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EVALUATION OF URINARY TRACT INFECTION IN CHILDREN WITH NEPHROTIC SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT: Urinary tract infection in nephrotic syndrome can be caused by gram negative bacteria such as E coli, klebsiella, enterobactor species, proteus species and gram positive bacteria, enterococcus species, staphylococcus saphrophyticus. Given the importance of the topic, the present study aims to Evaluation of Urinary tract infection in children with nephrotic syndrome.From the electronic databases, PubMed, Cochrane Library, Embase, ISI have been used to perform a systematic literature between 2010 and 2020. Therefore, a software program (Endnote X8) has been utilized for managing the electronic titles. Searches were performed with mesh terms. The quality of the studies included was assessed using the Newcastle-Ottawa Scale (NOS). For Data extraction, two reviewers blind and independently extracted data from abstract and full text of studies that included. Moreover, prevalence of UTI and prevalence of Spectrum of bacteria in urine cultures for each Organisms have been included in the meta-analysis.A total of 5263 potentially relevant titles and abstracts were found during the electronic and manual search. Finally, a total of SIX publications fulfilled the inclusion criteria required for this systematic review.The Prevalence of UTI in children with NS was 37.18% that is a significant figure and should be considered and it can endanger children's health.

KEY WORDS: Urinary tract infection, nephrotic syndrome, children

I. INTRODUCTION

One of the kidney disorders that causes the body to transfer a lot of protein in the urine is Nephrotic syndrome (NS). NS is usually caused by damage to the cluster of small blood vessels in the kidneys(1). Also NS is an important chronic disease and most common glomerular disorder with significant complications worldwide, affecting approximately 4.7 per 100,000 children per year(2). Symptoms of NS include edema, hypoalbuminemia, hyperlipidemia and massive proteinuria(3, 4). NS increases a child's susceptibility to infection, The most common infection in children with nephrotic syndrome who are diagnosed with a urinary tract infection is urinary tract infection(UTI)(5). UTI are among the most common infections in humans. Most UTIs are caused by bacterial infections and it is very common in childhood(6). About 8.4% of girls and 1.7% of boys in the first 8 years of life can develop UTI(7). Children may experience the first UTI at 6-12 months of age, with a prevalence of 30%(8). In the first year of life, girls and boys are equally involved in UTI, but later most cases occur in girls(9). Numerous symptoms, including high fever and sometimes secondary bacteria, may be seen(10). UTIs can be divided into three different categories: acute pyelonephritis (kidney infection), acute cystitis (bladder infection), and asymptomatic bacteriuria. However, there may be cases that cannot be categorized, but these categories can be helpful in diagnostic and managerial decisions(6). UTI is caused by both gram-negative and gram-positive bacteria, and in some cases may be caused by some fungi, such as Candida spp(11). urine culture accompanied is used to diagnose UTI, and specific clinical signs of acute UTI are effective for diagnosis(8). UTI is one of the most common infectious diseases in children with NS, which can lead to treatment failure and relapse(12). UTI in NS can be caused by gram negative bacteria such as E coli, klebsiella, enterobactor species, proteus species and gram positive bacteria, enterococcus species, staphylococcus saphrophyticus(13). Given the importance of the topic, the present study aims to Evaluation of Urinary tract infection in children with nephrotic syndrome.

ISSN- 2394-5125 VOL 7, ISSUE 15, 2020

II. METHOD

Search strategy

From the electronic databases, PubMed, Cochrane Library, Embase, ISI have been used to perform a systematic literature between 2010 and 2020. Therefore, a software program (Endnote X8) has been utilized for managing the electronic titles. Searches were performed with mesh terms:

((((((((((("Urinary Tract Infections/analysis"[Mesh] OR "Urinary Tract Infections/epidemiology"[Mesh] OR "Urinary Tract Infections/etiology"[Mesh] OR "Urinary Tract Infections/history"[Mesh] OR "Urinary Tract Infections/microbiology"[Mesh] OR "Urinary Tract Infections/mortality"[Mesh] OR "Urinary Tract Infections/pathology"[Mesh] OR "Urinary Tract Infections/urine"[Mesh])) OR "Bacteriuria"[Mesh]) OR "Pyuria"[Mesh]) OR "Schistosomiasis haematobia"[Mesh]) AND "Nephrotic Syndrome"[Mesh]) AND "Escherichia coli"[Mesh]) OR "Klebsiella pneumoniae"[Mesh]) OR "Staphylococcus aureus"[Mesh]) OR "Proteus mirabilis"[Mesh]) OR "Citrobacter"[Mesh]) OR "Enterobacter"[Mesh]) AND ("Child"[Mesh] OR "Adult Children"[Mesh] OR "Only Child"[Mesh]).

This systematic review has been conducted on the basis of the key consideration of the PRISMA Statement– Preferred Reporting Items for the Systematic Review and Meta-analysis(14), and PICO or PECO strategy (table1).

Selection criteria

Inclusion criteria

1. Randomized controlled trials studies, controlled clinical trials, and prospective and retrospective cohort studies.
2. in children
3. Full text
4. Prevalence of UTI
5. Spectrum of bacteria in urine cultures
6. in English

Exclusion criteria

1. in vitro studies, case studies, case reports, descriptive study and reviews.
2. Adults and elderly

Table1. PICO OR PECO strategy

PICO OR PECO strategy	Description
P	Population/ Patient:: children with nephrotic syndrome
E	Exposure/ Intervention: prevalence of UTI
C	Comparison: cases without UTI and with UTI
O	Outcome: prevalence of UTI and prevalence of Organisms

Data Extraction and method of analysis

The data have been extracted from the research included with regard to the study, years, study design, number of Patient, range of age, Spectrum of bacteria in urine cultures. The quality of the studies included was assessed using the Newcastle-Ottawa Scale (NOS) (15). The scale scores range from 0 (lowest grade) to 6 (highest grade). For Data extraction, two reviewers blind and independently extracted data from abstract and full text of studies that included. Moreover, prevalence of UTI and prevalence of Spectrum of bacteria in urine cultures for each Organisms have been included in the meta-analysis. Then, the forest plots and funnel plot have been evaluated with the use of a software program available in the market (i.e., Comprehensive Meta-Analysis Stata V16).

ISSN- 2394-5125 VOL 7, ISSUE 15, 2020

III. RESULTS

According to the research design, 5263 potentially important research abstracts and titles have been discovered in our electronic searches. At the first phase of the study selection, 4158 research have been with regard to the topics and abstracts. Therefore, fully assessed the complete full-text papers of the rest 90 studies in the second stage so that excluded 84 publications due to the lack of the defined inclusion criteria. Then, six papers remained in agreement with our inclusion criteria required (Figure 1). Table 2 reports the individual studies in this meta-analysis.

Sample size

Therefore, six studies (3 Retrospective and 3 Prospective) have been included. The Number of Patients a total was 471 (NS without UTI: 238, NS with UTI: 233), the range of age was 0-15 years (table1).

Bias assessment

According to Newcastle-Ottawa Scale, all studies had a moderate risk of bias (table1).

Overall prevalence

Prevalence of UTI in children with NS:

Prevalence of UTI was 37.18% (ES, 37.18% 95% CI -18.88%, 93.25% P= 0.19) among the 6 studies and heterogeneity found (I2 = 0%; P =0.99) (Figure2). There was no statistically significant difference for Prevalence of UTI among children with NS. Also there was no statistically significant difference between studies (p=0.99). Figure3 showed Funnel plot of Prevalence of UTI among children with SN.

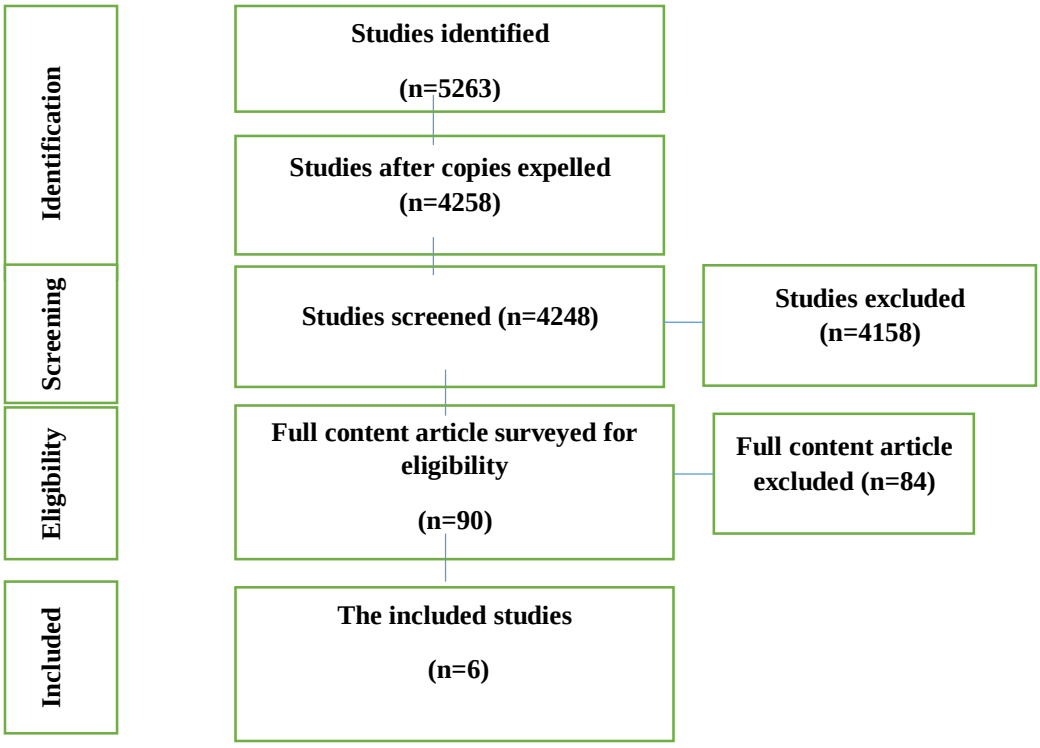


Figure 1. Study Attrition

ISSN- 2394-5125 VOL 7, ISSUE 15, 2020

Prevalence of Spectrum of bacteria in urine cultures:

Escherichia coli:

Prevalence of Escherichia coli was 38.83% (ES, 38.83% 95% CI 25.01%, 52.64% P= 0.00) among the 6 studies and heterogeneity found (I2 = 0%; P =0.92) (Figure4). There was statistically significant difference for Prevalence of Escherichia coli. Also there was no statistically significant difference between studies (p=0.92). Figure10 showed Funnel plot of Prevalence of Escherichia coli.

Klebsiella pneumonia:

Prevalence of Klebsiella pneumonia was 7.18% (ES, 7.18% 95% CI -6.64%, 20.99% P= 0.31) among the 6 studies and heterogeneity found (I^2 = 0%; P =1.00) (Figure5). There was no statistically significant difference for Prevalence of Klebsiella pneumonia. Also there was no statistically significant difference between studies (p=1.00). Figure10 showed Funnel plot of Prevalence of Klebsiella pneumonia.

Table2. Studies selected for systematic review and meta-analysis.

Study. Year	Design	Number of Patient				Range of age (years)	Spectrum of bacteria in urine cultures						Bias assessment
		G1		G2			E. coli	K. pneumoniae	S. aureu	P. mirabilis	C	E	
		M	F	M	F								
Sreenivasa et al. 2015 (16)	p	50				2-12	20	8	6	2	2	2	3/6
		20		30									
		12	8	18	12								
Basu et al. 2015 (17)	p	111				2-12	46	27	10	7	0	0	3/6
		81		30									
		NA	NA	NA	NA								
Gunawa et al. 2016 (18)	r	74				0-15	23	12	12	12	23	9	4/6
		34		40									
		15	17	33	9								
Dash et al. 2017 (19)	r	76				1-10	39.12	15.21	13.04	10.86	02.17	17.39	3/6
		46		30									
		34	12	16	14								
Pandya et al. 2018 (20)	r	59				1-12	42	6.5	6.5	6.5	6.5	32	4/6
		8		51									
		NA	NA	NA	NA								
Alhares et al. 2020 (21)	p	101				1.5 - 10	58.1	2.32	11.36	4.65	16.26	0	3/6
		44		57									
		NA	NA	NA	NA								

ISSN- 2394-5125 VOL 7, ISSUE 15, 2020

Staphylococcus aureus:

Prevalence of Staphylococcus aureus was 6.98% (ES, 6.98% 95% CI -6.83%, 20.79% P= 0.32) among the 6 studies and heterogeneity found (I^2 = 0%; P =1.00) (Figure6). There was no statistically

significant difference for Prevalence of Staphylococcus aureus. Also there was no statistically significant difference between studies (p=1.00). Figure10 showed Funnel plot of Prevalence of Staphylococcus aureus.

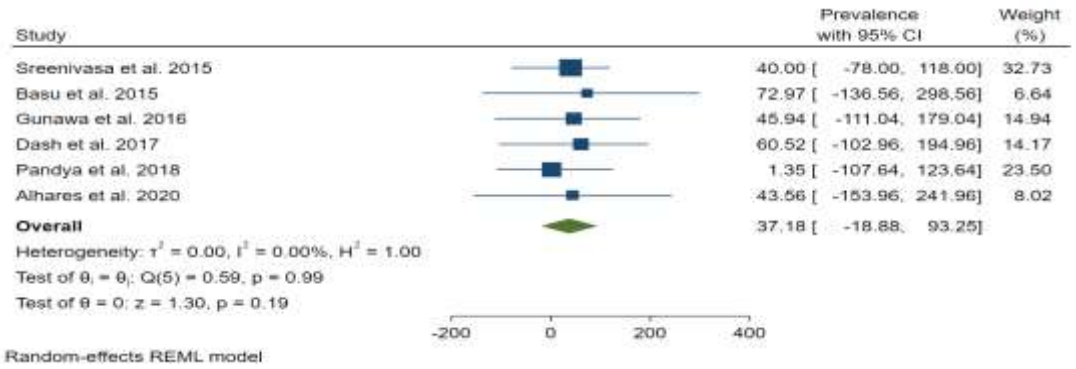


Figure2. Forest plots showed Prevalence of UTI among children with SN.

Proteus mirabilis:

Prevalence of Proteus mirabilis was 6.24% (ES, 6.24% 95% CI -7.58%, 20.05% P= 0.38) among the 6 studies and heterogeneity found (I^2 = 0%; P =1.00) (Figure7). There was no statistically significant difference for Prevalence of Proteus mirabilis. Also there was no statistically significant difference between studies (p=1.00). Figure10 showed Funnel plot of Prevalence of Proteus mirabilis.

Citrobacter:

Prevalence of Citrobacter was 6.75% (ES, 6.75% 95% CI -7.06%, 20.56% P= 0.34) among the 6 studies and heterogeneity found (I^2 = 0%; P =1.00) (Figure8). There was no statistically significant difference for Prevalence of Citrobacter. Also there was no statistically significant difference between studies (p=1.00). Figure10 showed Funnel plot of Prevalence of Citrobacter.

Enterobacter:

Prevalence of Enterobacter was 22.78% (ES, 22.78% 95% CI 2.28%, 43.29% P= 0.03) among the 4 studies and heterogeneity found (I^2 = 18.66%; P =0.52) (Figure9). There was statistically significant difference for Prevalence of Enterobacter. Also there was no statistically significant difference between studies (p=0.52). Figure10 showed Funnel plot of Prevalence of Enterobacter.

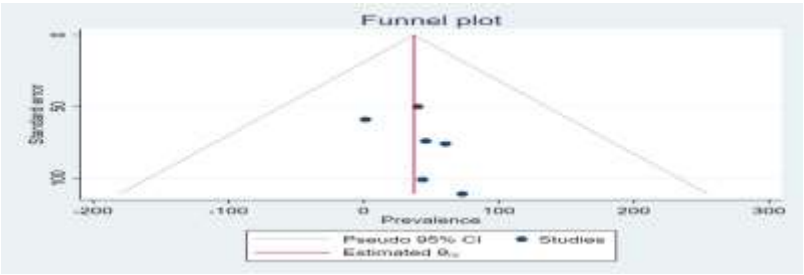


Figure3. Funnel plot showed Prevalence of UTI among children with SN.

ISSN- 2394-5125 VOL 7, ISSUE 15, 2020

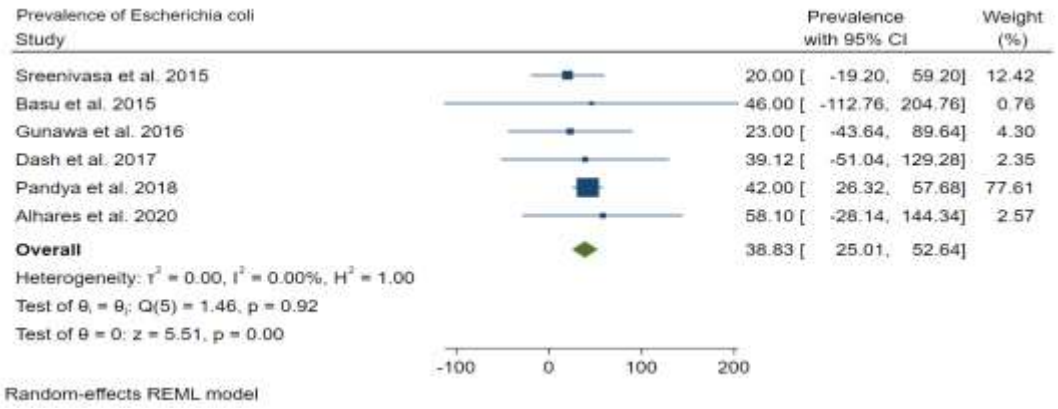


Figure4. Forest plots showed Prevalence of Escherichia coli.

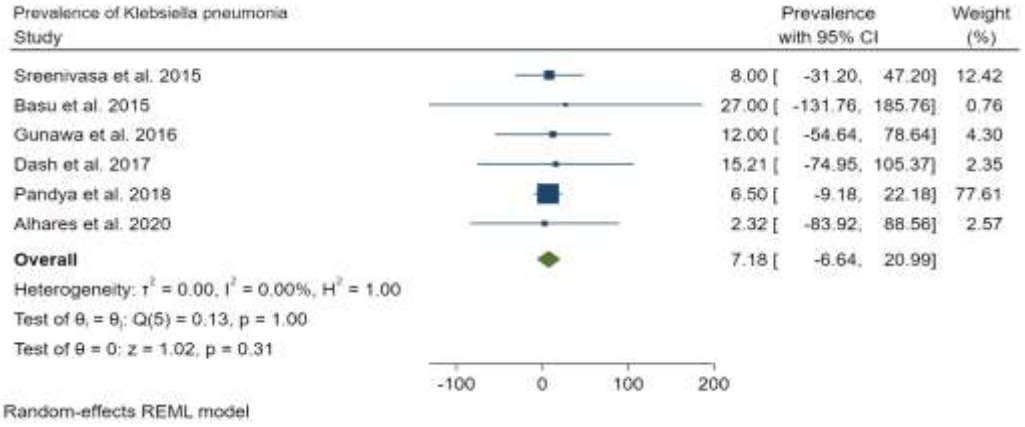


Figure5. Forest plots showed Prevalence of klebsiella pneumonia.

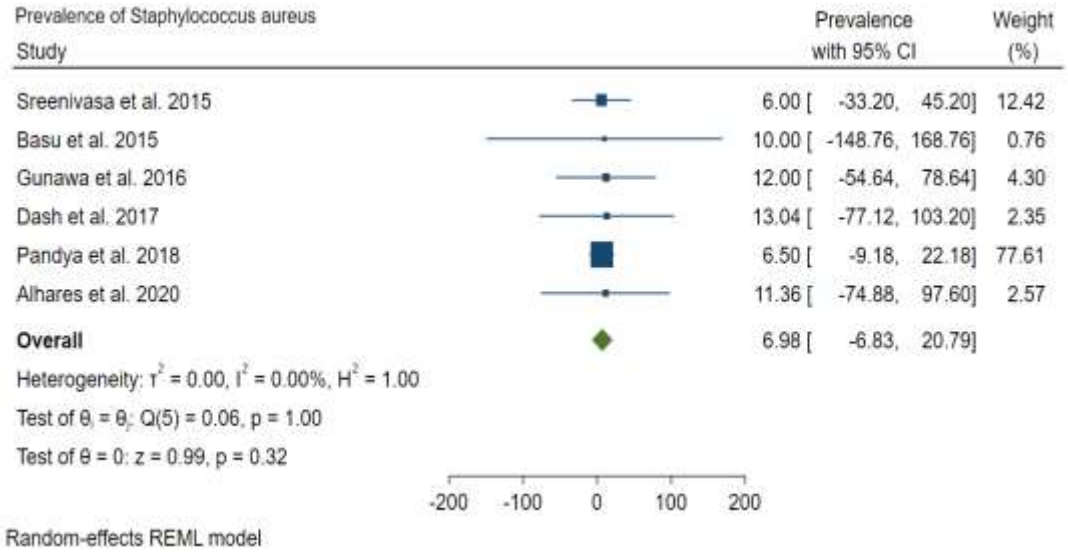


Figure6. Forest plots showed Prevalence of Staphylococcus aureus.

ISSN- 2394-5125 VOL 7, ISSUE 15, 2020

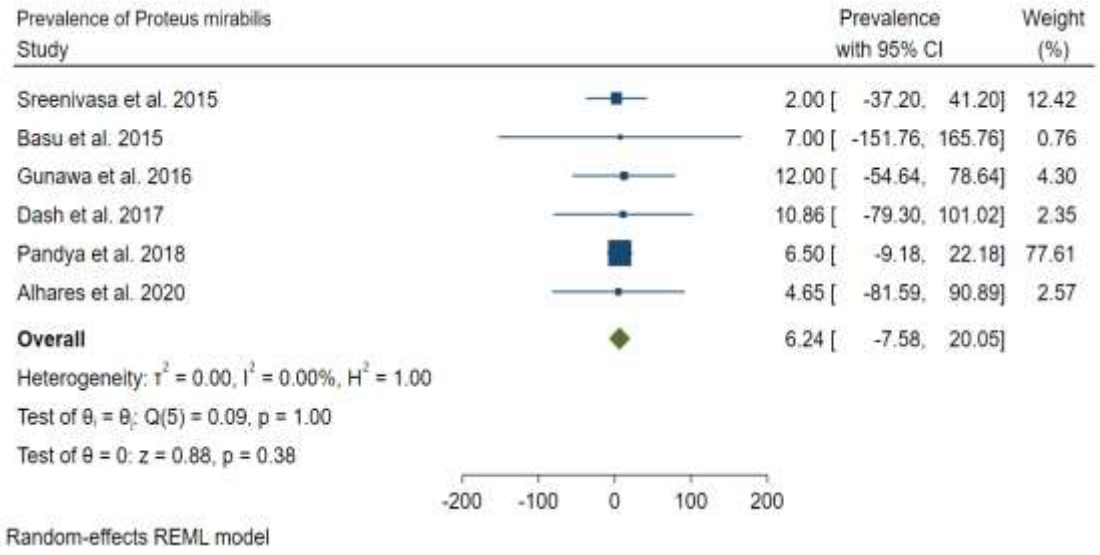


Figure7. Forest plots showed Prevalence of Proteus mirabilis.

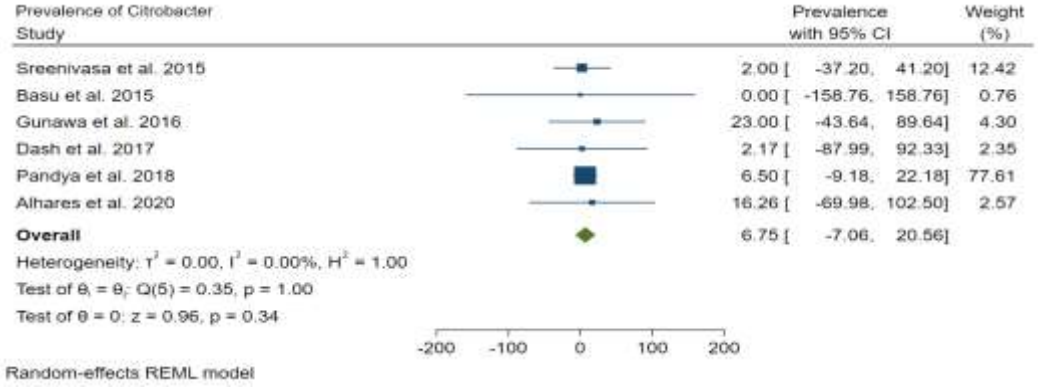


Figure8. Forest plots showed Prevalence of Citrobacter.

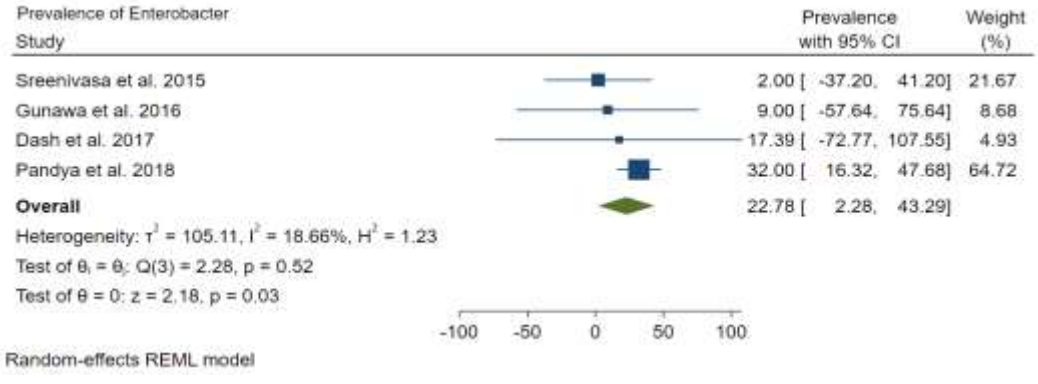
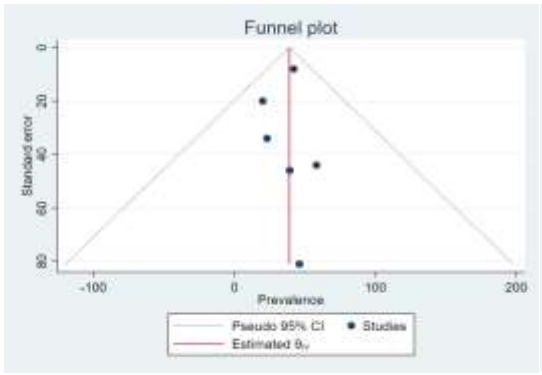
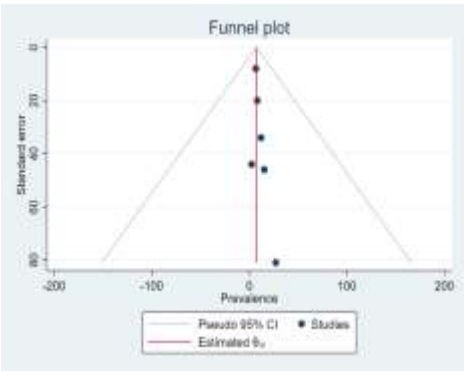


Figure9. Forest plots showed Prevalence of Enterobacter.

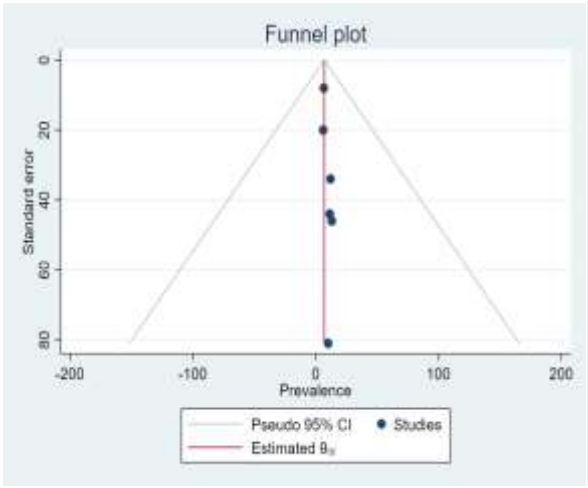
ISSN- 2394-5125 VOL 7, ISSUE 15, 2020



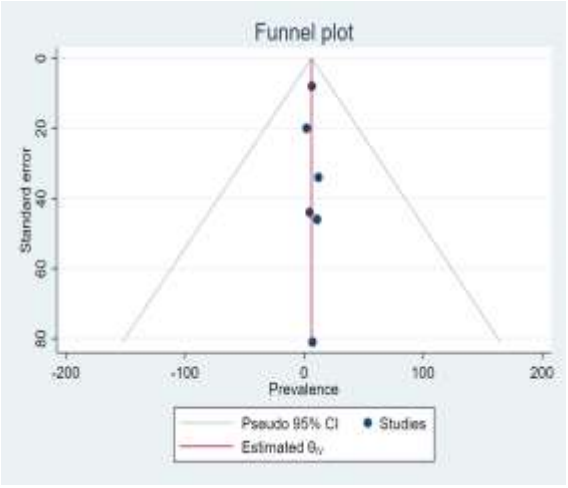
Escherichia coli



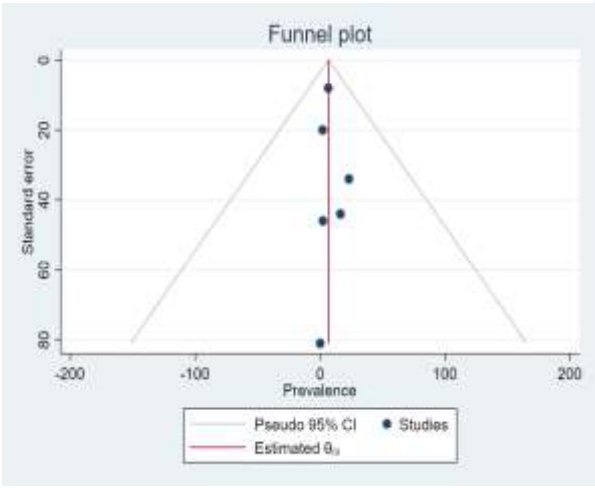
klebsiella pneumonia



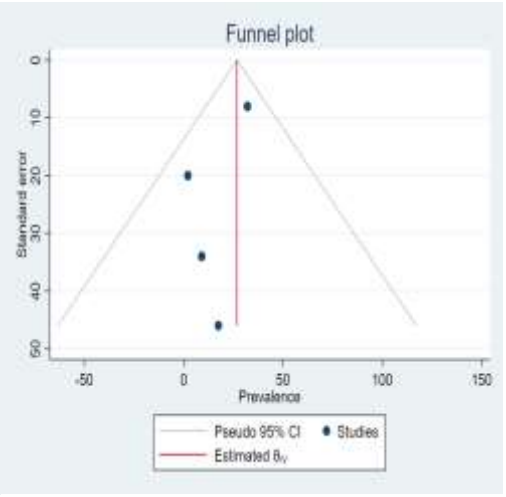
Staphylococcus aureus



Proteus mirabilis



Citrobacter



Enterobacter

Figure10. Funnel plot showed Prevalence of Organisms

IV. DISCUSSION

The present systematic review and Meta-analysis findings shows the Prevalence of UTI in children with NS was 37.18%. Escherichia coli was the most common organism isolated in 38.83% cases, then Enterobacter, Klebsiella pneumonia, Staphylococcus aureus, Proteus mirabilis, Citrobacter was 22.78%, 7.18% , 6.98%,6.24%,6.75%, Respectively. Sorkhi et al. (22) in a systematic review and Meta-analysis showed 21% of children with NS have UTI, This percentage of prevalence is lower than the prevalence of the present study, which can be attributed to the fact that the study used all available studies that were excluded in the present study. Another study (23) found

ISSN- 2394-5125 VOL 7, ISSUE 15, 2020

that the prevalence of UTI in girls was approximately 11.3% and in boys 3.6%, which is similar to the findings in Table 1. The high prevalence of UTI in girls may be due to the short distance from the anus to the bladder, which causes bacteria to reach the bladder faster and easier. a Meta-analysis study findings showed The prevalence of UTI in women was 3.1% higher than in men(24). Sorkhi et al. (22) showed Bacterial agents were the most common microorganisms, including Escherichia coli 28%, Klebsiella pneumonia 22.4%, and Proteus sp 8.6%, respectively. These results were not similar to the present study, but are consistent with the fact that Escherichia coli is the first factor. E. coli is accounts for more than 80% of all UTIs in the world(25). Therefore, it can be concluded that Escherichia coli can be considered as an important concern in children with NS. In another study, conducted by Adeleke et al., urine infection by Staphylococcus was most common followed by Klebisiella(26).A study conducted in China had shown enterococcus as the most common organism followed by E. coli(27). One of the goals of UTI treatment in children is to eliminate clinical symptoms, eradicate the cause, and prevent kidney failure as soon as possible. The Australian day-to-day trend is changing dramatically, and this could change the course of antibiotic susceptibility at different times and places. Gunawan et al.(18) (18) reported an increased risk of UTI in children with NS (OR 1.8; P=0.03). Dash et al. (19)study shows that 60.52% children with NS had UTI, this observation of high prevalence of UTI among NS patients have been reported by other studies(28, 29). The results of the present study can help to increase public awareness, parents to better respect the health of their children. This trend can also be helped by conducting forward-looking epidemiological studies. It is recommended that parents of children with NS and all those who deal with children with NS obtain sufficient information about the relationship between UTI and NS.

V. CONCLUSION

According to the findings, the most Prevalence of bacterial agents of UTI in children with NS was related to E. coli (38.83%) and the Prevalence of UTI in children with NS was 37.18% That is a significant figure and should be considered and it can endanger children's health. The prevalence of UTI also depends on geographical and economic conditions, and children who are poor in health care should pay more attention to this than other areas. Precautions should be taken when considering the high risk of UTI in children with ns.

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ISSN- 2394-5125 VOL 7, ISSUE 15, 2020

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