

# THE CLINICAL SIGNIFICANCE OF URINARY TRACT INFECTION AND ASYPTOMATIC BACTERIURIA IN TYPE 2 DIABETES MELLITUS PATIENTS IN THE GENERAL PRACTICES OF VARNA REGION - BULGARIA

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## ABSTRACT

**Background:** The urinary system of diabetics is one of their most frequently affected body systems. Periodic urine analysis reveals that asymptomatic bacteriuria is very often detected in this population.

**Objectives:** The aim of the study is to estimate the clinical significance of upper urinary tract infection (UUTI) and asymptomatic bacteriuria (ABU) in diabetics in a general practice setting, their clinical characteristics, incidence, course, evolution and complications.

**Methods:** We tested 560 patients with type 2 diabetes mellitus (DM) from 12 general practices of Varna region, Bulgaria in a prospective study. We traced ABU in the group for 2 years. There were 310 female patients (55.4%) mean age  $52.5 \pm 3.2$  years and duration of DM was  $8.5 \pm 2.8$  years.

**Results:** The results showed that in 11.14% ABU was significant. Only 4.82% of diabetics developed upper urinary tract infection and the complications from it were very rare: 0.89% pyonephrosis and 0.89% sepsis.

**Conclusions:** Our conclusion was that upper urinary tract infection in diabetics was not as severe as reported in the literature. Pyelonephritis had a benign course and only 16.6% of our patients developed chronic renal failure a few years later but the reason for its development was not diabetic nephropathy. All these facts show that ABU disappears spontaneously in most diabetics.

**Relevance to general practice:** We discuss the question: is it necessary for every case of ABU in diabetics in general practice to be treated and isn't it time to reevaluate the postulated antibiotic treatment for diabetics with ABU?

**Keywords:** Diabetes Mellitus (DM), Upper urinary tract infection (UUTI), Asymptomatic bacteriuria (ABU), general practice.

The urinary system of diabetic patients is one of their most frequently affected body systems. Periodic testing for asymptomatic bacteriuria in this group reveals that it is a common symptom, as in other immunocompromised patients (1,2,3). Few data, however, are available about the potential complications arising from asymptomatic bacteriuria (e.g. development of symptomatic infection and renal damage) in diabetics (4).

This review analyses several aspects of asymptomatic bacteriuria (ABU) and upper urinary tract infection (UUTI) in diabetic patients in 12 practices of Varna region, Bulgaria: incidence, frequency, sex

distribution, microbiological characteristics and upper urinary tract involvement.

### AIM OF THE STUDY

We screened for ABU in diabetic patients because of the higher risk for development of urinary and kidney infection in such patients (5,6,7).

The aim of our prospective 2 year study was to estimate the incidence of ABU and UUTI in type 2 Diabetes Mellitus (DM) patients and to determine clinical and microbiological characteristics, frequency incidence and sex distribution, course and evolution and also complications (upper urinary tract involvement). We selected the patients in order

TABLE 1: PRELIMINARY REQUIREMENT OF THE STUDY:

- |  |
|--|
| 1. Testing for ABU before treatment  |
| 2. Preserved intelligence/absence of serious senile metal changes                |
| 3. Age under 65 years  |
| 4. Lack of congenital or acquired kidney disease, urolithiasis, adenoma prostate |

to fulfill the certain preliminary requirements of the study (table 1).

## METHODS

All the patients in the study gave their informed consent for participation and further examination. The University Hospital Ethical Committee approved the study, where some of the additional examinations were made.

Out of the population of 12 general practices in Varna region, we screened for ABU patients without any urinary tract complaints at the time and no data for congenital or acquired kidney or prostatic diseases or urolithiasis in the past. We included in the study also healthy subjects, matched with the diabetics for age and sex, because in some literature reviews, the incidence of ABU in adult healthy patients, especially in women is shown to be higher in comparison with ABU in younger healthy people.

At the beginning of the study all patients were tested by two methods: self-screening test for ABU (a quick self-test, which is made when the patient gives a mid-stream urine sample in flasks with special culture) and parallel Microbiological Cultural methods - 3 times (a method of a mid-stream urine sample, with  $> 10^5$  organism/ml in pure culture taken as cutoff for significant bacteriuria). We tested all pts for ABU every 3 months during the 2-year study.

In patients with significant bacteriuria (3 positive, mid-stream urine samples, with  $> 10^5$  organism/ml in pure culture) we used additional examinations as:

- U/S of the urinary system
- Volhard test for kidneys' ability to concentrate urine
- J<sup>131</sup>- Hippuran Nephrography
- Urography

The patients in the study we divided into 2 groups: DM type 2 subjects (including patients with type 2 DM with insulin treatment) and healthy subjects as controls. The healthy subjects numbered 250, mean age  $54.2 \pm 3.2$  years (male 110/female 140). The diabetics numbered 560 individuals from 12 general practices of Varna region, of which 310 female (55.4%) and 250 male, mean age of  $52.5 \pm 3.2$  years and duration of disease  $8.5 \pm 2.8$  years. According to their age they were divided into 3 subgroups: 40 - 49 years n = 377 pts, 50 - 59 years n = 105 pts and 60 - 65 years n = 78 pts.

## RESULTS

The diagnosis of UUTI was established according to the clinical criteria: lumbar or abdominal pains, fever, nausea, vomiting, dysuria, etc.; laboratory criteria: multiple positive tests for significant bacteriuria and leucocyturia and other investigations: US urinary system

images showing UUTI, Volhard test with lower concentration ability of the kidneys and J<sup>131</sup>- Hippuran Nephrography and Urography with features of renal involvement during the 2 period study.

We established the distribution of ABU and UUTI in the group of diabetics as follows:

**1. Asymptomatic bacteriuria** – in 80 diabetics (14.28%) of all tested 560 diabetics and in 63 of them, a **significant bacteriuria** was persistent (78.75% of diabetics with ABU).

**2. Upper urinary tract infection** – developed in 27 diabetics (4.82% of all 560 diabetics)

**3. Pyonephrosis** after infected hydronephrosis – in 5 diabetics (0.89% of all 560 diabetics)

**4. Septicemia** due to urinary tract infection – in 5 diabetics (0.89% of all 560 diabetics)

Table 2. INCIDENCE OF ABU IN THE TWO GROUPS:

PATIENTS	SIGNIFICANT	NONSIGNIFICANT (NS)	NEGATIVE (STERILE)
DIABETICS N = 560	63 pts (11,25%)	17 pts (3,03%)	480 pts (85,72%)
HEALTHY N = 250	4 pts (1,6%)	-	246 pts

Table 3. SEX DISTRIBUTION OF ABU IN HEALTHY SUBJECTS:

SEX	STERILE AND NS	SIGNIFICANT	UPPER UTI
MALE N = 110	108 pts (98,2%)	1 pt (0,9%)	1 pt (0,9%)
FEMALE N = 140	136 pts (97,15%)	3 pts (2,14%)	1 pt (0,71%)

Table 4. SEX DISTRIBUTION OF ABU IN DIABETICS:

SEX	STERILE AND NS	SIGNIFICANT	UPPER UTI
MALE N = 250	234 pts (93,6%)	16 pts (6,4%)	7 pts (2,8%)
FEMALE N = 310	263 pts (84,84)	47 pts (15,16%)	20 pts (6,45%)

The microbiological characteristics of cases with significant bacteria in DM type 2 patients were: E.coli - 50,0% (n = 40 pts), Enterobacter - 12,5% (n = 10 pts), Klebsiella oxytoca-12,5% (n = 10 pts), Enterococcus - 12,5% (n = 10 pts) and Proteus mirabilis - 12,5% (n = 10 pts). The distribution of microorganism is given in Figure1.

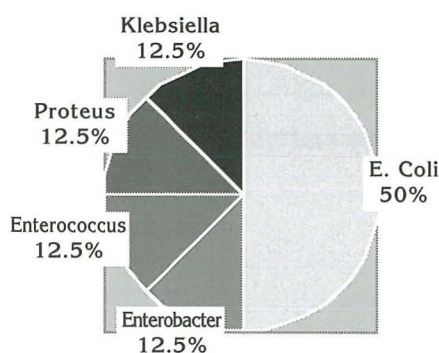


Fig.1. Distribution of the most common microorganisms among diabetics with significant bacteriuria in the study.

We compared the incidence of ABU among the two groups in our study (diabetics and healthy) and our results are tabulated (see Tables 2,3,4).

We have thus established a sevenfold higher frequency of significant ABU in diabetics in comparison with a healthy population. Sex distribution of ABU in diabetics and healthy subjects demonstrated female predominance.

Upper urinary tract involvement was 8.5 times higher in diabetics - (27 pts) 4.98% than in healthy individuals, (2 pts) 0.8%. The pathogenic microorganisms were similar in both groups.

## DISCUSSION

Only 27 (4.82%) diabetic patients out of the study group in the 12 general practices showed clinical evidence of upper UTI during the 2 year period. Although ABU was often present (14.28% -

80 pts), only 63 patients (11.25% of all diabetics in the study) had a significant ABU.

Complications were very rare among our diabetic patients: only 5 patients were diagnosed with infected hydronephrosis (pyonephrosis) which was only 0.89% of all diabetics and 5 patients complicated with septicemia due to UUTI (0.89% of all diabetics).

In our former investigations (1,8) we have established that UTI in diabetics presenting in general practice was not as severe as previously reported in the literature (2,5,9). Pyelonephritis exhibited a benign course, and only 16.6% of our patients developed chronic renal failure a few years later. All these facts show that ABU disappears spontaneously in most diabetic patients and does not necessarily progress to UUTI. We question the need for antibiotic treatment of asymptomatic bacteriuria in diabetics in general practice, in contrast to most recommendations (2, 7, 9).

## CONCLUSIONS

1. Periodic testing in type 2 DM patients in general practices of the Varna region, Bulgaria discovered ABU in 14.28%.
2. The incidence of significant ABU in diabetics is 7 times higher than in healthy subjects.
3. Significant bacteriuria in diabetics and healthy subjects shows female predominance.
4. The most frequent pathogenic agents in both groups are similar (E.coli over 50%, followed by Klebsiella and Proteus mirabilis).
5. In 11.25% of diabetics ABU, although significant, disappears spontaneously.
6. Only 4.98% of diabetics develop upper UTI vs 0.8% of healthy subjects.
7. Complications of UUTI are very rare: 0.89% pyonephrosis and 0.89% septicemia originating from urinary tract infection.

8. These facts led to discussion and reevaluation of the postulated antibiotic treatment of every ABU in diabetics.

• The data from this research project were presented at the meeting of the European General Practice Research Workshop, which was held in Ankara, Turkey, 8<sup>th</sup>-11<sup>th</sup> May 2003.

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