How to Cite:
Nada, D. W., Bahey, M. G., Oraiby, A. E. S., & Hanout, H. A. E. A. (2020). Evaluation of asymptomatic bacteriuria and urinary tract infections in Egyptian rheumatoid arthritis patients using biological and /or conventional DMARDs. *International Journal of Health Sciences*, *5*(S2), 1071–1085. https://doi.org/10.53730/ijhs.v5nS2.14118

Evaluation of asymptomatic bacteriuria and urinary tract infections in Egyptian rheumatoid arthritis patients using biological and /or conventional DMARDs

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***Abstract*---**Objective: To determine how frequently Egyptian RA patients receiving biological and/or traditional DMARDs experience asymptomatic bacteriuria and urinary tract infections (UTI). Methods: 100 RA patients and 100 age- and sex-matched healthy controls made up this cross-sectional study. For urine analysis and culture, each participant provided mid-stream urine sample. Each participant's blood was drawn for ELISA testing to measure the levels of IgG antibodies against Proteus mirabilis and E. coli, the most frequently isolated pathogen from RA patients' urine samples. Additionally, RA patients' clinical assessments were carried out. Results: (5%) of healthy controls and (40%) of RA patients had asymptomatic bacteriuria, respectively. E. coli (25%), followed by Proteus mirabilis (42.5%), were the two most frequently isolated organisms. IgG antibody levels against Proteus mirabilis were significantly different between the two study groups (P 0.001). Regarding the levels of IgG

antibodies against E. coli, there was no discernible difference between the two study groups (P 0.571). Proteus mirabilis IgG antibody levels were observed to significantly positively correlate with ESR, CRP, DAS28, m HAQ, duration of morning stiffness, and conventional DMARDs in RA patients. Conclusion: Patients with RA on conventional DMARDs and those utilizing conventional with biological DMARDs are more likely to experience asymptomatic bacteriuria and UTI with high frequency of P. mirabilis & E coli infections. Therefore, it is necessary to frequently screen RA patients in order to improve their clinical outcomes and their compliance to prescribed medications.

***Keywords*---**rheumatoid arthritis, asymptomatic bacteriuria, urinary tract infection, disease modifying antirheumatic drugs.

Introduction

One of the most prevalent systemic autoimmune diseases in humans is rheumatoid arthritis (RA). It is characterized by small joint damage and inflammation. Although the precise cause of RA is unknown, medical data suggests that people with inherited genetic risk factors are more likely to acquire the disease after being exposed to environmental triggers such infections, hormones, smoking, and nutritional variables [1, 2]. The clinical correlation between infection and RA has been demonstrated in numerous research. Infection is frequently identified in RA at an early stage and may appear before clinical arthritis, suggesting that infection plays a role in the development and aggravation of RA [3, 4].

Urinary tract infections (UTI) are among the most frequently found severe illnesses in RA patients. The immunological dysfunction underlying the disease process, immunosuppressive medications used to treat RA, and other immune-compromising coexisting conditions are only a few of the factors contributing to this elevated risk of infection [5]. UTI can affect the kidneys, ureters, bladder, and urethra, among other parts of the urinary tract. Women are more affected than men because of the female urethra's close proximity to the anus and vagina, as well as the fact that it is significantly shorter than the male urethra, making it easier for microorganisms to enter the bladder [6, 7]. Additionally, UTI is highly prevalent and recurrent in RA patients. Urine culture is the gold standard approach for diagnosing it. As a result of the emergence of antibiotic resistance, treatment is challenging. The key to successful therapy is selecting an antibiotic that is effective against the pathogen found in the antibiogram and has a low risk of causing resistance [8].

Asymptomatic bacteriuria, on the other hand, is typically underestimated. It is defined as the isolation of bacteria in significant amounts in the urine culture from a person without symptoms or signs of UTI and/or the isolation of the same bacterial strain >1 colony-forming unit (CFU) /mL in two consecutive urine cultures [9]. Moreover, modern approaches to the management of RA typically do not take into account the early phases of the disease's development and instead

just treat its symptoms. Long-term use of the currently available treatment options, including conventional and biological DMARDs, causes a number of serious adverse effects [10, 11].

Few studies have recently looked at the prevalence of UTIs or asymptomatic bacteriuria in RA patients without considering their use of DMARDs, and the others have only relied on registry data [5, 6, 12]. Therefore, the current study's goal is to ascertain how frequently Egyptian RA patients receiving biological and/or conventional DMARDs experience asymptomatic bacteriuria and urinary tract infections.

Methods

Study design and participants

100 RA patients were included in this prospective cross-sectional observational study that was conducted using the ACR/EULAR 2010 classification criteria for RA [13]. Additionally, 100 healthy volunteers matched in sex and age with patients' group , served as the control group over a period of 6 months (from October 2019 to March 2020) . This study was performed in Medical Microbiology & Immunology and Rheumatology & Rehabilitation Departments, Faculty of Medicine, Tanta University Hospitals. All requirements of the Declaration of Helsinki guidelines was followed during preparation of this study.

Exclusion criteria

Children, Pregnant women, Patients with anatomic disorder, pelvic relaxation, spinal cord injury, catheterization or active infection in other systems were all excluded.

Ethics-related considerations

The study protocol was approved by Local Research Ethics Committee, Faculty of Medicine, Tanta University (Approval code:35756). All procedures were carried out in accordance with the Helsinki Declaration and the responsible committee on human experimentation (institutional and national) ethical standards. All study participants provided informed consent after being informed of the study's objectives and that the information would only be used for scientific research.

Method

All participants was subjected to:

1-Clinical assessment including:

a) Through history taking as well as complete general & locomotor examinations.
b) Evaluation of disease activity score (DAS28). The number of swollen joints (out of the 28 joints), number of tender joints (out of the 28 joints), (ESR) or (CRP), and Patient global evaluation VAS make up [14]'s verified composite disease activity score (0–100 mm). The overall disease activity

score is then generated using these values as input into a challenging mathematical algorithm. DAS28 values of more than 5.1 indicate a disease that is very active, less than 3.2 indicate low disease activity, and less than 2.6 indicate remission.

c) Modified Health Assessment Questionnaire (MHAQ) [15], that perform a functional assessment that assesses the patient's response and accurately describes their typical abilities throughout the course of the previous week as well as gauges their level of disease-related impairment, discomfort, and quality of life. The result should fall between 0.0 and 3.0. Indicating a small functional loss is a score between 0.3 and 1.3, a moderate functional loss is one between 1.3 and 1.8, etc. A patient was deemed to have a high functional loss when their score rose by 1.8.

2-Laboratory assessment including:

- Complete blood Count with differential WBCs count
- Estimated sedimentation Rate (ESR) [16].
- High- sensitive CRP (HS-CRP) [17].
- RF titer [18].
- Anti CCP antibodies [18].
- Urine analysis.
- Urine cultures.
- Detection of Proteus mirabilis and E. coli IgG antibodies in the serum of the study subjects using ELISA.

3-Detection of Urinary tract infections and Microbiological assessment:

- Sample collection and processing:
  All study participants provided midstream urine samples, which were collected in sterile containers following cleaning with an external antiseptic agent. A midstream urine sample that had just been voided was used to inoculate 0.001 milliliters of Cysteine Lactose Electrolyte Deficient Medium (Oxoid UK) for bacterial count. Samples were incubated aerobically at 37°C for 24-48 hours after being inoculated on nutritional, blood, chocolate, and MacConkey agar plates (Oxoid, UK) as well. The isolates were phenotypically identified using Gram stain, colony morphology, and biochemical responses, which are common microbiological methods. They counted the colonies. Significant bacteriuria was defined as cultures 105 CFU/mL [19].
- Identification of bacterial isolates:
  Using Standard biochemical assays and the Gram stain (e.g., catalase, coagulase, oxidase, mannitol salt agar, DNase, triple sugar iron agar, citrate, urease, etc.) Additionally, in accordance with the manufacturer's instructions, the automated Vitek 2 Compact system (bioMerieux, France) confirmed the species identification. Proteus mirabilis, Escherichia coli, Klebsiella pneumoniae, Enterococci, Acinetobacter, and Pseudomonas aeruginosa were among the bacterial isolates examined.
- Identification of fungal isolates:
  Direct smears of lactophenol-cotton blue were examined under the microscope after immediate KOH wet mounting. After that, the specimens were grown on Sabouraud dextrose agar (oxoid UK) in the presence of chloramphenicol and with or without cycloheximide. The plates were incubated at room temperature and 37 degrees. According to

the manufacturer's instructions, the automated Vitek 2 Compact (bioMerieux, France) was used to separate the several species of Candida.
- Detection of Proteus mirabilis IgG and E. coli antibodies in the serum of the study subjects using ELISA.

Preparation of the antigen

In BHI broth, Proteus mirabilis colonies that had been kept on brain heart infusion (BHI) agar slants were sub cultured. The cultures were inoculated onto freshly made BHI agar plates containing 1:800 phenol and allowed to grow for 24 hours. After this time, the growth on the plates was gently scraped off with a sterile loop and suspended in 3 ml of sterile normal saline (0.9% w/v) saline. The organism was then thermally destroyed by keeping the culture suspension in a heater set at 60 °C for 30 minutes. After that, the culture suspension was centrifuged for 15 minutes at 3000 RPM. The pellet was washed three times with 400 l of PBS-T after the supernatant was discarded. The pellet was gently added carbonate-bicarbonate buffer following the third wash, and the turbidity was adjusted to 4McFarland turbidity standard tubes.

Coating the ELISA plates with the tested microbial antigens

Each well of the ELISA plate was filled with 100 l of the prepared antigen solution. Three hours were spent incubating the plate at 37°C with aluminum foil on top. The sensitized plate was then overnighted stored at 4^0 C. Each well was aspirated, then washed three times with 400 l of PBS-T as the wash buffer. The plate was blocked by adding 150 l of 1% bovine serum albumin solution and letting it sit at 37 °C for two hours. The plate was washed three more times.

ELISA steps

Following a 1:10 PBS dilution, duplicate serum samples were added to the matching wells, which were then incubated at 37°C for 90 minutes. With PBS-T solution, the wells were rinsed three times. Each well received 100 µl of the Horse Radish Peroxidase conjugated with anti-human IgG. The wells were three times rinsed after being incubated at 37oC for 90 minutes. 100 µl of the chromogenic substrate were added. The plate was incubated at 37°C and out of the light for 20 minutes. To each well, 50 l of the stop solution was added. Using an ELISA reader (Stat fax 303 plus) set to 492 nm, the optical density (OD) of each well was ascertained in less than 30 minutes. Each duplicate's mean OD was computed.

Statistical analysis

The study was conducted with SPSS version 20. (Statistical Package for Social Science). The results were represented by the mean and standard deviation. The student t test was used to evaluate normally distributed quantitative data. The number and percent distributions were derived using qualitative data. In addition, Pearson's correlation coefficient (r) was computed to determine the relationship between two variables.

Results

The mean age of the patients was 53.17± 10.64 years. There was a total of 75 (75%) females and 25 (25%) were males. About 70 (70%) patients had sedentary lifestyle while 30 (30%) had active lifestyle. The mean duration of RA diagnosis was 18. 46 ± 6.73 years and the mean duration of morning stiffness was 59.70 ± 18.59 minutes. The majority of RA patients were active, and a mean DAS28 of (4.23 ±1.22). 40 (40%), 30 (30%), 25 (25%) and 5 (5%) of the patients had moderate disease activity, low disease activity, clinical remission and high disease activity, respectively. The majority of patients (70%) were receiving methotrexate and/or leflunomide with hydroxychloroquine, which were administered to almost all patients as conventional DMARDs. In addition, (30%) of patients were receiving either Golimumab , Adalimumab or Etanercept as biological DMARDs. (Table 1) Forty out of 100 investigated case group (40%) have asymptomatic bacteriuria (ABU) in comparison to 5 out of 100 investigated control group (5%). There is highly statistically significant difference between both studied groups regarding the frequency of ABU (P< 0.001). (Table 2) . In all urine samples of RA patients, P. mirabilis was detected in 17 (42.5%) , E. coli was detected in 10 (25%), Acinetobacter Baumanii in 1 (2.5%)cases, Klebsiella Pneumonie in 5 (12.5%) cases, Candida albicans in 2 (5%), Enterococcus faecalis in 3 (7.5%) cases while pseudomonas aeruginosa in 2(5%) cases. while in the control group (60 %) were E. coli and (40%) were Enterococcus faecalis. (Table 3) . Moreover, Our study demonstrated that there is highly statistically significant difference between both studied groups regarding Proteus mirabilis IgG antibodies levels (P< 0.001). However, there is no statistically significant difference between both studied groups regarding E. coli IgG antibodies levels, although the level of E. coli IgG antibodies among the case group (0.54 ± 0.15) is higher than this of the control group (0.51 ± 0.07) (P 0.571). (Table 4). As regard Proteus mirabilis IgG antibodies levels our study demonstrated that there is a statistically significant difference among RA patients. The highest level of Proteus mirabilis IgG antibody was detected in RA patients with Proteus mirabilis ABU (P< 0.036) (Table 5).

A statistically significant positive correlation was demonstrated between levels of P. mirabilis IgG antibodies and the levels of ESR, CRP, duration of morning stiffness, DAS28 , m HAQ , number of swollen &tender joints , conventional DMARDs as well as combined DMARDs & Biologics . (Table 6) Additionally, UTI represented 35.24 % in a patient using combined drugs, which is nearly the same as patient using DMARDs only (34.98%) with distribution of microorganism as shown in (Table7).

Discussion

RA is one of the chronic inflammatory illnesses whose causes are uncertain. Among the related risk factors [20] are the tyrosine phosphatase gene, HLA-DR gene, cytokine coding gene, and peptidyl arginine deiminase gene. It has been postulated that a range of environmental variables, including as cigarette smoking, atmospheric pollutants, and occupational irritants, can function as triggers for the onset of RA in predisposed individuals, resulting in synovial hyperplasia and bone destruction [12]. Early rheumatoid arthritis is characterised by modifications in the innate and adaptive immune systems, which result in the

production of auto-antibodies chasing a variety of molecules and changed self-epitopes [21]. Urinary tract infections, one of the most common types of infections in the local population, play a crucial role in the pathogenesis of rheumatoid arthritis (RA) by initiating tissue damage that exposes previously hidden self-antigens or leads to the creation of super antigens. Additionally, antigenic protein similarities between invading pathogens and host tissues may trigger an immune response that targets host tissues [11].

Consequently, the purpose of our cross-sectional study was to determine the frequency with which RA patients developed asymptomatic bacteriuria and UTI. The participants were divided into two groups: the case group, composed of 100 individuals with RA (75 females and 25 males), had a mean age of (53.17 10.64) years, whereas the control group, composed of 100 individuals who appeared to be in good health (70 females and 30 males), had a mean age of (52.21 10.34) years. The two groups were nearly identical with regard to gender and age.

Our findings demonstrated that there was a very statistically significant difference in ABU frequency between the two study groups. It was found in 40% of the urine samples from RA patients and only in 5% of the urine samples from healthy controls. P. mirabilis was the most prevalent organism in our research (42.5%), however it was not isolated from the control group. Following P. mirabilis, E. coli was the second most often isolated organism. It was isolated from the urine of RA patients and control participants, respectively, in amounts of 25% and 60%. These results were consistent with those of Senior et al. [5], who observed a slightly higher percentage of P. mirabilis isolation from the urine of RA patients (33 percent) compared to 48 healthy persons of the same gender (four percent) Georgiadou et al. discovered no significant differences in ABU frequency between RA patients and healthy controls [22].

We investigated the connection between P. mirabilis IgG antibodies and RA using ELISA. A highly significant difference was seen between the RA patient and control groups (1.48 0.41 versus 0.41 0.08) Raj Kumar et al. showed that the mean antibody titer against P. mirabilis in RA was 1.74 0.6, which was substantially higher than the 0.13 0.3 in the control group [23].Christopoulos *et al.*, on the other hand, utilized three artificial amino acid peptides. Each of them included an amino acid sequence that was similar to the P. mirabilis enzyme [11]. They discovered that RA patients had much greater levels of antibodies against these synthetic peptides than healthy controls. These synthetic amino acid peptides are utilised to identify the precise epitopes of cross-reactivity between P. mirabilis and human tissue antigens. Based on cross-reactivity or molecular mimicry between Proteus hemolysin and RA-associated HLA-DRB1 alleles as well as between Proteus urease and type XI collagen, extensive data collected over the past four decades suggest that subclinical urinary tract infection by P.mirabilis contributes to the etiopathogenesis of RA [24]. Many residents of fourteen nations, including United Kingdom, United states of America, England & Netherlands, have found patients with RA to have elevated levels of antibodies against P. mirabilis [2]. In addition, rheumatoid arthritis patients had significantly higher antibodies to P. mirabilis but not to more than 20 other bacteria, such as E. coli [25]. Similar to how Streptococcus causes rheumatic fever and valvular complications in cardiac muscles [26, 27], this immune system's response is the

release of additional self-tissue antigens, followed by the secretion of additional autoantibodies, proliferation of pathological progression, and development of classical rheumatoid arthritis. These antibodies will attach to the joint tissue and will be cytopathic to the joint tissues, which transport proteus cross-reactive antigens. Numerous investigations have confirmed the proteus anti-bodies' specificity in RA patients. In contrast to the pathogens present in the urine sample, Deighton *et al.*, found that RA patients had considerably higher levels of antibodies against P. mirabilis [28]. Due to the molecular resemblance between self-antigens and proteus, patients with infections caused by proteus species create antibodies not only against this bacterium, but also against the molecules of self-tissue that carry the cross-reactive antigens [29]. These antibodies would bind to the joint tissue that transports the proteus cross-reactive antigens and be cytopathic. In addition, this protective reaction may stimulate the release of new self-tissue antigens, resulting in the production of additional autoantibodies, the expansion of the pathogenic process, and the development of the typical form of RA.

In the present study, E. coli was the second most frequent isolated organism from RA patients (25%), so it was indicated to evaluate its association with RA (if any) in comparison to Proteus mirabilis. We found no significant differences between both study groups regarding E. coli IgG antibodies. In the current study, the highest levels of P. mirabilis IgG antibodies were detected in 17 RA patients with P. mirabilis ABU. The mean level of these antibodies was (1.61 ± 0.16) versus (1.21 ± 0.4) in other 83 RA patients. Our results showed a significant positive correlation between P. mirabilis IgG antibodies levels and the levels of the ESR and CRP in RA patients. It is consistent with the results published by Rashid and Ebringer [25]. The increase in ESR and CRP levels is typically a side effect of the immunological interaction between high titer P. mirabilis antibodies and the HLA epitopes in synovial tissues, which activate complement and other inflammatory cascades. The majority of our RA patients (70%) were receiving conventional DMARDs, in addition to (30%) receiving biologics . A statistically significant positive correlation was demonstrated between levels of P. mirabilis IgG antibodies and duration of morning stiffness, DAS28 , m HAQ , number of swollen & tender joints , as well as conventional DMARDs.

Chandrashekar *et al.,* [30] investigated whether medical therapy may increase the concentration of anti-Proteus antibodies in patients with rheumatoid arthritis and found results that are similar to these ones. 32 RA patients' blood samples were taken. All of the patients were given the go-ahead to use methotrexate, hydroxychloroquine, and an adequate dosage of non-steroidal anti-inflammatory medication. 11 cases had reached clinical remission after a year, but the remaining 21 patients were still experiencing significant disease activity. After a year of consistent therapy, anti-proteus anti-bodies titers were noticeably high in instances with RA. Contrary to our findings, this rise did not differ significantly between patients with clinical remission and those with high disease activity.

However, numerous studies found that, when compared to conventional DMARDs, patients receiving anti-TNF medication had a lower prevalence of serious infections, but a higher rate of severe skin and soft tissue infections [31]. An analysis of 18 randomized clinical studies involving a patient receiving anti-

TNF therapy revealed that at approved doses, there is no increased risk of serious infection. According to Attar A *et al.*, who demonstrated a higher rate of infection being connected with DMARDs [32], in our analysis DMARDs were associated with the greatest rate of urinary tract infections. Germano *et al.,* however, demonstrated that utilizing DMARDs alone was linked to a lower infection rate than using biologics [33]. The latter could have been caused by two factors. First off, we did not ignore the impact of steroids in our analysis, and secondly, more patients use DMARDs than biologics. Studies that compared patients with active Rheumatoid arthritis to those with active osteoarthritis or other Rheumatoid diseases in many situations found that those with active Rheumatoid arthritis have a higher risk of infections [34]. TNF plays a crucial part in regulating the likelihood of infection in the human body. Notably, TNF enables the macrophage to release in a maintenance manner and to develop an organism-defense mechanism [35]. Interleukin 1 (IL 1) and tumor necrosis factor (TNF) are crucial for the treatment of rheumatoid arthritis (RA). They work by counteracting the effects of cytokines that promote inflammation. TNF inhibitors, in particular, have a counterproductive effect on infection management and may even increase the likelihood of infection development in animal models [34]. These cytokine inhibitors, such as infliximab, etanercept, adalimumab, and anakinra, are used in individuals with active illness to lessen joint deterioration. These medications are now used extensively in the treatment of RA, particularly in individuals who did not react to disease-modifying antirheumatic medications (DMARDs). Biologic therapy patients are more likely to have previously contracted an infection than those on other types of medication. Aldauig B. A *et al* .,[36] in their study suggested the presence of particular concern for upper respiratory tract infections besides 100% increase in URTI among patients using biologics (TNF inhibitors). Hence , urinary tract infections were increased by 33.33%. Data were gathered from 173 RA patients, of them 15 patients were using Biologics agents. Similar results were listed by Listing J and Attar S .M [32, 37] in their study that estimated the incidence rate of serious and non-serious infections in patients with rheumatoid arthritis (RA) who were using biologics as a treatment. Furthermore, Furst DE. [38]revealed that Patients with RA are more likely to contract infections, such as tuberculosis, than people in general. Tumor necrosis factor (TNF) inhibitors are more likely to cause infections than traditional disease-modifying antirheumatic medications (DMARDs), particularly early in the course of treatment, according to long-term clinical trials and post-marketing investigations. The urinary tract, skin, and soft tissues are the most often infected areas, along with the respiratory tract (including pneumonia). In light of our RA Patients taking either DMARDs or biologics with or without the usage of steroids and those taking both DMARDs and biologics were studied to determine whether the combination of the two medicines increased the risk of infections. However, it was discovered that the overall UTI rate in patients taking combination medications (35.24%) was not statistically greater than the rate in individuals taking DMARDs alone (34.98%). However, this lower prevalence can be contributed to the difference in a number of each sample. So, for better assessment of infection risk in each type of drugs and the most common type of infection they encounter, a large multicenter cohort study would be an advantageous method to identify these infections. It can also help in assessing their outcomes and determining how this could affect the patient's adherence to the treatment.

Conclusion

Patients with rheumatoid arthritis on conventional DMARDs or conventional DMARDs in combination with biological DMARDs are more likely to develop silent bacteriuria and urinary tract infections (UTI) with a high incidence of P. mirabilis and E. coli infections. Therefore, frequent screening of RA patients is required to enhance their clinical results and adherence to recommended drugs.

Declaration of interest

It is stated by the authors that they have no competing interests. The authors alone are responsible for the writing and content of the paper.

Funding information: None reported

Availability of data and material: The raw data supporting the conclusions of this article will be made available by the authors on demand without undue reservation.

Acknowledgements: not applicable**.**

Abbreviations

RA: Rheumatoid arthritis, UTI: Urinary tract infection, DMARDs: Disease Modifying Antirheumatic drugs, ESR: Erythrocyte sedimentation rate, CRP: C reactive protein, DAS28: Disease activity score in 28 joints, m HAQ: modified health assessment questionnaire

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Table 1: Basic Demographic data of RA patients (n=100)

Variables	(mean ± SD)
Age, (years)	53.17± 10.64
Sex M/F (%)	25 / 75
Duration of rheumatoid arthritis , (years)	18. 46 ± 6.73
Duration of morning stiffness, (min.)	59.70 ± 18.59
Number of swollen joints	4.51 ± 2.01
Number of tender joints	5.04 ± 1.52
DAS 28	4.23 ±1.22
m HAQ	1.15 ± 0.59
ESR 1st h (mm/h)	55.78± 21.55
CRP (mg/dl)	32.54± 6.98
UTI: Urinary tract infection, DAS28: Disease activity score in 28 joints, m HAQ: modified health assessment questionnaire ,ESR: Erythrocyte sedimentation rate, CRP:C-reactive protein	

Table 2: Frequency of asymptomatic bacteriuria among studied groups

Variables	RA patients		Control subjects		P-value
	N0	%	N0	%	
Significant Asymptomatic bacteriuria	40	40%	5	5	<0.001*
Non-Significant Asymptomatic bacteriuria	60	60%	95	95	

Table 3: Asymptomatic bacteriuria causative organisms isolated from urine samples of RA patients and controls

Isolated organism	RA patients(N=40)		Control(N=5)	
	No	%	No	%
Escherichia coli	10	25	3	60
Proteus mirabilis	17	42.5	0	0
Klebsiella pneumonae	5	12.5	0	0
Candida albicans	2	5	0	0
Enterococcus faecalis	3	7.5	2	40
Pseudomonas aeruginosa	2	5	0	0

Acinetobacter Baumanii	1	2.5	0	0

Table 4: E coli & P. mirabilis IgG antibodies among studied RA patients

Variables	RA patients	Control subjects	T-test	P-value
P. mirabilis IgG: (Mean ± SD)	1.48 ± 0.41	0.41 ± 0.08	10.31	<0.001*
E coli IgG: (Mean ± SD)	0.54 ± 0.15	0.51 ± 0.07	0.120	0.571

Table 5: Comparison between P. mirabilis ABU and levels of P. mirabilis IgG antibodies in RA patients

Variables	P. mirabilis IgG antibodies (Mean ± SD)	T-test	P-value
Patients with P mirabilis ABU (N=17)	1.61 ± 0.16	1.857	< 0.036*
Patients without P mirabilis ABU (N=83)	1.21 ± 0.4		

Table 6: Correlation between P. mirabilis antibodies level and the acute phase reactants, different clinical parameters as well as DMARDs therapy in studied RA patients

Variables	P- mirabilis IgG antibodies	
	r	P value
Age, (years)	0.435	0.83
Duration of rheumatoid arthritis, (years)	0.192	0.362
Duration of morning stiffness, (min.)	0.345	0.006*
Number of swollen joints	0.321	0.025*
Number of tender joints	0.513	<0.001*
DAS 28	0.346	<0.001*
m HAQ	0.431	0.001*
ESR 1st h (mm/h)	0.419	<0.001*
CRP (mg/dl)	0.362	0.004*
Conventional DMARDs (n=10)	0.341	0.01*
Biological DMARDs(n=2)	0.442	0.08
Combined Conventional &Biological DMARDs (n=5)	0.621	0.05*

Table 7: Distribution of microorganisms isolated from Rheumatoid arthritis patients with Urinary tract infections

Isolated organism	RA patients (N=100)	
	Negative growth (N=65) Positive growth (N=35)	
	No	%
Escherichia coli	12	34.2
Proteus mirabilis	10	28.5
Klebsiella pneumonae	7	20
Candida albicans	4	11.4
Enterococcus faecalis	2	5.7