ABSTRACT:
Background: Urinary tract infections (UTIs) are some of the most common infections in childhood. It is well established that breastfeeding reduces the risk of some respiratory tract infections in childhood, but it is still questionable if it has an effect on the rate and severity of UTI.

Aim: To investigate the role of breastfeeding on the occurrence and severity of UTIs in children aged 0-3 years in Varna, Bulgaria.

Methods: A case-control study was performed in Varna between 2013 and 2015. The frequency, duration and type of breastfeeding practices were assessed in children (from birth till 3 years) diagnosed with UTIs (cases) and in healthy children (controls). Descriptive analysis, parametric and nonparametric methods were used to analyse the collected data. SPSS version 17 was applied. For statistically significant differences a p-value of less than 0.05 was accepted.

Results: 216 controls and 108 cases were included in the statistical analysis. The average age of patients and controls was 17.7 ± 1 months. The median of the duration of breastfeeding and exclusive breastfeeding for the cases was 3.5 and 0 months respectively compared to the significantly longer duration in the controls - 6 months and 2 months respectively. Controls were breastfed and exclusively breastfed 2 times longer, and the UTI was not accompanied by high temperature in breastfed cases compared to non-breastfed cases (p <0.05).

Conclusions: Longer breastfeeding and exclusive breastfeeding contributes to protection against the development and lowers severity of UTIs in infants and small children.

Keywords: breastfeeding, urinary tract infections, protection, infants, small children,

INTRODUCTION/BACKGROUND:
Urinary tract infections (UTIs) are among the most common inflammatory diseases worldwide [1, 2]. This is due to anatomic and physiological characteristics of the urinary system that favor the colonization of urinary tract with virulent microorganisms, most commonly from the area around the urethra. They are associated with serious medical and financial consequences. Despite the risk of underestimation as sometimes, they are difficult to diagnose in early childhood [3], they form a significant part of morbidity in both outpatient and inpatient settings. In childhood, UTIs are the second most common diseases after those of the respiratory system [4]. Their reoccurrence places at risk the development of immature kidneys in the growing child. This tendency is also one of the main reasons for the development of chronic kidney diseases in childhood [5].

There are a number of scientific publications for the protective effect of breast milk against infections in the neonatal and breastfeeding period [6]. Benefits of breastfeeding for the prevention of acute otitis, gastroenteritis, severe infections of the respiratory tract and skin are undoubtedly [7, 8]. Mechanisms of this effect in UTIs have been studied. The possibilities are:
1/Antiadhesive oligosaccharides in breast milk might reduce the risk of ascending infections in breastfed babies [9, 23].
2/If left undisturbed by antibiotic treatment, the intestinal flora is quite constant and is more beneficial than that in formula or mixed fed babies, which also might provide long-term protection, which may explain the preventive effect far beyond the cessation of breastfeeding- till 3 years of age.
3/In addition, lactoferrin (with a role in the non-specific immune response) and secretory Ig A (with a role in antigen-specific secretory responses) execute powerful antibacterial effects and are present in the urine of breastfed infants [10, 24].

A search of the scientific databases for the last 5 years, such as EMBASE, MEDLINE, PUBMED shows that still in practice, the effect of breastfeeding on the incidence and severity of urinary tract infections in childhood is less studied and proven.

AIM of the study is to investigate the role of breastfeeding in the development and severity of UTIs in infants and children in early childhood.

MATERIALS AND METHODS:
This study was designed as a prospective case-control study. It was performed in Varna between June 2014 and
December 2016 in the Diagnostic and consulting center “St Marina”.

Cases:

Children 0–3 y of age were eligible for the study if they were with a symptomatic UTI. Inclusion criteria were:
1. Clinical signs such as fever of 38°C or higher, failure to gain weight, irritability, strong-smelling urine, crying during urination; 2. Urinalysis - bacteriuria, defined by one of the following: for midstream clean catch samples, a positive culture result is defined as at least 50,000 colony-forming units per mL (cfu/ml), where one strain is detected; for Culture of a urine specimen from a sterile bag attached to the perineal area- two separate specimens with a positive culture result of >100,000 cfu/ml, where one and the same strain is detected in both specimens; 3. Laboratory tests-leukocytosis and high C-reactive protein (CRP) > 5mg/l.

Controls:

Controls were recruited among infants or small children referred to the same medical center for a well-child visit or prophylactic ultrasound examination, in whom UTI was excluded. They had no history of previous UTI or of urinary tract anomalies. The selection aimed at two control subjects per case, matched for gender and age.

Exclusion criteria: Children with a diagnosed congenital abnormality of the urinary tract or whose parents were unable to understand the questionnaire were excluded.

A direct individual questionnaire consisting of 21 questions was developed, including questions regarding demographic data, initiation, duration and type of breastfeeding, complementary feeding practices.

Statistical analysis: Descriptive analysis; Analysis of variance of quantitative indicators - calculating the average (mean, median), standard deviation, standard error of the average, 95% confidence interval (CI). Risk (OR) for the UTI between exposed and non-exposed to the breastfeeding and exclusive breastfeeding children was calculated. Parametric methods: T-Test Student Fischer; Nonparametric methods: a method of Kolmogorov-Smirnov, a method of Mann-Whitney, a method of Kruskal-Wallis; Graphical method for displaying results. Statistical significance was determined at the highest level of significance p < 0.05. In the statistical processing of material was used statistical software package SPSS (v. 17.0).

The Research Ethics Committee of the Medical University “Prof. Dr Paraskev Stoyanov”- Varna, Bulgaria approved the study (Protocol No.37/ 15.05.2014). A written informed consent was obtained from parents before participation in the study.

RESULTS:

216 controls and 108 cases were included in the final analysis, of which 216 girls- 144 controls (33.3%), 72 cases (33.3%) and 108 boys- 72 controls (66.7%), 36 cases (66.7%). 80.5% of the controls and 55.6% of the cases in the male group were either circumcised or had no phimosis.

The mean age of cases and controls was similar (17.7 ± 1 months). There were 42.6% (46) infants in the group of cases (Figure 1).

Fig. 1. Distribution of children with UTIs (%) according to their age (months)

At the moment of the diagnosis of urinary tract infections, 94 children (87%) were breastfed. Never breastfed were 13% (n = 14) of children. The majority of infected children (57.4%) were not breastfed exclusively. Exclusive breastfeeding among children with urinary tract infections continued till 3.39 ± 0.3 months, and water was given to them at the age of 1.74 ± 0.2 months. The highest was the share (48%) of exclusively breastfed children with urinary infections.
tract infections till the second month (Figure 2). Among the cases with UTIs ten children (22% of the cases) within the age of 5-6 months were breastfed exclusively.

**Fig. 2.** Duration distribution in the group of the exclusive breastfed up to six months in children with UTIs

The mean age of initiation of complementary feeding among our respondents was 4.85 ± 0.1 months.

Afebrile cases were breastfed twice as long compared to febrile cases - median of 8 months compared to a median of 3 months respectively (p <0.05 Mann-Whitney U 1476). The average age till which afebrile cases were breastfed exclusively case was higher than that of the febrile cases - 2.13 ± 0.5 months versus 1.18 ± 0.2 months (p <0.005) (Figure 3).

**Fig. 3.** Distribution cases (%) according to the presence of fever and breastfeeding practices

Babies with UTIs, with low CRP (0-5mg/l), were significantly longer breastfed compared to those with high CRP (> 5 mg/l) - median 4 months versus median 2.5 months.

Comparison between cases and controls in our study showed that the duration of breastfeeding and exclusive breastfeeding were significant factors for urinary tract infections in the age period 0-3 years. The median duration of breastfeeding and exclusive breastfeeding in the cases was 3.5 and 0 months respectively versus the significantly longer duration in the controls - 6 months and 2 months respectively (p <0.005 Mann-Whitney U 9978, respectively Mann-Whitney U 9332) (Figure 4).

**Fig. 4.** Duration of breastfeeding and exclusive breastfeeding

The duration of exclusive breastfeeding is associated with a protective effect on the occurrence of urinary tract infections in our study with a relative risk (OR) of 0.842 (95% CI 0.758-0.935).

In the control group prevail children that have been breastfed up to six months (exclusive, predominant breastfeeding or mixed feeding). Among the cases, those who received breast milk up to six months were only 48 (38.9%) versus 114 (53%) healthy children of the same age (p<0.05) (Figure 5). Distribution of cases and controls according to the type of feeding at the time of the infection is shown on Figure 6.

**Fig. 5.** Breastfeeding practices among the tested groups

**Fig. 6.** Duration of the cases and controls according to the type of feeding by the time of the study (%)
Breastfeeding children up to 12 months of age in our study demonstrated a credible reduction in the risk of urinary tract infections compared to their peers, who were entirely replacing feeding at OR 0.390 (95% CI 0.154-0.984).

**DISCUSSION:**

The selected age period provides an opportunity to assess the short- and long-term effects of breastfeeding on children’s health with minimal risk of recall error.

According to the scientific literature, UTIs are more common among females, due to the shorter female urethra and its proximity to the anal area, facilitating an infection due to colonic bacteria [11, 12].

Breastfeeding has protective effects on morbidity, mortality [13], against diarrhoea [14], otitis media [15], infantile respiratory infections [16], and other bacterial infections.

The duration of breastfeeding of children with UTIs was lower than that of the controls. The European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Food Safety Authority (EFSA) recommend that in countries with a low infectious disease such as countries in Europe, breastfeeding should continue until the mother and the child wish [17, 18]. Studies that reveal the health benefits of natural nutrition on the urinary system indicate the duration of exclusive breastfeeding [19, 20] as the main indicator. WHO, ESPGHAN and the American Pediatric Academy recommend that children should only exclusively breastfeed until six months [17, 21]. The average duration of UTIs among cases in our study was low and did not meet current recommendations.

The median of complementary feeding of children with UTIs (fifth month) corresponds to the current four to six month (week 17 and week 26) recommendations. Introduction of solid foods is associated with risks to the child’s health, growth and development.

Several small clinical studies have found similar to our results- term-born babies who are breastfed develop less urinary tract infections than formula-fed controls [19, 22, 23]. A case-control study conducted in Iran by Falakazlaki and Ahmadiafshar compares 50 children under the age of one with UTIs and 50 healthy children in the same age group. Breastfed babies were found to have a significantly lower risk of urinary tract infection compared to formula and mixed feeding [24]. Children of mixed diet had a reduced risk of urinary tract infections compared to complementary feeding. The authors conclude that longer breastfeeding is associated with a lower risk of urinary tract infections, which suggests that breastfeeding has a protective effect against urinary tract infections.

**CONCLUSIONS:**

1. Urinary tract infections in the age period 0-3 years occur predominantly in children with mixed and predominant breastfeeding.

2. The duration of breastfeeding and exclusive breastfeeding is negatively correlated with the risk for UTIs- longer breastfeeding leads to a lower rate of UTIs.

3. The duration of breastfeeding and exclusive breastfeeding are significant protective factors for the severity of UTIs in children under three years of age.

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