

## Assessment of Exclusive Breastfeeding Effect against Urinary Tract Infection in Infancy

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### ABSTRACT:

#### BACKGROUND:

Urinary tract infection is the third most common pediatric bacterial infection in developing countries. Exclusive breastfeeding as World Health Organization recommendations in infants provides the simplest method that provides protection against infant's infections including UTI.

#### OBJECTIVE:

To assess the possible protective effect of exclusive breastfeeding on infant UTI.

#### PATIENTS AND METHODS:

A case control study was carried out in Children Welfare Teaching Hospital from March to September 2018. The study group included 300 infants (100 cases and 200 controls). Cases were selected from Pediatric Nephrology Department when clinically suspected as UTI. Controls were selected from the patients of other diseases in the hospital. Both cases and controls were divided according to the type of feeding during first 6 months of life into three groups: Exclusive breastfeeding, bottle feeding and mixed feeding.

#### RESULTS:

Infants exclusively breastfed for 6 months, shown to have a lower risk of UTI 12% than partially breastfed 68% or bottle fed peers 20%. This protective effect after fixation of other variables (P value=0.0001). The study also showed that lack of circumcision in male infants, having a previous history of UTI and use of antibiotics inappropriately were significant risk factors for UTI in infants.

#### CONCLUSION:

This study showed a protective role of breastfeeding on UTI in infancy. Other risk factors for the UTI were uncircumcised male infants, positive history of UTI and improper use of antibiotics.

**KEYWORDS:** Breastfeeding, Urinary tract infection, Infancy

### INTRODUCTION:

Urinary tract infection (UTI) is considered as the third most common pediatric bacterial infection in developing countries after those of the gastrointestinal and respiratory tract. It constitutes a common cause of morbidity which in association with abnormalities of the urinary tract resulted in long term complications, including hypertension and chronic renal failure. UTI defined by clinical presentation of UTI together with the presence of single pathogenic organism in urinary tract with growth of more than 100,000 CFU (colony-forming unit) per ml by urine culture <sup>[1]</sup>. Risk factors of UTI including: age & gender, lack of circumcision for male infants, constipation, having a previous history of UTI, inappropriate use of antibiotics, lack of perineal hygiene & poor socioeconomic status <sup>[2]</sup>.

Complications of UTI in properly managed infants are rare, they may progress to renal failure especially when they have urinary tract abnormalities. Cystitis, pyelonephritis, renal abscess, renal scar formation and later adulthood hypertension <sup>[3]</sup>.

Exclusive breastfeeding is defined as the practice in which the infants receive only breast milk and not even water, other liquids or food during the first 6 months of life, with the exception of vitamins or medications. World Health Organization (WHO) recommends breastfeeding as the main source of feeding for babies for the first 6 months of life and encourages mothers to consider breastfeeding as the only feeding source between 6 months and 2 years old <sup>[4]</sup>. Breastfeeding is associated with decreasing acute illnesses, during the first 6 months of the baby's life exclusive breast feeding can reduce under-five of age mortality by 13% in developing countries as estimated by the United Nations

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Children's Fund (UNICEF) [5].

It has been shown to be associated with lower incidence of atopic dermatitis and asthma in early childhood [6]. Formula feeding is defined as feeding of an infant by a prepared formula instead of breastfeeding, it is indicated when the mother has an illness that could be passed on to the baby through breast milk [7]. Mixed feeding is the feeding of the babies with breast milk and formula milk, or breast milk with any complementary feed simultaneously [8].

Some defense factors in the breast milk can prevent urinary tract infection in infants. The breast milk contains immunoglobulin A (IgA) antibodies that can bind to microbes such as *E. coli*. Also breast milk contains Lysozyme an enzyme that is capable of degrading the outer wall of bacteria, acting synergistically with lactoferrin [9,10].

### **PATIENTS AND METHODS:**

**Study design:** A retrospective case control study.

**Setting:** The study was carried out in Children Welfare Teaching Hospital.

**Data collection time:** From March to September 2018.

**Case definition:** Infants from 6 months to 1 year of age diagnosed with UTI by a specialist and confirmed by investigation either urine analysis (having >10 pus cells/HPF) or urine culture (having urine growth was >10<sup>5</sup> CFU/ml), and documented to be free from anatomic abnormality of the urinary tract by ultrasound.

**Control definition:** Infants from 6 months to 1 year of age having any acute illness other than UTI and confirmed to be free from UTI by general urine exam (GUE).

### **Exclusion criteria:**

- 1) Infants with documented anatomic abnormality of the urinary tract associated with UTI such as vesicouretric reflux.
- 2) Infants with documented urinary tract obstruction.
- 3) Infants with neurogenic bladder.

The study groups included 300 infants during the period from first of March to the end of August 2018. They were 100 case infants diagnosed with UTI admitted to the pediatric ward or attending outpatient, and 200 control infants who were in the hospital for reasons

other than UTI. The selection aimed at 2 control subjects per case. A detailed history, physical examination, measurement of temperature and ultrasound of the patient was done. Cases were selected from Pediatric Nephrology Department when clinically suspected as UTI by fever >38°C, poor feeding, vomiting, diarrhea, abdominal pain, malodorous urine or tender renal angle then they were confirmed by urine analysis or urine culture. Controls were selected from the patients admitted to hospital for other diseases and having a negative urine analysis. Data was obtained by a questionnaire paper prepared by the researchers aided by informations from previous studies, and reviewed by 2 nephrologists; this questionnaire was filled by the researcher by interview with the infants' mother.

Both cases and controls were divided according to the type of feeding during first 6 months of life into three groups: Exclusive breastfeeding, bottle feeding and mixed feeding infants. Both cases and controls were searched for risk factors of UTI including: gender, male infant circumcision (circumcised/ uncircumcised), constipation was considered if the infant had less than 2-3 bowel movement per week was divided to (constipated/not constipated) [11], previous infant history of UTI having at least one previous episode of UTI was considered as a positive history divided to (positive history/negative history), inappropriate use of antibiotics was considered if the antibiotics were given to the infants without doctor's prescription [12], mean diaper change per day divided as (<5 and ≥ 5 per day), socioeconomic status (SES) of the infant's family is the social class of the family it was measured by a combination of education of the mother, occupation of the mother or her husband and family income (having their own house or own car). After analyzing the family's SES it was classified into four groups: (Poor SES 0-4, Fair SES >4-8, Good SES >8-12 and Excellent SES >12 ) [13]. Both Good and Excellent SES were considered as one category in the results because only one variable belonged to Excellent SES class.

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### DATA ANALYSIS

Data were analyzed for both descriptive and inferential statistics using (IBM-SPSS) version 24. Descriptive statistics were displayed by using frequencies, percentage and distribution tables. While inferential statistics were presented by using Odd's ratio (OR) and 95% confidence interval (CI) were calculated. Binary logistic regression was used to find out associations between different studied variables and getting UTI. (P value < 0.05) was considered as a cutoff point for discrimination of significance.

### RESULTS

The association of cases and controls with different variables was shown in table 1. There was a significant association between type of feeding and getting UTI. The percentage of cases who had exclusive breastfeeding was significantly lower than controls (12% and 57% respectively). Regarding cases who had mixed feeding the percentage of cases was higher than controls (68% and 41% respectively). While the percentage of cases who had bottle feeding was significantly higher than controls (20% and 2% respectively). (P value= 0.001).

Regarding the infant's gender the percentage of cases was 36% in females which was lower in controls 48%. While in males the percentage of cases was higher than controls (64% and 52% respectively). There was significant association between infant gender and UTI (P value= 0.048). A lower percentage of cases than controls had circumcision (65.6% and 84.6% respectively). While a higher percentage of cases than controls were not circumcised (34.4% and 15.4% respectively). The association between circumcision and getting UTI was statistically significant (P value= 0.004). Regarding constipation the percentage of cases who were not constipated was lower than controls (84% and 99% respectively). While among cases who had constipation the percentage was significantly higher than controls (16% and 1% respectively). The association between constipation and getting UTI was statistically significant (P value= 0.001).

The percentage of cases who had a negative previous history of UTI was lower in cases than controls (42% and 95% respectively).

A higher percentage of cases than controls gave a positive previous history of UTI (58% and 5% respectively). The association between having a previous history of UTI and getting future UTI was significant (P value= 0.001). A significant association was found between the use of antibiotics inappropriately and getting UTI. The percentage of cases who used antibiotics only with prescription was much lower in cases than controls (16% and 79% respectively). While the percentage of cases who used antibiotics inappropriately was significantly higher than that of controls (84% and 21% respectively). (P value= 0.001).

There was a significant difference between cases and controls with respect to their mean diaper change per day (P value= 0.001). The percentage of cases with mean diaper change of  $\geq 5$  was lower than controls (46% and 66% respectively). While in those with mean diaper change of <5 per day the percentage of cases was higher than controls (54% and 34% respectively). The percentage of cases who belong to good SES family was lower than controls (20% and 30% respectively). Regarding the percentage of cases that belong to fair SES family was 38% compared to 42% controls. While the percentage of cases who belong to poor SES family was significantly higher than controls (42% and 28% respectively). Poor SES families had a significant association for the infants to develop UTI in comparison with good SES families (P value= 0.001).

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Table (1): The association of cases and controls with different variables

| Type of Feeding in 1 <sup>st</sup> 6 months | Group  |    |          |     | OR        | 95% CI      | P value     |       |
|---|--------|----|----------|-----|-----------|-------------|-------------|-------|
|   | Cases  |    | Controls |     |           |             |             |       |
|   | No.    | %  | No.      | %   |           |             |             |       |
| Exclusive Breastfeeding                     | 12     | 12 | 114      | 57  | Reference |             |             |       |
| Mixed feeding                               | 68     | 68 | 82       | 41  | 0.12      | 0.07 - 0.25 | 0.001       |       |
| Bottle feeding                              | 20     | 20 | 4        | 2   | 0.02      | 0.01 - 0.07 | 0.001       |       |
| Gender                                      | Female | 36 | 36%      | 96  | 48%       | 0.61        | 0.37 - 0.99 | 0.048 |
|   | Male   | 64 | 64%      | 104 | 52%       |             |             |       |
| Male circumcision                           | Yes    | 42 | 65.6     | 88  | 84.6      | 0.34        | 0.16 - 0.73 | 0.004 |
|   | No     | 22 | 34.4     | 16  |           |             |             |       |
| Constipation                                | No     | 84 | 84       | 198 | 99        | 0.05        | 0.01-0.23   | 0.001 |
|   | Yes    | 16 | 16       | 2   | 1         |             |             |       |
| Previous history of UTI                     | -ve    | 42 | 42       | 190 | 95        | 0.04        | 0.02-0.08   | 0.001 |
|   | +ve    | 58 | 58       | 10  | 5         |             |             |       |
| Inappropriate antibiotic use                | No     | 16 | 16       | 158 | 79        | 0.05        | 0.03-0.09   | 0.001 |
|   | Yes    | 84 | 84       | 42  | 21        |             |             |       |
| Diaper changed per day                      | ≥5     | 46 | 46       | 132 | 66        | 0.44        | 0.27-0.72   | 0.001 |
|   | <5     | 54 | 54       | 68  | 34        |             |             |       |
| SES class                                   | GOOD   | 20 | 20       | 60  | 30        | Reference   |             |       |
|   | FAIR   | 38 | 38       | 84  | 42        | 0.74        | 0.39-1.39   | 0.342 |
|   | POOR   | 42 | 42       | 56  | 28        | 0.44        | 0.44-0.85   | 0.013 |

In order to determine the independent effect of modifiable variables on the occurrence of infant UTI, a logistic regression analysis was carried out. Table 2 shows the results which indicate that infant UTI was significantly and independently affected by exclusive breastfeeding during the first 6 months of life which may act as a protective factor against UTI during infantile life

after fixation of other variables (P value=0.0001). Also the infant UTI was significantly affected by having positive previous history of UTI, inappropriate use of antibiotics and lack of circumcision that may act as risk factors in developing UTI among infants (P value= 0.0001, 0.0001 and 0.031) respectively.

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Table (2): Regression of the occurrence of infant UTI in relation with significant variables

| Significant Variables        | B     | P value | OR    | 95% CI       |
|------------------------------|-------|---------|-------|--------------|
| Type of feeding              | -2.81 | 0.000   | 0.06  | 0.01 - 0.27  |
| Constipation                 | -0.08 | 0.966   | 0.93  | 0.03 - 31.54 |
| Previous UTI                 | 3.13  | 0.000   | 22.85 | 4.72 - 10.53 |
| Inappropriate antibiotic use | 3.01  | 0.000   | 20.37 | 5.59 - 11.27 |
| SES                          | 0.12  | 0.391   | 1.13  | 0.86 - 1.47  |
| Male circumcision            | -0.18 | 0.031   | 0.41  | 0.07 - 0.95  |
| Diaper changed per day       | 0.08  | 0.734   | 1.08  | 0.70-1.67    |
| Constant                     | -2.28 | 0.559   | 0.10  |              |

### DISCUSSION:

This case control study suggested a potential protective effect of breastfeeding on UTI during the first year of life. Breast-fed infants had a lower risk of UTI compared to mix-fed and formula-fed infants. The desired effect of breastfeeding was supported by a local study which was done by Hammdi M., in Iraq 2007<sup>[14]</sup>. Another regional study supported this result was done in Iran, by Ahmadiashar A. et al, from 2004 to 2005, showed that breastfeeding has a possible protective effect against UTI and the longer duration of breastfeeding<sup>[15]</sup>. The same results was found by Mårild S. et al in Sweden 2004 and Lee S.J. in Korea 2015<sup>[16,17]</sup>. This protective role of breastfeeding might explain the role of breast milk as a part of the natural defense against UTI.

So far, the result of Gensure R. et al, in USA, from 2001 to 2006 was against these results. No protective effect of breastfeeding against UTI was found. The influence on this result was other potential confounders, such as breastfeeding effects on rates of other illnesses, admission of breastfed children with gastroenteritis to the hospital, and vitamin D supplementation in the breastfed and bottle-fed infants which increase the risk of UTI, could affect these results<sup>[18]</sup>.

Regarding the previous history of UTI, the present study showed that majority of cases with UTI had a positive previous history of UTI compared to controls.

Similar results was found by Larcombe J., in United Kingdom 2010 and Schlager T.A. et al 2000<sup>[19,20]</sup>. This recurrence is explained by

unresolved bacteriuria after the first attack of UTI due to inadequate antimicrobial therapy after the first attack of UTI, non compliance of the treatment, malabsorption and drug resistance. Inappropriate use of antibiotics had significant relation with UTI, was also found in this study. The same result was reported by Falcão M.C. et al 2000 and Chang S.L. et al in USA 2006<sup>[21,22]</sup>. Since the use of these antibiotics is necessary for treatment of undetermined infection. The inappropriate use of broad spectrum antibiotics may change the infant's natural flora increasing infections by opportunistic microorganisms fungal urinary tract infections, mainly *Candida albicans* well exemplify this fact.

Furthermore; UTI in the first year of life affecting males mostly, as these findings were supported by results obtained by Mårild S. et al in Sweden 2004<sup>[16]</sup>. This study found also that uncircumcised boys were at a higher risk for UTI compared with circumcised boys. Same finding was supported by earlier studies done by and Hammdi M. in Iraq 2007 and Kose E. et al, in Turkey 2013, which showed that the number of uncircumcised boys with UTI was significantly higher than circumcised boy with UTI and circumcision could decrease the risk of UTI in infants<sup>[14,23]</sup>.

These results are explained by that uncircumcised male infants are at risk of colonization of mucosal surface of the foreskin with pathogens which causes ascending bacteriuria. Additionally; the logistic regression

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analysis showed no independent effect of constipation on UTI which may be caused by a subjective definition of constipation obtained by the mother. While other studies claimed that constipated infants are more likely to have UTI than non-constipated infants which was consistent with the results found by Hoque S.A et al 2010 and Zaffanello M. et al 2018 showing the significant impact of constipation on pediatrics UTI [24,25].

Although this study showed no direct effect of SES on the risk of UTI, owing to that even though the families had poor SES their infants undergo proper perineal washing technique and using sanitary diapers. However; poor SES families expose their infants to some risk factors of UTI such as malnutrition, using of unsanitary diapers, infrequent diaper change. This findings was obtained by Salunkhe S. et al, in India 2016 and Mohammed M.T. et al 2016 [26, 27].

### CONCLUSION:

Exclusive breastfeeding may provide a protection against infant UTI during the first year of life. As breast-fed infants had a lower risk of UTI compared to mixed-fed infants and formula-fed infants. Uncircumcised male infants, in addition to those who had a positive previous history of UTI and those who were given antibiotics inappropriately were found to have an increased risk of infant UTI. No association was found between risk of UTI with infant's constipation, poor SES families and mean diaper change per day.

Encourage the mothers to exclusively breastfeed their infants at least until the age of 6 months, as it is the simplest healthiest and least expensive method to prevent infant UTI.

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