

Impact of Joint Urology clinic with infectious disease specialist to manage recurrent UTIs effectively

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Abstract

Objective: To evaluate the investigations and treatment patient had prior to being referred to specialist recurrent UTIs Clinic in NHS Hospital, as well as, to assess the difference in antibiotic use before and after being treated in specialized recurrent UTI clinic.

Study design: Retrospective comparative observational study

Place and duration: At specialized recurrent UTI Clinic, Department of Urology in Western General Hospital during 1st August 2019 and 1st March 2020.

Methodology: All patient seen in specialized recurrent UTIs clinic were audited. Specialized recurrent UTI clinic consist of urology consultant, infectious disease consultant and pharmacist. All patient seen in this clinic had either two cultures proven UTIs in last six month or three culture proven UTIs in a year. Patient with cystitis like symptoms without culture proven UTIs are excluded from study. Patient demographics, underlying abnormality, workup and management in the primary care, culture results, and relevant prescriptions were extracted from the electronic record. Patient are followed up after 6 months to access reduction in number of UTI episode and antimicrobial use to complete audit cycle.

Results: A total of 44 patients were studied with female (93.18%), age varies from 17 years to 91year with a mean age of 64.2 +/- 2.3 years. Majority of patients were in 7th decade of life (31.82%). The underlying pathology was observed in majority (86.36%) of the patients and among them the complex urological surgery was the commonest risk factor (23.68%), followed by post coital UTI (13.15%). In pre-clinic patients, number and quantity of both routine and non-routine antibiotics used is high (Mean+/- SD, 2.85±3.75, p-value 2.162, 95% CI 3.71 to 5.13 and OR 4.52) as compared to postclinic patients i.e., Mean+/- SD, 1.15±1.85, p-value 0.452, 95% of CI 1.61 to 2.32, OR value 2.43. In preclinic, 32% patients were on more than two and 41% patients were on two antibiotics routine and non-routine antibiotics with higher levels of daily defined dosages i.e., Mean+/- SD, 1.98±2.792, p-value 2.352. In post clinic, 82% patients were on only one and 13.64% received no antibiotic during follow up period. The daily defined dosages among these patients were also quite low in both routine and non-routine antibiotic group i.e., Mean+/- SD, 1.18±1.72, p-value 0.0031, which is also significant statistically.

Conclusion: Overall, patients found it really helpful to discuss their symptoms with a consultants in Multidisciplinary team approach. The number of acute infections and antibiotic use was lower in the six months after the intervention.

Keywords: Female, Recurrent UTI, Management, Antibiotics, Recurrent UTI clinic, Daily defined dosage

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I. Introduction

The first documented evidence of urinary tract infections (UTIs) was found in 1550 BC in Egypt and it's still among the commonest bacterial infections all over the world [1]. It affects around 150 million people globally each year with an incidence of 12.6% in female and far less (3%) in male [1,]. Collectively, it represents the 2nd most common bacterial infection after respiratory tract infection which is encountered in primary care. This leads to enormous burden on health care system and data in literature shows that it accounts for its reported that it accounts for 1±3% of all consultations and approximately 30±50% of all antimicrobial prescriptions in primary care (General Practitioner (GP) consultations) [2,3].

Almost 75% of female have episode of UTI at least once in their lifetime and literature has reported that the E Coli (*Escherichia coli*) is the commonest pathogen in 70–95% of cases [2]

Most of the UTIs are treated effectively with antibiotics but recurrent UTI is a common and troublesome problem especially in female. Recurrent UTIs, is labelled when a patient had reinfection and relapses which is defined traditionally as more than two episodes of uncomplicated UTIs in last six months or more than three infection episodes in the preceding years [4]. Literature has reported that there is a J-shaped distribution in UTI prevalence, which increase gradually with age. Up to 27% of college-age girls has developed UTI with one recurrence at least in six months. Almost up to 50 to 55% of females over 55 years age has been reported recurrent UTI [5,6]. The recent literature evidence from microbiology has suggested that some of the patients with persistent lower urinary tract symptoms are having chronic infection of the urothelial cells lining the bladder due to greater tendency of uro-pathogens especially coliform to adhere to uroepithelium [7,8]. The same tendency of uro-pathogens is also observed in vagina epithelium along with enhanced susceptibility of vaginal colonization [7].

Although, these urinary infections are usually not life-threatening but are difficult to manage usually especially at primary care setup. Moreover, the high incidence of these infections significantly affects the patient's quality of life and enhances the economic burden over health care [5]. During last 2 to 3 decades the risk factors, pathogenesis, management and prophylaxis of UTI has been attracted wide attention and investigated well. The commonest risk factors among female includes sexual interaction, spermicidal agents use, early onset 1st UTI event and history of UTIs to mother. In some female with recurrent UTIs, the inherited factors are also important. Whereas many factors which were thought to predispose recurrent UTIs in ladies in past, like pre- and post-coital voiding patterns, urinary frequency, wiping methods and douching have not been proved as risk factors now in literature. Whereas in healthy post-menopausal female, the behavioral risk factors for young women either mechanical or physiological which affect emptying of bladder are reported to be predominantly more strongly associated with recurrent UTI [7]. Recently, it has been reported that up to 95% of female has consulted their GP for their recent episode of and antibiotics were prescribed in 74% of patients [9]. Whereas the Duane et al [10] has observed that only 35.8% of urine which were cultured for suspected UTIs has met the laboratory threshold for UTI. They concluded that not all symptomatic episodes are due to urine infection so other causes should also be looked for.

The NICE (National Institute for Health and Care Excellence) has concluded that insufficient data or evidence-based protocols are available to guide the clinicians in managing the recurrent UTIs [9]. Instead of treating these infections with antibiotics alone, the change in the trend in the form of guidelines, specialist clinics for recurrent UTI has been emerged in successful management. More aggressive management is suggested, such more emphasis on medical prophylaxis and risk factors avoidance[1]. Different strategies are recommended to prevent recurrent urinary infections like awareness about association of recurrent UTIs and sexual intercourse frequency, usage of spermicide products and so on. The prophylaxis with low-dose antimicrobials continuously or intermittently have been reported effective in uncomplicated recurrent UTIs management. In postmenopausal female, Estrogen is found very effective in recurrent UTIs prevention [11,12]. The exciting new modalities in recurrent UTI prevention or prophylaxis comprises of vaccine, methenamine Hippurate, intravesical instillation and/or probiotics use in these patients [3,13]. Moreover, the understanding of UTI pathogenesis will also helpful in use of safer and effective modalities in prevention of these recurrent infections [14].

In this study we were able to offer management to patients with recurrent UTI and analyze the results. The study is also an excellent example of a hospital specialists working in a team to improve patient outcome and to assess any benefits of adherence to guidelines. This study will enhance the clinician trust on adherence to the SIGN/NICE guidelines in the treatment of recurrent UTI. Thus, the objective of this study was to investigate the work up and treatment patient received prior to being referred from a primary care practice in NHS Location to Hospital, as well as, to assess the difference in antibiotic use before and after being treated in specialized recurrent UTI clinic.

II. Methodology

This retrospective comparative observational study was conducted at the Department of Urology in specialized recurrent UTI clinic at Western General Hospital, UK from 1st August 2019 and 1st March 2020. The data of all patients with recurrent UTI who are attending the specialist UTI clinic were retrieved from the hospital data base. Specialized recurrent UTI clinic consist of urologist, infectious disease specialist and pharmacist. All patient who received treatment at least of six months duration before clinic and has completed six months follow up in specialist UTI clinic were included. In addition, patients seen in this clinic had either two cultures proven UTIs in last six month or three culture proven UTIs in a year. Patient with cystitis like symptoms without culture proven UTIs are excluded from study. The demographic data, any comorbidities or underlying pathology, previous investigations and treatment for UTIs at primary care and treatment given in specialized UTI clinic were retrieved carefully and meticulously and recorded on separate performa. The patients who The special emphasis was given on the pre and post clinical daily defined dosage (DDD), number of routine and non-routine UTI antibiotics prescribed in pre and post UTI clinic period, and difference in usage of antibiotics in pre-clinical and post clinical duration. The criteria for the diagnosis of recurrent UTI were two cultures proven UTIs in six month or three culture proven UTIs in a year. The mid-stream urine was tested in all patients to diagnose the UTI and for culture and sensitivity of micro-organism. Patient were followed after 6 month to access improvement in number of UTI and decrease in antibiotic usage.

Data analysis: All data retrieved from hospital record and analyzed with SPSS23 version. In age the mean and SD were calculated where as 95% confidence interval and % age was calculated in age groups and risk factors. The number, quantity and Daily defined dosages were assessed through mean with SD, p-value, OR and 95% of CI in both pre-clinical and clinical patient.

III. Results

A total of 44 patients were studied with age varies from 17 years to 91year with a mean age of 64.2 +/- 2.3 years. Majority of patients were female (93.18%, n=41) as compared to male (n=3, 6.82%). Most of patients were in 7th decade of life (n=14, 31.82%) followed by 8th decade (n=7, 15.92%). Only 2.27% patients were from 2nd decade of life (Table-I).

Table-I: Frequency of age distribution (N=44)

AGE GROUP	n	%	95% Confidence Interval (CI)
< 20	1	2.27%	2.11 to 2.35
21 – 30	4	9.09%	9.01 to 9.20
31 – 40	5	11.36%	11.25 to 11.48
41 – 50	3	6.82%	6.75 to 6.89
51 – 60	6	13.63%	13.50 to 13.77
61 – 70	14	31.82%	31.51 to 32.14
71 – 80	7	15.92%	15.75 to 16.09
>80	4	9.09%	9.01 to 9.19
TOTAL	44	100	

Table-II shows the frequency of different comorbidities associated with UTI among patients studied. Only in 13.64% (n=6) patients with recurrent UTI no co-morbidities were found as compared to 86.36% (n=38) with co-morbidities. The complex urological surgery was the commonest risk factor (n=9, 23.68%) associated with UTI followed by post coital UTI (n=5,13.15%). The long-term catheterization of the bladder was observed in 10.52% (n=4) patients.

Table-II: Frequency of co-morbidities/risk factors associated in patients with recurrent UTI. (N=44)

Co-morbidities	Frequency	% of total	95% CI
Recurrent UTI without underlying pathology	6	13.64%	11.39 to 15.67
Recurrent UTI with underlying pathology	38	86.36%	83.82 to 89.08
<i>Post coital</i>	5 (13.15%) % in group		11.87 to 15.98
<i>Fecal incontinence</i>	3 (7.89%) % in group		4.39 to 5.67
<i>Long term catheterization</i>	4 (10.52%) % in group		9.05 to 11.17
<i>Intermittent Catherization</i>	2 (5.26%) % in group		4.39 to 6.07
<i>Complex urological surgery</i>	9 (23.68%) % in group		21.73 to 25.36

Table -III shows frequency of different treatment modalities offered to the patients in UTI clinic. Methenamine is the commonest treatment modality (50%, n=22) used followed by topical estrogen therapy (40.90%, n=18)prophylactic antibiotics were used in 22.72% (n=10)and D-Manose in 20.45% (n=9) patients. Our 2.27% (n=1) has also received E coli vaccine.

Table III: Frequency of different treatment strategies used in UTI clinic (N=44)

Treatment advised	N (%)	95% CI
Methenamine	22 (50%)	48.72 to 52.12
Topical Estrogen	18 (40.90%)	39.33 to 42.17
D-Mannos	9 (20.45%)	18.95 to 22.03
Prophylactic antibiotics	10 (22.72%)	21.45 to 24.32
Intra-vesical instillation	2 (4.5%)	3.70 to 5.21
E coli vaccine	1 (2.27%)	1.87 to 3.05
0.5% Chlorhexidine Sol	3 (6.81%)	5.11 to 8.03
Cystoscopy + ureteral dilatation	6 (13.63%)	11.97 to 15.12

Data shows that the other than urine culture, the only investigation done in patients with recurrent UTI prior to attending specialist UTI clinic was Urinary tract US Scan (n=22, 50%) and flexible cystoscopy (n=16, 36.36%). The comparison of urine culture sent 06 months before and 06 months after attending UTI clinic of all 44 patients shows a statistically significant difference in culture patten of micro-organisms especially in positive culture i.e. 50% (n=22) in pre-UTI clinic as compared to 34.13% (n=15) post UTI clinic (P vale - 4.76). The 27.84% (n=12) specimen shows no growth before attending UTI clinic as compared to 42 33.34% (n=15) specimens (p value- 1.73 as shown in figure 1.

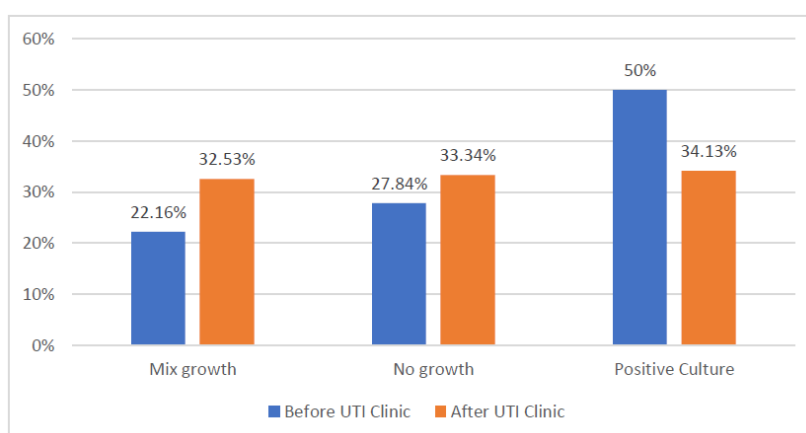


Fig 1: Comparison of urine culture 06 months before and 06 months after attending UTI clinic (N=44)

Figure-2 shows the frequency of number of routine and non-routine antibiotics used, quantity and daily defined dosage used in patient with recurrent UTI six months before attending the UTI clinic. The number and quantity of both routine and non-routine antibiotics used in majority of patients is high (Mean+/- SD, 2.85±3.75, p-value 2.162, 95% CI 3.71 to 5.13). The OR was analyzed as 4.52 in these patients. Almost 32% (n=14) patients were on more than two routine and non-routine antibiotics where as 41% (n=18) patients were on two antibiotics. Higher daily defined dosages among these patients were

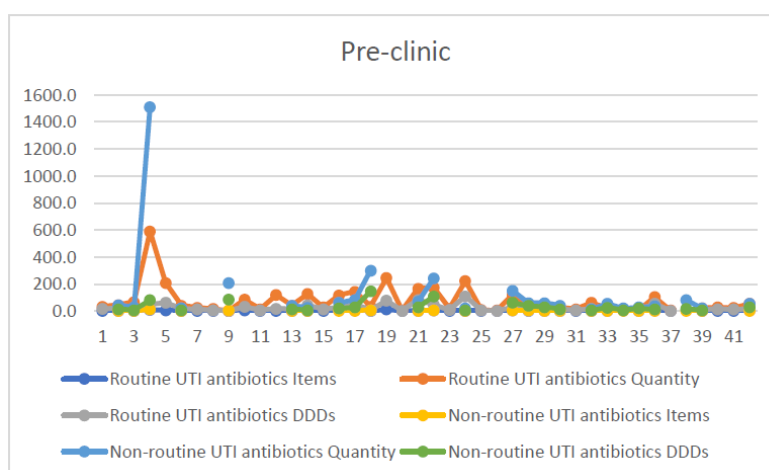


Fig - 2: Frequency, quantity and daily defined dosage (DDD) in patient before attending UTI Clinic (pre-clinical) (N=44)

Analyzed to be higher i.e. Mean+/- SD, 1.98±2.792, p-value 2.352 in both routine and non-routine antibiotics.

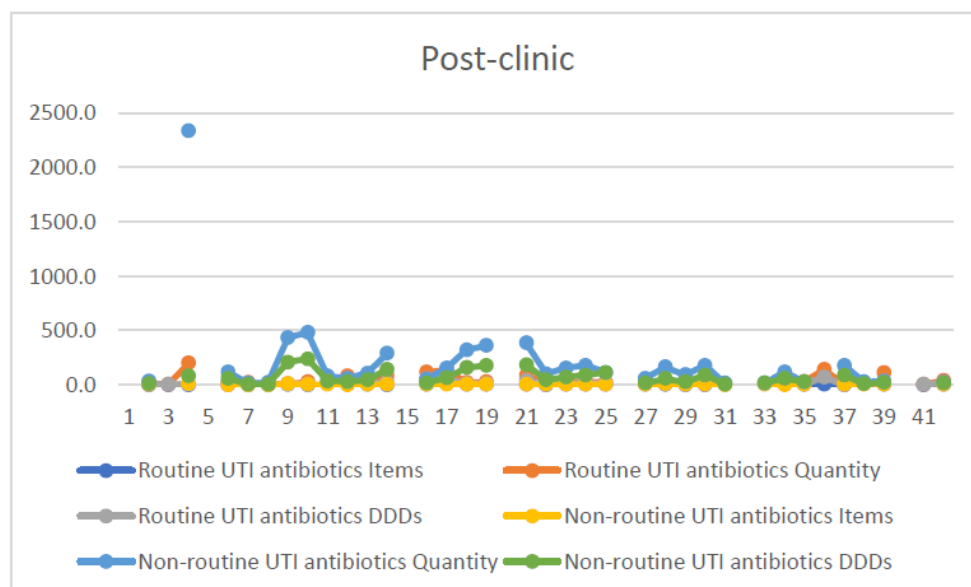


Fig - 3: Frequency, quantity and daily defined dosage (DDD) in patient after attending UTI Clinic (post-clinical) (N=44)

In figure-3, the frequency of number of antibiotics used, their quantity and daily defined dosage used in patient up to 06 months after attending UTI clinic. The number and quantity of both routine and non-routine antibiotics used in patients were less i.e., Mean \pm SD, 1.15 \pm 1.85, p-value 0.452 and 95% of CI 1.61 to 2.32. The OR value was analyzed as 2.43 in these patients. These values lower and are statistically significant as compared to pre-clinical group patients. Almost 82% (n=36) patients were on only one antibiotic during follow up period. No antibiotics were prescribed to 13.64% of patients (n=6) and only 4.36% (n=2) patient required more than one antibiotic in follow up period. Higher daily defined dosages among these patients were also quite low in both routine and non-routine antibiotic group i.e. Mean \pm SD, 1.18 \pm 1.72, p-value 0.0031, which is also significant statistically.

IV. Discussion

The UTIs is a common urological problem with a significant patient load over General Practitioner with an almost 30 \pm 50% of antimicrobial prescriptions at primary care clinics [15]. Therefore, the meticulous patient's assessment is very crucial as suboptimal diagnosis and management will end up in failure in treatment, resistance to antibiotics and recurrent UTIs. In this regard, patients' education in self-care improvement, timely referral to specialist clinic, shared decision making, most likely will improve the outcome especially in reducing recurrent UTI episodes and reduces morbidities [16,17]. It has been reported that many patients with uncomplicated UTI symptoms having no meaningful improvement or benefit with antibiotic therapy, but the evidence base in this regard is complex and there is a lack of appropriate shared decision-making guidelines for primary care doctors to guide them in symptomatic care and antibiotic treatment.

UTI is common in post-menopausal group especially in aging population i.e., after the age of 60 years. The majority of our patients were in 7th decade of life (31.82%) with a mean age of 64.2 \pm 2.3 years which is consistent with literature finding [14,15,18,19]. The clinical presentation may varies at different age groups as also observed by Arinzon et al [20]. They observed that the clinical presentation in older and younger female is slightly different which is not only by voiding itself and by local symptoms but also by un-specified generalized symptoms which are important in older female. They grouped these symptoms as local constant, voiding-related and generalized symptoms. In patients usually the local symptoms were predominant followed by voiding and generalized symptoms. In post-menopausal female the storage and generalized unspecific symptoms are predominant. The study observed that unspecified symptoms like low back ache, lower abdominal pain, nausea, cold chills and constipation were significantly correlated with advancing age. The Palma et al [21] has observed in female with GSM that the reason of increase prevalence of recurrent UTIs in advancing age (>65) is due to vulvar vaginal atrophy, pH > 5. (79.1%) and vaginal infections which usually starts 1 to 6 years after menopause. They conclude that the symptoms of GSM are common and usually under diagnosed and under-treated. Measures to improve its early detection and its appropriate management are needed.

Among the pathogenesis and one of the reason other than antimicrobial resistance causing difficulty to treat recurrent UTIs is the progression of intracellular bacterial communities (IBCs) in bladder urothelium. This has been reported in literature as another possible mechanism in pathogenesis [6]. Studies shows that *E. coli*

replicate and causing bacterial collection intracellularly, and then entered the bladder lumen. These IBCs remain quiescent even for longer period despite antibiotic treatment and then escape into bladder causing recurrent UTI. It is difficult to detect these IBCs in urine specimens. The immunofluorescence evidence shows that up to 18% of female having acute uncomplicated cystitis had bladder IBCs [6,22].

It's very important to exclude possible risk factors through a comprehensive evaluation and investigations in recurrent UTIs. The evaluation comprises of a detailed history review and a clinical examination to look for any anatomical urogenital anomalies, voiding dysfunctions, immunodeficiency, and any health behavioral issues [6,23]. The commonest well known urogenital anomalies are obstruction and calculi [23]. In our patients the most common risk factors other than age were post coital UTI (11.36%), incomplete emptying of the bladder (9.09%), among urological procedure, duplex kidney (4.54%) and ileal conduit (4.54%) are commonest. The other factors like voiding dysfunction, chronic pain, increase urinary frequency, sense of incomplete emptying and ureteral catheterization were also noticed. Proper assessment and information gathering is very important as a first step in management of recurrent UTI. The current guidelines recommend that in recurrent UTIs, the increase RU is an independent risk factor and it should be assessed before planning any management [4,13]. The behavioral risk factors such as sexual intercourse, frequency, sex partner, use of spermicide agents, local hygiene, voiding habits (i.e., hesitating or voluntary deferring of urination) should be considered in patients with recurrent UTI [23]. Studies shows that the odds ratio of recurrent UTIs is more than 10.3 in female who have more than 9 times intercourse in last month. Similarly hesitating or deferring oneself for 1 h were strongly associated with recurrent UTIs [4,7,11]. In female, the urodynamic studies observed that increased abdominal pressure (>28mmH₂O) during voiding is common finding in patient with recurrent UTI [9,12]. In a systematic review by Geisen et al [24] to assess the symptoms and signs diagnostic accuracy in suspected UTI has concluded that the diagnostic accuracy in UTI improves considerably by combining the signs, symptoms assessment with dip-stick tests (especially tests for nitrites). This will be helpful in use of flowchart stepwise approach. The Michaels et al [25] in their review has recommended evidence-based approaches for UTIs evaluation. They stressed of initial targeted history with special emphasis on features of a local cause, risk factors identification and UTI symptoms.

During past years the psychological factor's role in recurrent UTIs has gained wide attention of clinicians [1,15]. By using different personality questionnaire, the Hunt and Waller has observed that the neurotic personality type females are more prone to recurrent UTIs [1]. However, due to limited data more research is required to draw some precise conclusion. The dietary habit's role is also not clear except a moderate association was reported with soft drinks and UTI with a lack of strongest evidence [15].

The functional and structural anomalies of the genito-urinary tract are also associated with asymptomatic bacteriuria with an exceedingly high prevalence of UTIs even in healthy females. These patients frequently found to have positive urine cultures. The asymptomatic bacteriuria is rarely associated with adverse outcomes, though in some cases screening and treatment is recommended [6,8]. The Bonkat et al [26] has recommended routine screening by mid-stream urine culture for asymptomatic bacteriuria because it reduces the risk of recurrent UTIs. As asymptomatic bacteriuria is usually not associated with long-term adverse outcomes. Therefore, the screening and treatment is not recommended in these young healthy females. The structural and functional anomalies commonly observed among our patient were duplex kidney, ileal conduit (22.22% each), followed by vesico-ureteric reflux, ureteral stricture, ureteric re-implantation and urethroplasty (11.11% each)

In a review of UTIs diagnosis and treatments, the most diagnostic symptoms comprise of dysuria, change in frequency, urgency and presence or absence of vaginal discharge especially in pre-menopausal females and reported that the UTIs may have different presentation among older females. Other UTI symptoms are tenderness (suprapubic, vaginal, and/or urethral), haematuria. It's important to note that systemic symptoms like nausea, vomiting, fever, back pain, flank pain are usually indicator of ascent of infection to upper urinary tract[27].

Literature mentioned that the most relevant findings on clinical examination are to look for signs of infectious or atrophic vaginitis, STIs, vulvo-vaginal disease, urethritis etc. If any recurrent or complicating features are suspected of detailed history and physical examination, the urinalysis and urine culture should be arranged as first line investigation. In suspected urethritis, a urethral, vaginal, endocervical, or urine nucleic acid amplification test for *N. gonorrhoeae* and *Chlamydia trachomatis* is recommended. Subsequently, the secondary evaluation findings, laboratory tests, and imaging studies enable the clinician to progress in through a logical evaluation of UTI and in deciding an appropriate management or referral to UTI clinic [8,9,22].

As per NICE Guidelines, a urine sample should be sent for culture in all women with suspected lower UTI who are pregnant, older than 65 years, have persistent symptoms or if treatment fails, have recurrent UTI, catheterized or who have recently been catheterized, have risk factors for resistant or complicated UTI and have visible or non-visible haematuria. However, in patient with recurrent UTI Urine cultures are frequently obtained in primary care, even in the absence of urinary symptoms [28]. Asymptomatic bacteriuria is often treated in these patients, and accounts for a substantial burden of inappropriate antimicrobial use. Effective strategies to

improve urine culture ordering and antimicrobial utilization in primary care for recurrent UTI patients need to be implemented. Asymptomatic bacteriuria, generally defined as bacteriuria in the absence of urinary symptoms, is relatively common in adults, but in most cases should not be treated. Therefore, appropriately sent urine culture only if patient with recurrent UTI is symptomatic will help to reduce economical burden as well as inappropriate use of antibiotics [9]. A review of Urological Infections Guidelines by panel of urologists on management guidelines for UTIs in specialist clinic does not recommend treatment in asymptomatic bacteriuria, among post-menopausal ladies because the antibiotic treatment does not show significantly beneficial effects in resolution of asymptomatic bacteriuria or reducing the rate of recurrent symptomatic UTIs after comparing with placebo or no treatment (average RR 0.68, 95% CI 0.46 to 1.00; n=210). Moreover, the screening or treatment is not recommended for asymptomatic bacteriuria the urine dipsticks is not recommended among older females in diagnostic pathway for recurrent UTI. The urine cultures are recommended to check for resistance if UTI is suspected [20].

This guideline produced by the NICE Public Health and Social Care Guidelines Team of anti-microbial treatment for UTIs has stressed more on rationale use of antibiotics and to reduce antibiotic resistance. It is recommended that the advice should be given on self-care to all those with expected UTI and mid-stream urine specimens should be sent [28].

A study on population older than 70, to assess antibiotic resistance of urinary tract has observed a high level of bacterial resistance and as a first line tool recommended that all older adults with suspected UTI should have a urine culture [29]. The resistance against antibiotics is a commonest problem which is becoming critical to address all over the world. Some proactive solutions of this issue are mandatory to slow down this surge in antibiotic resistance because of economic burden over health resources and may leads to crisis future. In this regard, the safe, effective alternatives would be very helpful to reduce antibiotic prescription and incidence of drug resistance [13]. By using this strategy and guidelines, the prophylactic antibiotics were used only in 22.72% of our patients and majority of patients were treated with alternative treatment modalities as per their indication.

The use of methenamine salts (methenamine Hippurate) is one of the possible alternatives, which is generally safe and act as bacteriostatic agent through the production of formaldehyde from hexamine and it does not cause any antibiotic resistance. It gives mild gastrointestinal symptoms, can be used in pregnancy and only major problem is to be used with caution if there is dehydration, or liver and renal disease. The Bakhit et al [30] has reported significant reduction in the symptoms of UTI in patients without renal tract abnormalities in their review. The NICE guidelines, recommended that the Methenamine (hexamine) Hippurate should not be used generally due to acidic urine requirement for its antimicrobial activity and also found ineffective for upper urinary-tract infections. But it has a prophylactic role in treatment and prophylaxis of recurrent or chronic uncomplicated lower urinary-tract infections [9]. Methenamine is the commonest treatment modality used in almost 50% of our patients with very good results on follow up after six months.

The Vaginal estrogen supplementation is another well-known option used in treatment and prevention of recurrent UTIs, which is widely supported in literature [21,28]. Estrogen lack leads to vaginal epithelium atrophy, increase in vaginal pH and reduction in endogenous vaginal flora (lactobacillus). Literature has proved that a reduction in estrogen during post-menopausal state leads to decrease in vaginal mucosal blood flow, increased hypoxia and marked increased mucosal permeability, which is attributed to the increased rate of UTIs. The topical estrogen cream useful in enhancing blood flow and associated with a quicker response to bladder infection [31]. The topical estrogen therapy was used in majority (40.90%) of our patients as almost more than 60% of our female patients were from post-menopausal age. Topical estrogen cream local application is found very effective in our experience and to be used when ever indicated.

Another agent, D-mannose, a simple sugar has been proved to hinder the bacteria adhesion to the urothelium as reported by Domenici et al [32]. The and D-Manose is used in 20.45% of our patients and shows good results.

The 0.5% chlorohexidine solution which is used to clean urethral meatus prior to ISC has also reported to be helpful in reducing the UTIs in patient with voiding dysfunction. Bacteria in UTI can easily adhere to the urothelium of bladder because it is porous nature, proliferate there and cause recurrent UTIs [1]. The intravesical installations is another alternative, which is a theorized pathways that it is helpful in restoring the abnormalities of the GAG layer of urothelium which is a hydrophilic coating and barrier within the bladder. The Dimethyl sulfoxide (DMSO), heparin or pentosan poly sulphate, reported to restore the GAG layer of the bladder in a subset of patients by reducing incidence of UTIs [3,31].

Immunotherapy, as an alternate non-antibiotic treatment strategy is also increasingly becoming an attractive alternative in the UTIs treatment. In several randomized placebo-controlled trials reported in literature to reduce the frequency of UTI recurrence, the Uro-Vaxom® (OM-89, OM Pharma), an immuno-modulator, against 18 different strains of *Escherichia coli* shows enhanced humoral and cellular immune responses by stimulating macrophages, lymphocytes and also found to increasing the levels of circulating endogenous

IgA/IgG antibodies [33]. It is recommended in SIGN guideline but its endorsement in the European Association of Urology Guidelines is still awaited. The E coli vaccine is used in 2.27% and intravesical instillation was done in 4.54% of our patients with no recurrent episode of UTI were found after 06 month follow up.

The benefits to carrying out clinics in multidisciplinary approach were that patients felt comfortable and travelling times and costs were reduced to avoid multiple visits to different specialties. The urologist could access past consultation records and consider illness in context of the patient's life while infectious disease consultant can review patient culture results and sensitivities and pharmacist help to extract patient use of antibiotics and other routine medication. Therefore, recommending patient appropriate treatment to manage symptoms effectively with better outcome. We gained valuable knowledge from working in collaboration in this study.

V. Conclusion

Overall, patients found it really helpful to discuss their symptoms with a consultants in Multidisciplinary team approach. The number of acute infections and antibiotic use was lower in the six months after the intervention.

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