase.

groups. The decision level corresponds to the concentration was ≥95% of the samples tested are positive. The decision levels for each residue from discrete test regions arrayed on the biochip.

Statistical Analysis

Statistical analysis was performed using the SPSS package program, version 11.5 (Chicago, IL, USA). Values, which are normally distributed, were expressed as mean and standard deviation. The Mann-Whitney U test was used to compare unpaired data among the groups. Analysis of variance (ANOVA) was used to compare maternal dietary habits among mother with positive or negative antibiotic residues in their human milk. Games-Howell test was used to compare subgroups in cases where there was a statistically significant difference between the groups. A p-value of less than 0.05 was considered statistically significant.

Results

The HUMAP study included 83 mothers, ranging from 17 to 41 years (mean 29.7 ± 6.2 years). Human milk samples were obtained from the mothers between 7 and 90 days after birth (mean 35.9 ± 2.1 days). The study included 32 (32/83; 38.5%) mothers who had their first gestation. The deliveries were either normal or spontaneous (36/83; 43.4%) or Cesarean section (47; 56.6%). Cefazoline sodium was administered to 49 (59%) mothers; 31 (37.3%) mothers received the antibiotic from 24 to 72 hours after birth, while 19 mothers (22.8%) received a 7-day course of cefazoline sodium after birth. The study included 34 (34/83; 40.9%) mothers who did not receive antibiotics during the pregnancy, delivery or lactational periods. The average gestational weeks of the infants in the study ranged from 26 to 42 weeks, with a mean of 37.7 ± 2.41 weeks. Breastfeeding alone was used on 59 (71.1%) of the infants, while 24 (28.9%) consumed both human milk and formula. The demographic and antenatal factors, antibiotic use and maternal dietary habits are summarized in Table I. The antibiotic and other drug residues detected in the milk of 83 mothers are summarized in Table II. Quinolones residues were detected in 12 (14.5%) of the human milk samples. There was no difference in maternal age, gestational week or sampling time between the mothers who had quinolone residues in their human milk and those who did not ($p > 0.05$). Six of the mothers whose milk had quinolone residues gave birth through normal spontaneous transmission, and six gave birth through Cesarean section. Quinolone residues were detected in the human milk samples of 8/34 (23.5%) mothers who did

Table II. Antibiotic and other drug residues identified in the human milk of the mothers included in the study.

Antibiotic or other drug residue	N (%)	Antibiotic or other drug residue	N (%)
Amphenicol	2/83 (2.4)	Phenylbutazone	1/83 (1.2)
Apramycin	-	Pirlimycin	-
Bacitracin	2/83 (2.4)	Polymyxin	4/83 (4.8)
Baquiloprim	-	Ractopamine	-
Beta-lactams*	71/83 (85.5)	Rifaximin	-
Cefuroxime	5/83 (6.0)	Quinolones**	12/83 (14.5)
Cephalexin	-	Spectinomycin	-
Chlormadinone	1/83 (1.2)	Spiramycin	-
Dapsone	-	Streptomycin	-
Dexamethasone	2/83 (2.4)	Sulfaguanidine	-
Erythromycin	-	Sulfapyridine	1/83 (1.2)
5-hydroxy flunixin	-	Sulfamethazine	1/83 (1.2)
Gentamycin	-	Sulfonamides	1/83 (1.2)
Hygromycin	-	Tylosin	-
Kanamycin	-	Tolfenamic acid	-
Lincomycin	-	Trimethroprim	-
Melamine	3/83 (3.6)	Tetracyclines	-
Meloxicam	-	Tobramycin	2/83 (2.4)
Metamizole	2/83 (2.4%)	Virginiamycin	-
Neomycin	-	Methylprednisolone	-
Nitroxinil	-	Aflatoxin M1	-
Novobiocin	-		

*Beta-lactams residues penicillin (penicillin G, ampicillin, dicloxacillin, amoxicillin, cloxacillin, nafcillin and penicillin V) and cephalosporin (cefalonium, ceforperazone, cefapirin cefquinome, ceftiofur, cefacetril and cefazolin) groups.
**Quinolones residuea for; enrofloxacin, ciprofloxacin, danofloxacin, difloxacin, marbofloaxacin, oxolinic acid and flumequine.

not take antibiotics during pregnancy, at birth or after birth. There was no history of quinolone use during pregnancy, at birth, or after birth in any of these mothers. All 12 mothers with quinolone residues present in their milk samples exclusively fed their babies with breastfeeding. Beta-lactam residues were detected in 71 (85.5%) of the human milk samples Table II. There was no difference in maternal age, gestational week or sampling time between the mothers who had beta-lactam residues in their milk and those who did not ($p > 0.05$). Beta lactam residues were detected in the human milk samples of 29/34 (85.2%) mothers who did not take antibiotics during pregnancy, at birth or after birth. Beta lactam residues were detected in the human milk samples of 42/49 (85.7%) mothers who received antibiotics at birth and/or for seven days after birth. There was no difference in the percentage of beta lactam residues in the human milk ($p > 0.05$) of the mothers who did not take antibiotics during pregnancy and those who received antibiotics at birth and/or for seven days after birth ($p > 0.05$). There was no difference in the maternal dietary habits of the mothers whose milk was positive or negative for beta-lactams or quinolones ($p > 0.05$ for both). Cefuroxime was also detected in five (6%) of the human milk samples. Other antibiotic residues (i.e., amphenicol, bacitracin, polymyxin and tobramycin) were detected among a minority of the human milk samples; however, none of the enrolled mothers had a history of using these antibiotics. The non-antibiotic drugs metamizole and dexamethasone were detected in 2/83 (2.4%) of the human milk samples; neither of these mothers had taken these drugs (Table II).

Discussion

This study provides the first reported evidence that beta lactams and quinolones antibiotic residues have been detected in the human milk samples of mothers who have no history of using antibiotics during the pregnancy, birth or lactational periods. The amount of antibiotics in the mother's milk is in part determined by the levels of antibiotics in the mother's circulation that pass into her milk through passive diffusion. Other factors include the antibiotic's molecular size, distribution volume and half-life[13,14]. In our study, beta lactams antibiotic residues were most commonly

found in the human milk samples, especially among mothers who had not received antibiotics. Beta-lactams residues in this test include positive samples of penicillin (penicillin G, ampicillin, dicloxacillin, amoxicillin, cloxacillin, nafcillin and penicillin V) and cephalosporin (cefalonium, cefoperazone, cefapirin cefquinome, ceftiofur, cefacetril and cefazolin) groups. Positive results might be associated with cefazoline use at birth and after; however, we observed positive beta-lactams residues especially among mothers who had not received antibiotics. More than 10 million women in the United States have reported receiving antibiotic treatment during pregnancy or at birth. The problems associated with antibiotic use during pregnancies and in breastfeeding mothers are often overlooked[15]. Antibiotic use during pregnancies and in breastfeeding mothers is typically used to treat community-borne infections and mastitis. Antibiotics are also prophylactically used for Group B Streptococcus infections and in conjunction with Cesarean sections. Studies[13,14] have shown that antibiotics can be safely used during pregnancy without causing serious adverse effects in infants. Beta lactam antibiotics are the most commonly used antibiotic group during pregnancy and lactation periods and are generally regarded as safe for infants[13,16]. In our study, the second most commonly detected antibiotic residue was quinolone, but none of the mothers had a history of quinolone use. Quinolones residue test includes positive detection limit for enrofloxacin, ciprofloxacin, danofloxacin, difloxacin, marbofloaxacin, oxolinic acid and flumequine. Quinolones are among the most widely used antibiotics, and quinolone resistance has become a significant problem in many countries[17]. Fluoroquinolones are easily transferable from the mother to her baby through breast milk. Quinolones are not recommended for use in pregnancy or in children because the drug has been associated with arthropathic effects in experimental models[14]. Theoretically, human milk should not include quinolone residues, but given our study results, additional extensive studies are needed to determine the potential effects of quinolone residues in human milk on infants. Although serious side effects have not been reported, it is thought that antibiotics may affect the composition of the intestinal microbiota[18]. Recently, Pereira et al[19] evaluated the effects of antibiotics residue containing milk on microbiota composition and related functions in calves. This study showed that drug residues, even at very low concentrations, resulted in a significant difference in relative abundance of microbiota composition and changes in the functional profile of microbial populations. For this reason, we believe that beta lactams antibiotic residues, which we detected in the milk of mothers both with and without antibiotic use, may adversely affect antibiotic resistance and alter the microbiota composition. Although this study provided no information on the source of the antibiotic residues detected in the human milk, the antibiotic residues were thought to derive from the mothers' food. Despite numerous studies on the safe use of antibiotics, there is insufficient data on the effects of foodborne and long-acting antibiotics on infants[14]. Antibiotics have long been used in veterinary practice for the treatment and prophylaxis of infections; however, in recent years, antibiotics have also been widely used to accelerate animal weight gain[10]. Antibiotic residues can be found at different concentration levels in foods of animal origin such as fish, beef, poultry, milk, and milk products[10,20]. Antibiotics may be fed to animals as a source of indirect human contamination. Antibiotics are also used directly during the production, processing and storage of dairy milk products[10]. Humans can consume these antibiotic residues in food sources, affecting mothers during pregnancy and breastfeeding. While several quinolones are acceptable for treatment of beef, poultry, and fish in many countries of the World, contaminated poultry tissues with harmful concentrations of drug residues may occur[19]. In Turkey, ciprofloxacin, enrofloxacin, marbofloxacin, danofloxacin, difloxacin, sarafloxacin, flumequin, and oxolinic acid are approved quinolones for usage in animal production, upper limit has been defined by the regulatory authorities[20]. In 2013, Er et al[20], have been detected quinolones antibiotic in 45% of chicken samples and 58% of beef samples in Turkey, while detected levels were low except two samples. Antibiotic residues in food have many pathological effects, including the transfer of antibiotic resistant bacteria to humans, immunopathological effects, autoimmunity and carcinogenesis as well as renal/liver and bone marrow toxicity[10]. The most frequently used antibiotics in animals are sulfonamide, tetracycline, beta lactams, macrolides and aminoglycosides; the most common antibiotics detected in our study were in the beta lactam group. While it is thought that the mothers' diets provided the source of the antibiotic residues detected in our study, parameters that would have demonstrated this were not studied. Although the impacts of food-based an-

tibiotic residues on human health are not clearly known, antibiotics can cause different side effects depending on the intake period and the age of the host[10]. Antibiotic residues can be detected and analyzed using different techniques, including enzyme linked immunosorbent assay, high performance liquid chromatography and liquid-gas or paper chromatography[10]. In the current report, we used a multi-array system to detect antibiotics and other drug residues in human milk. For residue prevention on a commercial scale, similar rapid screening procedures will be needed to identify antibiotic residues and to provide instant grading and prohibition of foods containing antibiotics. The multi-array, multi-chip technology used in this study allowed us to simultaneously evaluate more than 40 drugs. We found positive milk samples for antibiotic residues above detected levels, however limitation of this study we did not perform exact amount of antibiotics in human milk samples. Also, we detected positive results for beta-lactams and quinolones groups; we have no chance to show detailed antibiotic subgroups. Researches conducted in recent years have shown that breastfeeding has a marked effect on the intestinal microbiota of newborn babies from the first days of life. The maternal milk microbiota has a determinative effect on several pregnancy-related factors, the delivery pattern and maternal nutrition[3,21]. In a Canadian study[22] between 2010 and 2012 on the use of antibiotics to prevent group B streptococcal infection, the maternal milk microbial content was found to be different for three months after delivery, a condition that continued for twelve months in mothers who had delivered through Cesarean section. There are no investigations on the effects of antibiotic residues in human milk on the intestinal microbiota of babies whose mothers did not use antibiotics in pregnancy or at birth. In the next section of our study, we plan to evaluate the effects of breast milk antibiotic residues on breast milk microbiota.

Conclusions

Although minor antibiotic use does not cause serious side effects for infants during the breastfeeding period, antibiotic intake in subtherapeutic doses may lead to antibiotic resistance in infants. The long-term use of antibiotics, especially at low doses, may play a role in the spread of antibiotic resistance. The main strategy for preventing the consumption of foodborne antibiotic residues is to provide the necessary training and legal regulations for the rational use of antibiotics[23]. Rapid tests, such as those used in our work, could be beneficial in identifying contaminated food products. In the European Union countries, regulations have been enacted on the quantity and detection of antibiotic residues in foodstuffs, and it has been suggested that antibiotic residues should be evaluated at certain intervals for food safety[24]. As with other toxins and pollutants, the first and most important step to prevent antibiotic residue contamination is to increase awareness of the problem. Further prevention strategies should be implemented with the collaboration of regulatory authorities.

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Conflict of Interest

The Authors declare that they have no conflict of interest.

References

1) Eidelman AI. Breastfeeding and the use of human milk: an analysis of the American Academy of Pediatrics 2012 Breastfeeding Policy Statement. Breastfeed Med 2012; 7: 323-324.
2) Berti C, Agostoni C, Davanzo R, Hyppönen E, Isolauri E, Meltzer HM, Steegers-Theunissen RP, Cetin I. Early-life nutritional exposures and lifelong health: immediate and long-lasting impacts of probiotics, vitamin D, and breastfeeding. Nutr Rev 2017; 75: 83-97.
3) Dieterich CM, Felice JP, O'Sullivan E, Rasmussen KM. Breastfeeding and health outcomes for the mother-infant dyad. Pediatr Clin North Am 2013; 60: 31-48.
4) Le Doare K, Holder B, Bassett A, Pannaraj PS. Mother's milk: a purposeful contribution to the development of the infant microbiota and immunity. Front Immunol 2018; 9: 361.
5) American Academy of Pediatrics Committee on Drugs. Transfer of drugs and other chemicals into human milk. Pediatrics 2001; 108: 776-789.
6) Warth B, Braun D, Ezekiel CN, Turner PC, Degen GH, Marko D. Biomonitoring of mycotoxins in human

breast milk: current state and future perspectives. Chem Res Toxicol 2016; 29: 1087-1097.

7) Holmes AH, Moore LS, Sundsfjord A, Steinbakk M, Regmi S, Karkey A, Guerin PJ, Piddock LJ. Understanding the mechanisms and drivers of antimicrobial resistance. Lancet 2016; 387: 176-187.
8) Ramatla T, Ngoma L, Adetunji M, Mwanza M. Evaluation of antibiotic residues in raw meat using different analytical methods. Antibiotics (Basel) 2017; 6: pii: E34.
9) Moreno-Bondi MC. Antibiotics in food and environmental samples. Anal Bioanal Chem 2009; 395: 875-876.
10) Nisha AR. Antibiotic residues - A global health hazard. Veterinary World 2008; 12: 375-377.
11) Langdon A, Crook N, Dantas G. The effects of antibiotics on the microbiome throughout development and alternative approaches for therapeutic modulation. Genome Med 2016; 8: 39.
12) Newton ER, Hale TW. Drugs in breast milk. Clin Obstet Gynecol 2015; 58: 868-884.
13) Mathew JL. Effect of maternal antibiotics on breast feeding infants. Postgrad Med J 2004; 80: 196-200.
14) de Sá Del Fiol F, Barberato-Filho S, de Cássia Bergamaschi C, Lopes LC, Gauthier TP. Antibiotics and breastfeeding. Chemotherapy 2016; 61: 134-143.
15) Martinez de Tejada B. Antibiotic use and misuse during pregnancy and delivery: benefits and risks. Int J Environ Res Public Health 2014; 11: 7993-8009.
16) American Academy of Pediatrics Committee on Drugs. Transfer of drugs and other chemicals into human milk. Pediatrics 2001; 108: 776-789.
17) Kim ES, Hooper DC. Clinical importance and epidemiology of quinolone resistance. Infect Chemother 2014; 46: 226-238.
18) Azad MB, Konya T, Persaud RR, Guttman DS, Chari RS, Field CJ, Sears MR, Mandhane PJ, Turvey SE, Subbarao P, Becker AB, Scott JA, Kozyrskyj AL; CHILD Study Investigators. Impact of maternal intrapartum antibiotics, method of birth and breastfeeding on gut microbiota during the first year of life: a prospective cohort study. BJOG 2016; 123: 983-993.
19) Pereira RVV, Carroll LM, Lima S, Foditsch C, Siler JD, Bicalho RC, Warnick LD. Impacts of feeding preweaned calves milk containing drug residues on the functional profile of the fecal microbiota. Sci Rep 2018; 8: 554.
20) Er B, Onurdag FK, Demirhan B, Ozgacar SÖ, Oktem AB, Abbasoglu U. Screening of quinolone antibiotic residues in chicken meat and beef sold in the markets of Ankara, Turkey. Poult Sci 2013; 92: 2212-2215.
21) Gomez-Gallego C, Garcia-Mantrana I, Salminen S, Collado MC. The human milk microbiome and factors influencing its composition and activity. Semin Fetal Neonatal Med 2016; 21: 400-405.
22) Mazzola G, Murphy K, Ross RP, Di Gioia D, Biavati B, Corvaglia LT, Faldella G, Stanton C. Early gut microbiota perturbations following intrapartum antibiotic prophylaxis to prevent group B streptococcal disease. PLoS One 2016; 11: e0157527.
23) Founou LL, Founou RC, Essack SY. Antibiotic resistance in the food chain: a developing country-perspective. Front Microbiol 2016; 7: 1881.
24) https://ec.europa.eu/food/safety/chemical_safety/vet_med_residues_en.