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**DIAGNOSTIC APPROACHES AND CLINICAL MANAGEMENT IN
HYDRONEPHROSIS DURING PREGNANCY**

ABSTRACT

on

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The defense materials are available at the Scientific Department of MU-Varna and are published on the MU-Varna website (www.mu-varna.bg).

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ABBREVIATIONS USED

ACB - alkaline-acid balance
ACOG - American College of Obstetricians and Gynecologists
AH - arterial hypertension
AKI - acute kidney injury
ALAT - Alanine Aminotransferase
ARDS - acute respiratory distress syndrome
ARF - acute renal failure
ART - assisted reproductive technologies
ASA - acute surgical abdomen
AST - Aspartate aminotransferase
CKF - chronic kidney failure
CNS - central nervous system
CRP - C-reactive protein
CT/ST - computed tomography
CVP - central venous pressure
DJ - Double J -stent
E.coli - Escherichia coli
EAU - European Association of Urology
EGDT - Early Goal Directed Therapy
ERPF - effective renal plasma flow
FDA - Food and Drug Administration
FFP - fresh frozen plasma
g.w. - gestational week
G6FDH - glucose-6-phosphate dehydrogenase
GBS - Group B Streptococcus
GF - glomerular filtration
GIT - gastro-intestinal tract
GPF - glomerular plasma filtration

H2RAs - H2 receptor antagonists

HELLP - Hemolysis, Elevated Liver enzymes and Low Platelets

HGB - Hemoglobin

HN - hydronephrosis

IUGR - Intrauterine Growth Restriction

Leuc - Leukocyte

MAP - Mean Arterial Pressure

mGy - milligray

mmHg - millimeter of mercury

MRI - nuclear magnetic resonance

NSAIDs - nonsteroidal anti-inflammatory drugs

NSCAT - native computed axial tomography

NSCAT - native spiral computed axial tomography

pCO₂ - Partial pressure of Carbon dioxide

PCS - pyelocalyx system

PE - preeclampsia

PNS - percutaneous nephrostomy

PPIs - Proton Pump Inhibitors

PTU - Polskie Towarzystwo Ultrasonograficzne

RAAS - reninangiotensin aldosterone system

RPF - renal plasma filtration

RUG - retrograde ureterography

U/S - ultrasound examination

URS - ureterorenoscopy

UTS - urinary tract system

USA - United States of America

UTI - urinary tract infection

UUT - upper urinary tract

WEB - water-electrolyte balance

INTRODUCTION

Pregnancy is an anatomically and physiologically changing state involving a series of adaptive processes in the maternal organism in response to the developing fetus. Many of these changes begin soon after fertilization and continue throughout pregnancy. Knowing them is the main goal of the obstetrician-gynecologist, so that they can be differentiated from pathological conditions and promptly diagnosed and treated.

Dilatation of the upper urinary tract is a common condition accompanying pregnancy. It has long been known that up to 90% of pregnant women experience such a change. In the majority of cases, the condition is transient and does not affect both the health of the mother and the development of the fetus. After childbirth, the processes undergo a reverse development without lasting consequences. This adaptive phenomenon is referred to as the so-called "physiological" hydronephrosis. It is possible that at a different stage of pregnancy, this course is changed and acquires pathological characteristics. They are a serious threat to both the woman and the developing individual.

With the increase in the incidence of chronic kidney disease and the tendency for women to plan and become pregnant at an older age, the control of kidney disease during pregnancy is an increasingly common reason for visits to nephrologists, urologists, and obstetricians. Women with renal disorders face several challenges in pregnancy due to the increased physiologic demands on the kidney and the risk of disease progression, the potential teratogenicity of drugs, and the increased risk of complications such as preeclampsia and preterm birth. The challenges posed by the underlying disease process during pregnancy require an interdisciplinary team to ensure good outcomes for mother and fetus. During this period may be the first time a woman is diagnosed with kidney disease or hypertension as a result of kidney damage.

Pregnant women suffering from UUT obstruction in a large percentage of cases (gradual, protracted onset and long-term course) do not know about the problem, and often pain symptoms are associated with contractile activity of the uterus. This leads to untimely diagnosis and treatment, metabolic and electrolyte disorders, manifestation of renal failure or exacerbation of existing one, as well as irreversible damage to the renal parenchyma and function, sometimes leading to fatal consequences for the mother and/or the fetus.

When a physiological dilatation turns into pathological HN requiring medical intervention is a debatable question with an ambiguous answer. Until now, there is no definitive standpoint /guideline that indicates the management of a pregnant woman with HN.. The main debate is when and who should conduct active treatment? The question of the diagnostic approach and the method of treatment is also debatable. The improvement and accessibility of ultrasound examination and the mass penetration of MRI are a prerequisite for analysis and modification of diagnostic algorithms.

The above gives rise to the need to deepen research and create a diagnostic-therapeutic algorithm adapted to clinical practice.

GOAL AND OBJECTIVES

1. Purpose

To compare diagnostic approaches and to study clinical management in pregnant women with hydronephrosis in the first and second half of pregnancy.

To achieve the main goal, we set ourselves the following tasks:

1 . Tasks

Tasks:

1. To study the Bulgarian and foreign literature on modern trends in the diagnostic and treatment management of hydronephrosis during pregnancy.
2. To perform a prospective and retrospective analysis of a group of patients with symptomatic hydronephrosis, diagnosed and treated in the Department of Pathological Pregnancy at SBAGAL "Prof. Dr. D. Stamatov" city of Varna and Urology Clinic at the MHAT "St. Anna" in the city of Varna for the period 2019-2021 with the aim of creating current complex diagnostic and therapeutic algorithm.
3. To clarify the effectiveness of the diagnostic methods used in the practice of obstetricians and gynecologists and urologists during the first half of pregnancy.

4. To evaluate the effectiveness of the diagnostic methods used in the practice of obstetricians and gynecologists and urologists during the second half of pregnancy.
5. To specify the indications, treatment methods and complications during the first half of pregnancy
6. To systematize the indications, treatment methods and complications in the second half of pregnancy
7. To compose and propose an algorithm for behavior in hydronephrosis during pregnancy.

MATERIAL AND METHODS

The dissertation was developed based on the results of a clinical study of 184 pregnant patients with evidence of symptomatic hydronephrosis. Patients with physiological hydronephrosis and pregnant minors were excluded. The criteria for inclusion in the study (including) were pregnant women with evidence of unilateral or bilateral hydronephrosis, complicated by an inflammatory process, manifestations of renal failure, renal colic, with pronounced pain syndrome and/or vegetative symptoms. The study was retrospective and prospective in nature. All patients were urgently hospitalized in the Department of Pathological Pregnancy at SBAGAL "Prof. Dr. D. Stamatov" city of Varna and Urological Clinic at the MHAT "St. Anna" city of Varna for the period 2019-2021. Medical history, clinical results, laboratory, imaging, microbiological and intraoperative data were used for diagnosis. Based on them and the patient's consent, treatment was carried out - conservatively and/or surgically.

The sources of information we used were: the available digital database, discharge summaries, histories of diseases, operational journals of SBAGAL "Prof. Dr. D. Stamatov" city of Varna and Urological Clinic at the MHAT "St. Anna" city of Varna for the period 2019-2021.

1. Demographic characteristics

Table 1. Distribution by age

	number	%
All	184	100%
Age ≤ 20 years 34	Ag	Age ≤ 20
Age >21 years and ≤30	Ag	Age >21
Age >31 years and ≤40	Ag	Age >31
Age ≥41 years 7 3.80%	Ag	Age ≥41

Table 1 shows the age distribution. There is a prevalence of pregnant women aged 21-30 years 42.94% (79 patients). Second in frequency are the age range 31-40 years 31.78% (64 pregnant). It is noteworthy that 3.80% (7 pregnant women) are over 41 years old.

Table 2. Distribution by side of affected kidney from hydronephrosis

	number	%
All	184	-
Right-sided HN	143	77.71%
Left-sided HN	27	14.67%
Bilateral HN 14 7.61%	14	7.61%

In confirmation of the anatomical premises, right-sided HN in pregnant women prevailed 77.71% (143 women), compared to left-sided 14.67% (27 women), and bilateral involvement was observed in 7.61% (14 patients) (Table 2.).

Table 3. Distribution by term of pregnancy

	number	%
All	184	100%
Pregnancy up to 20 g.w.	35	19.02%
Pregnancy over 20 g.W.	149	80.98 %

When studying the distribution according to the term of pregnancy indicator, in 80.98% (149 patients) of the studied patients with hydronephrosis were after 20 g.w., and 19.02% (35 patients) were before 20 g.w. (Table 3.)

In Fig. 1 we summarized the data of the examined group by age, side of involvement and term of pregnancy.

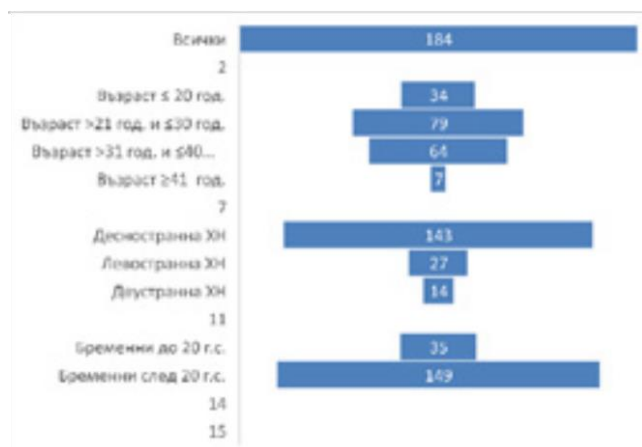


Fig. 1. Distribution of female patients by age, side of involvement and term of pregnancy

We used different methods to achieve the main goal, categorizing them as follows:

2. Diagnostic methods

2.1. Medical history

Pregnant women were diagnosed during their stay in the Department of Pathological Pregnancy or in emergency conditions in an emergency room with the following most common complaints:

- Pain - unilateral or bilateral in the lumbar region, with colic or constant character, with varying strength and intensity, with irradiation along the course of the corresponding ureter, suprapubically and towards the labia majora. Less often – to the contralateral lumbar region. Sometimes they are accompanied by disturbances in urination - dysuria, pollakiuria, macroscopic hematuria.
- Uterine contractions - in a large percentage of cases premature, regular, painful, but painless, with long-lasting intensity are also found.
- Vegetative symptoms - nausea with/without vomiting, sometimes long-standing and recurrent - most often observed in the first trimester of pregnancy, characteristic of hyperemesis gravidarum, but may be a manifestation of kidney failure and/or uroinfection;
- Fever - in part of the pregnant patients, the main complaint was an elevated body temperature above 37°C, episodes of chills (characteristic of obstructive pyelonephritis), headache,

dizziness, edema - preferentially in the lower limbs, loss of appetite, general weakness, asthenodynamia, characteristic of progressive kidney failure;

- accompanying diseases: anamnestic data on renal calculus, with previous episodes of renal crises, pyelonephritis, congenital anomalies of US, diabetes mellitus (incl. Gestational DM), AH.

2.2. Physical status

- Obstetrical palpation – a subjective marker for the duration of pregnancy, to establish uterine contractility and sensitivity and assess the risk of premature birth.

- Gynecological examination - a mandatory component of the obstetric-gynecological examination to determine the pelvic score and pathology accompanying pregnancy.

- Succusio renalis- a symptom of pain when tapped in the corresponding lumbar region, specific for kidney pathology.

- increased body temperature - pointed to the presence of an inflammatory process.

- Arterial pressure and pulse: Arterial hypertension is a frequent expression of preeclampsia, or in case of impaired kidney function; tachycardia - a suspected sign of an inflammatory process or a disorder in ACB.

2.3. Laboratory researches

In the clinical laboratory of SBAGAL "Prof. Dr. D. Stamatov" city of Varna and Urological Clinic at the MHAT "St. Anna" in the city of Varna for the period 2019-2021, complete blood count, biochemistry (blood sugar, serum urea, serum creatinine, AST, ALAT) CRP, standard urine - sediment, ionogram, coagulation status of all studied patients were examined as a matter of urgency during their hospitalization. We additionally examined ACB, total protein, and serum albumin in indicated cases. In pregnant women with evidence of hydronephrosis, we looked for laboratory data pointing us to complications.

2.4. Microbiological studies

Microbiological examination of urine: the materials are cultured on selective and differentiating nutrient media on arrival in the laboratory. After incubation for 24 hours, a quantitative assessment and identification of the microorganism is made, using manual and automated methods (VITEK 2 compact). In parallel with the identification process, antibiotic sensitivity testing of the etiological microorganism is carried out. Antibigrams are made using the manual

disk-diffusion method of Bauer-Kirby, Muller-Hinton agar or by determining the minimum inhibitory concentration of VITEK 2 compact. Interpretation of results for antibiotic sensitivity (sensitive, intermediate, resistant) is done using the latest EUCAST version.

2.5. Imaging methods

Imaging methods confirmed hydronephrosis, which accompanied the complaints. Diagnosing the cause of UTS obstruction is difficult in the pregnant woman.

2.5.1. Ultrasound diagnosis of UTS, abdominal ultrasound

Ultrasound examination is a main component of the obstetric and gynecological examination. Its widespread use is based on its easy availability, speed and ease of application and, last but not least, the safety of the method. The non-invasive nature of ultrasound and its informative value defines it as a basic examination in medical practice. Ultrasound examination is characterized by specificity and accuracy close to 100% in relation to the diagnosis of hydronephrosis.

We applied transabdominal ultrasound examination to all patients included in the study. The primary task was to objectify fetal vitality and embryonic/fetal biometry - supplementing history information to determine gestational age. A mandatory component included locating the placenta and its maturity, as well as determining the amount of amniotic fluid. The presence or absence of pathological changes affecting the developing fetus and/or uterus. Due to the high percentage of pain symptoms, accompanied by regular uterine contractions and the risk of premature birth, in some cases we used a transvaginal ultrasound examination. We measured the length of the cervix and visualization of "funneling", which are predictors of the probability of early termination of pregnancy. In the first half of pregnancy, especially in the first trimester, transvaginal ultrasound examination was more often applied, especially in obese patients, to assess pregnancy and diagnose pain symptoms.

In terms of differential diagnosis, ultrasound examination in pregnant women plays a major role. In addition to diagnosing pregnancy and its accompanying complications, it is also widely advocated for visualizing UTS. During a scan in both lumbar areas, the number and localization of the kidneys were assessed, their dimensions in transverse, longitudinal and oblique diameters, as well as parenchymal thickness were measured. Visualization and evaluation of the bladder was a mandatory component during the study. Data on hydronephrosis and its likely non-obstetric causes were actively sought. Through a transvaginal scan, we actively looked for

the cause of the hydronephrosis present, in some cases it was a concretion in the lower parts of the ureters.

Patients with high-grade and symptomatic hydronephrosis were subjected to control ultrasound examinations after the symptoms subsided - twice within one month after discharge from the hospital. They were applied with a view to prevention of recurrence and/or factors complicating pregnancy, as well as timely treatment.

We classified cases according to the Onen, SFU system (1993) modified in 2007. It states that depending on the severity of PCS dilatation, hydronephrosis is divided into 4 (four) degrees (Fig. 2).

First degree - independent expansion of only the renal pelvis or several calyces;

Second degree – the renal pelvis is expanded including all calyces;

Third degree – expansion of the renal pelvis, of the renal calyces, accompanied by a reduction to ½ of the parenchyma;

The fourth degree – expansion of the renal pelvis, of the renal calyces combined with a reduction of more than ½ of the parenchyma.

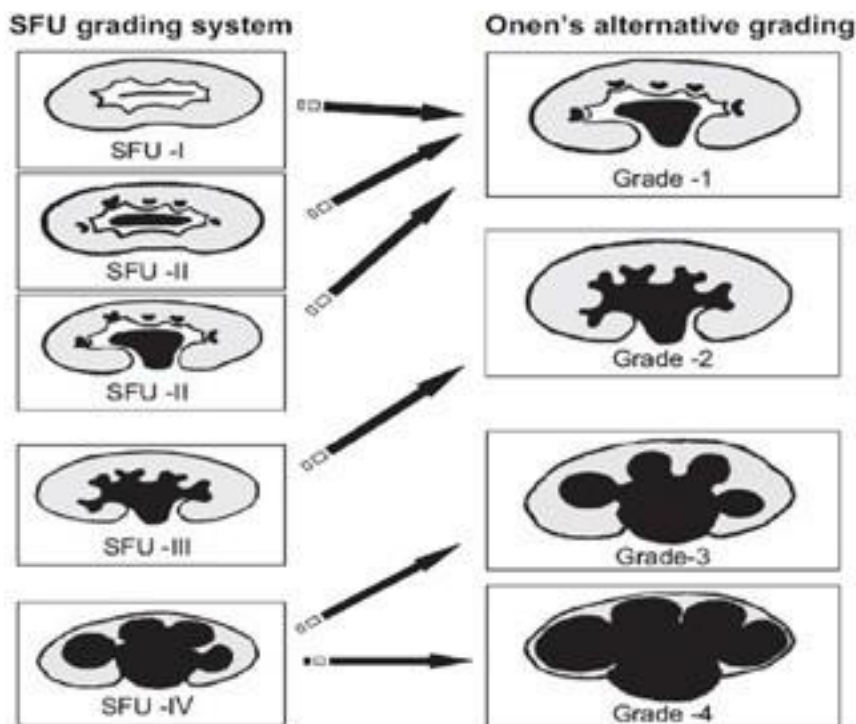


Fig. 2. Comparison of the two main ultrasonic classifiers systems. SFU and 2. Onen (Jose de Bessa Jr et al. 2018)



Fig. 3. Kidney - normal ultrasound image



Fig. 4. Echographic image of a kidney with HN I degree



Fig. 5. Echographic image of a kidney with HN II degree



Fig. 6. Echographic image of a kidney with HN III degree

The treatment approach for hydronephrosis during pregnancy, regardless of the cause, is general.

Elucidation of the etiological factor during pregnancy is hampered by the limitations of imaging studies.

Given the above, in our study we did not perform additional imaging diagnostic tools to clarify the etiology. (x-ray, urography, CAT). Definitive urological treatment of obstructions unrelated to pregnancy is carried out after delivery.

2.5.2. Nuclear magnetic resonance imaging

In case of differential diagnostic difficulties and the need to clarify the obstructive cause, MRI is the method of choice. Its use is based on its safety during pregnancy.

In the present study, we used MRI as an exception. The choice of diagnostic method was based on the scarcity of ultrasound data and the need for information on topographic-anatomical areas determining the course of therapeutic behavior. Despite the reported data on the possibility of using low-dose CT, after a detailed discussion with the patients, a decision was made for MRI before CT, mainly because of its safety during pregnancy. The lack of ionizing radiation and the possibility of re-application, in order to monitor the state of the UTS was included into consideration when selecting an imaging method.

Another advantage of MRI compared to CT is the quality of the imaging of the organs in the small pelvis and the possibility of establishing a large number of pathological conditions of the

female reproductive system and the fetus, as well as a potential cause of hydronephrosis during pregnancy.

The diagnosis of hydronephrosis and ureteral dilatation is not difficult with MRI because of the long relaxation times of fluids (urine) and the low density of the T1-weighted image with obliteration of the border between cortex and medulla.

In the course of our study, we did not use intravenous contrast material. Nevertheless, native MRI has a high diagnostic value.

In patients with urinary tract infections, the ability to study the diffusion of water molecules (diffusion weighted imaging) is a unique advantage of MRI, contributing to the imaging differential diagnosis.

Its limited use in emergency diagnostics and high cost are the reasons for its rare application.

3. Therapeutic methods

The main therapeutic methods we used in the treatment of symptomatic HN are conservative and operative. Conservative treatment was carried out in the Pathological Pregnancy Department at SBAGAL

"Prof. Dr. D. Stamatov" city of Varna, and surgical urological treatment in the Urological Clinic at the MHAT "St. Anna" city of Varna.

The indications for urological treatment, after consultation with a urologist, which we followed were:

1. Not influencing the uroinfection 48h. after the start of antibiotic treatment.
2. Failure to influence or increase the pain syndrome.
3. Patients with III degree hydronephrosis
4. Patients with threatening or developing urosepsis.
5. Clinical and laboratory data for the development of OBU
6. A relative indication is a single functioning kidney, bilateral hydronephrosis and a high degree of hydronephrosis.

We successfully treated the remaining patients conservatively.

3.1. Conservative treatment

A main component of conservative therapy is analgesic and antispasmodic treatment.

In all patients we used Paracetamol 10 mg/ml 100 ml for intravenous administration, in a dosage 3-4 times a day. The dosage regimen was determined individually, depending on the pain relief and/or temperature reduction in febrile pregnant women. The main emphasis in the dosage was the maximum effect at the minimum dosage regimen, despite the lack of data on the teratogenicity of the drug and its classification in group "B" FDA.

In the case of a weak effect on the symptoms (absence of anamnestic data on alegria), in single doses we administered Analgin (Metamisole sodium) 500mg/ml 2ml amp. i.m.

An alternative medication that was considered was Lidol (Pethidine hydrochloride) 50 mg/ml amp.2ml. Observing the basic rule: minimum dose, maximum effect during pregnancy, we carried out treatment with doses of 25-100 mg 3 to 4 times daily intramuscular applications, and in no case did we exceed the maximum single dose of 100 mg and the maximum daily dose of 600 mg. We observed a positive effect with Lidol 50 mg i.m.

Other drugs that we used to treat pain of renal origin were antispasmodics. In some cases we used Papaverine amp. 20ml/ml 2ml and Buscolysin amp. 20 mg/ml 1 ml. in one with 500 ml infusion solution and/or Drotaverin amp. 20 mg/ml 2ml, Buscolysin amp. 20 mg/ml 1 ml i.m.

Along with the analgesic and spasmolytic therapy, we applied tocolysis to copy the uterine activity. Cormagnesin amp 400 10 ml dissolved in Serum glucose or Physiological solution 500 ml infusion was mainly used. One ampoule of 10 ml solution for injection contains 4095 mg of magnesium sulfate heptahydrate, corresponding to 2000 mg of magnesium sulfate. In cases of high risk of prematurity, we used 2 to 3 ampoules in a slow intravenous drip.

Another tocolytic medication that we administered was Nifedipine. 20 mg tab. The dosage regimen aimed at effective relaxation of the myometrium was 20 mg p.o. in 8 hour intervals. In addition to tocolysis, nifedipine, by blocking calcium influx and suppressing ureteral peristalsis, also had an analgesic effect.

In the period 18-20 and cervical length less than 25 mm, the patients were indicated for administration of Progesterone 200 mg once daily, vaginally administered until 34 g.w., with the aim of preventing late spontaneous abortions and premature birth.

Rehydration: The second major component of our conservative treatment included intravenous rehydration. We combined it with oral hydration in patients without severe vegetative symptoms. In all cases, we applied Ringer's lactate, physiological serum, and glucose solutions according to the blood sugar levels of the patients. The amounts of infused solutions ranged from 1000 to 2000 ml per 24 hour interval. In parallel, we monitored basic vital signs, with the aim of correcting the infused fluids if necessary.

The third benchmark in the treatment of pain symptoms was antibiotic treatment.

In the case of a clinical-laboratory constellation correlating with an infectious process, we empirically started with a broad-spectrum antibiotic. After receiving a result for the type of causative agent and its antibiogram, correction followed if necessary.

Most often we used Ospamox 500 mg, in four doses in 24 hours. Second in frequency of application was Ceftriaxone 2 g fl., which we administered in infusion of 100 ml of physiological solution. Before the first application, a negative scarification sensitivity to the medication was necessarily reported. The usual dosage was 1 fl once a day, and in more severe cases it was also required twice every 12 hours. interval.

In cases of significant bacteriuria, without leukocytosis and an increase in CRP, we prescribed Fosfomycin 3 g sachets, in the evening before going to bed, twice in 48 hours, as an antibacterial course for the sanitation of POS. Due to its safe action profile, being eliminated through the OS and not crossing the placental barrier, fosfomycin is indicated during pregnancy. There is no evidence of a teratogenic effect in its application, which makes it suitable and preferred for urinary tract infections.

In cases with predominant vegetative symptoms, the use of antiemetic preparations was necessary. Degan 10mg 2ml amp (Metoclopramide hydrochloride) was administered by intramuscular/intravenous infusion twice daily. An alternative medication is Ondansetron (Zofran) 2 mg/ml, in a double dose regimen by intravenous infusion. We applied the latter to a group of patients not affected by Degan and after the first trimester of pregnancy, in view of the safety of the preparation.

Additionally, in our group of patients, it was applied vitamin therapy. Especially in cases with a prolonged course of symptoms, a mandatory component were vitamins of group B- B1, B6 and B12, as well as vit. C. For the prevention of POS, we included nutritional supplements containing American cranberry, which has a proven preventive effect. It is based on reduced

adhesion activity of bacteria in the urinary tract (especially *Escherichia coli*) and their faster elimination from the body.

For correction of hypokalemia, the inclusion of KCl 150mg/ml amr., intravenous perfusor infusion, in a dose strictly determined by laboratory parameters, was considered. In case of evidence of accompanying hypoproteinemia and hypoalbuminemia, it was immediately corrected by infusing PZP or human albumin 20% 100ml.

The common anemia during pregnancy required the administration of iron preparations. Because iron deficiency anemia is the leading etiology. Administration of iron-containing preparations was an invariable part of the treatment.

Patients with evidence of pre-eclampsia and high blood pressure were treated with antihypertensive therapy, mostly with Dopegit 250 mg tablet, three times a day, one tablet p.o.

3.2. Surgery

Surgical treatment of pregnant women was carried out in a urology clinic for the above indications and after consultation with a urologist. The endourological methods of retrograde ureteral stenting (RUS) and percutaneous nephrostomy (PNS) were used. The effect that was aimed and achieved with these methods is an initial desobstruction of the affected kidney and ensuring adequate drainage of the UTS until delivery.

3.2.1. Ureteral stenting (retrograde) RUS

Ureteral stents are an endourological device for desobstruction. They are ureteral catheters, which are most often placed retrogradely. They have memory bends of different shapes and sizes at both ends that hold the stent and prevent its migration in the proximal and distal direction. Ureteral endoprotheses are widely used for rapid and minimally invasive restoration of ureteral patency, regardless of the obstructive cause. In pregnant women, it was the main method of surgical treatment.

Regardless of their high-tech production, endoprotheses are perceived by the body as a foreign body in the UTS. They cause unpleasant symptoms that often require additional treatment. The tolerance of pregnant women to stents is individual and is influenced by the material of manufacture, the coating and the shape of the memory curve. Preoperative determination of stent length is another factor determining discomfort. It is related to the irritation of the bladder wall. There are various formulas and relationships established empirically after studies to determine the correct length of the stent according to the height and habit. We followed the

formula of Ho et al., according to which stent length = $0.125 \times \text{height} \times 10 + 0.5$ cm. In general, the length of the stent should be selected so that the distal curve does not cross the midline of the ureter contralaterally bubble. In stented pregnant women, stents with a length of 24 cm and 26 cm were most often used, respectively 6 fr or 7 fr.

Description of the methodology. In the practice of the Urology Clinic "St. Anna" MHAT-Varna, in pregnant women with symptomatic hydronephrosis indicated for surgical treatment, DJ stent placement was most often practiced using a semi-rigid ureteroscope. Manipulation will be performed through sedation, spinal or local anesthesia depending on experience, preferences and pre-anesthesiology consultation. After bladder penetration, rapid orientation for the ureteral ostiums followed. A hydrophilic 0.0035 or 0.0038 inch guidewire with the flexible (soft) end is inserted through the endoscope into the corresponding orifice. With slow movements of small "steps", the latter is pushed cranially, without applying pressure. The assistant with the ultrasound of the corresponding kidney monitors the entry of the tip of the guide into the renal pelvis. It also tracks its positioning. The endoscope is withdrawn and reinserted into the bladder, releasing the guide. Under ultrasonic and visual control (metric marking) the endoprosthesis is instilled along the guide. The latter is configured under ultrasound control while removing the guidewire. If necessary, the distal end is reconfigured using a URS clip.

This technique is the least traumatic and, at the same time, allows, in the event of an obstruction during the passage of the driver, prompt endoscopic penetration into the ureter and performing RUG and/or ureteroscopy. The use of hydrophilic guides provides safe passage through the fetally compressed portion of the ureter, or bypassing an intraluminal obstruction. In pregnant women, this is of utmost importance, as it reduces the likelihood of trauma and perforation (from the guide) of the ureter. Most often, we installed hydrophilic stents with both ends open, with a duration of stay in the urinary tract from 1 month to 6 months. We preferred the introduction of more rigid endoprotheses because of their resistance to external compression and a lower number of recurrences of the obstruction. After placing the endoprosthesis, we took urine for uroculture. Post-procedurally, we temporarily placed a foil urethral catheter, with a view to reducing vesicorenal reflux.

3.2.2. Percutaneous nephrostomy under ultrasound control

Percutaneous nephrostomy was rarely used for deobstruction during pregnancy. The reason for this is the low quality of life associated with the external urinary collector combined with the need for prolonged persistence of drainage (until the end of pregnancy). We placed PNS in case

of inability to pass retrograde through the stenotic area and failed stenting, as well as advanced obstructive purulent pyelonephritis and/or septic conditions. The main advantage is that it is carried out under local anesthesia, as well as the short operating time and the lack of pre-operative preparation.

Description of the methodology: Due to the impossibility of pregnant women lying on their stomachs, we performed the procedure on the back in a supination position under 30° to 45° lateral inclination. An alternative is to place the PNS in a sitting position. Most often, we performed the nephrostomy according to the following methodology: position of the patient - lying on his back (supination), with a textile roll placed longitudinally under the ipsilateral scapula to the pelvis. The angle that should make the dorsal surface and the operating table is 30°. The location of the 11th and 12th rib is established. Under ultrasound control with an abdominal convex transducer equipped with an interventional guide and index marker, a position is selected along the posterior axillary line lateral and caudal 1 to 2 cm from the 12th rib. In doing so, a longitudinal section of the kidney across the entire width is imaged. The marker should cross the posterior lower or posterior middle cup along the longitudinal axis. The line of the posterior group of calyces is projected on the surface of the kidney with a relatively avascular zone - Braudel's line. This allows safe puncture and creation of a nephrostomy tract.

After determining the most suitable puncture site, anesthetic lidocaine 10 ml 1% is infiltrated subcutaneously and deeply. A small incision was made with a sharp scalpel (#11).

The puncture was performed under ultrasound control using a Franzen needle. The echopositive needle tip follows the guide marker and thus penetrates the target calyx. After we removed the catheter, our urine flow indicated successful penetration of the PCS. We took a urine culture. A "J" guide with a soft end was inserted through the needle, which we positioned in the pyelomonas through echography. This was followed by removal of the needle and dilatation of the nephrostomy tract along the guide to a size of 1–2 fr. larger than the nephrostomy catheter. We placed the nephrostomy 6-8 fr along the guide. We configured the latter under ultrasound control, the goal being to screw a "pigtail" into the renal pelvis. We fixed with stitches to the skin.

Thanks to modern sonographers, the placement of the PNS completely under ultrasound control, the results are close to the classical in combination with X-ray methodology. But the harm to the fetus, the pregnant woman and the staff is significantly reduced. Another advantage is the lower cost, since no contrast, special X-ray operating room and equipment are required.

4. Statistical methods

For the purposes of this study, we will apply the following statistical methods:

1. Graphic and tabular method - with the help of graphs and tables, the frequency distribution of the considered signs (age groups, side of hydronephrosis, degree of hydronephrosis, symptoms, therapy - conservative and operative, etc.) is presented, divided by research groups, the average values and standard deviations, 95% confidence intervals of change in means. Histograms, diagrams, pie charts, etc. are used to visually present the results.

2. Descriptive analysis - we calculate derivative quantities that describe the regularities in the phenomena, without looking for the reasons that gave rise to them.

3. Methods of analysis of relationships and dependencies

3.1. correlation analysis – a statistical method by which the degree (closeness or strength) of the relationship between two or more phenomena is measured, when the dependence between them is of a correlation type. Correlation coefficients and their derivatives - coefficient of determination (determination) and coefficient of indeterminacy (indeterminacy) are used as measures of correlation dependence. A basic measure of the tightness of the relationship is the correlation coefficient (r). It represents a normalized value that takes values from (-1) to $(+1)$. We will use nonparametric and parametric correlation coefficients. When the correlation dependence is straight, the calculated correlation coefficient is positive. When the correlation dependence is reversed, the calculated correlation coefficient is negative.

3.2. regression analysis – a set of statistical methods, which are used to model relationships and dependencies between mass phenomena and processes, represented by statistical series on interval scales. Correlation-type relationships are measured and the form of the relationship between two or more correlated phenomena is investigated. It is established by means of modeling. The chosen model for describing the studied relationship must necessarily have a specific analytical (mathematical) form. Regression analysis solves the following tasks:

3.2.1. determination of the form of the dependence between the variables with graphic and analytical methods;

3.2.2. determination of the regression function and estimation of its parameters;

3.2.3. verification of statistical hypotheses about the reliability of regression models and their parameters.

We will consider univariate regression models in which the variables are represented by static series statistics. We will mark the result variable with Y, and the factor variable with X.

RESULTS

In the present work, we studied and analyzed 184 pregnant patients with evidence of symptomatic hydronephrosis. All patients were urgently hospitalized in the Department of Pathological Pregnancy at SBAGAL "Prof. Dr. D. Stamatov" city of Varna and Urology Clinic at the MHAT "St. Anna" city of Varna for the period 2019-2021. We surveyed the women according to the following indicators:

- Socio-demographic indicators
- Clinical symptoms
- Laboratory indicators
- Microbiological studies
- Visual research methods
- Country and extent of the affected kidney
- Conservative treatment
- Surgery

1. Demographic indicators

They are described in the Material section. Demographic characteristics

2. Clinical symptoms

2.1. Pain

The first and leading symptom in the patients we examined was pain. It was expressed by pain in the abdominal area (low or high located, corresponding to the location of the uterus, in its different terms) and/or lumbar area, predilection for the affected kidney. The irradiating

character was not emphasized, probably because of the anatomical changes that occur in US. In women with a history of kidney stone disease, irradiation along the course of the ureter was observed more often. In some cases, it had a chronic-recurring nature. In others, it had suddenly appeared.

Table 4. Distribution according to the presence of pain symptoms:

	number	%
All	184	-
All patients with pain symptoms	83	45.11%

Out of all 184 patients admitted for treatment, pain symptoms were observed in 83 of them (45.11%). (Table 4.)

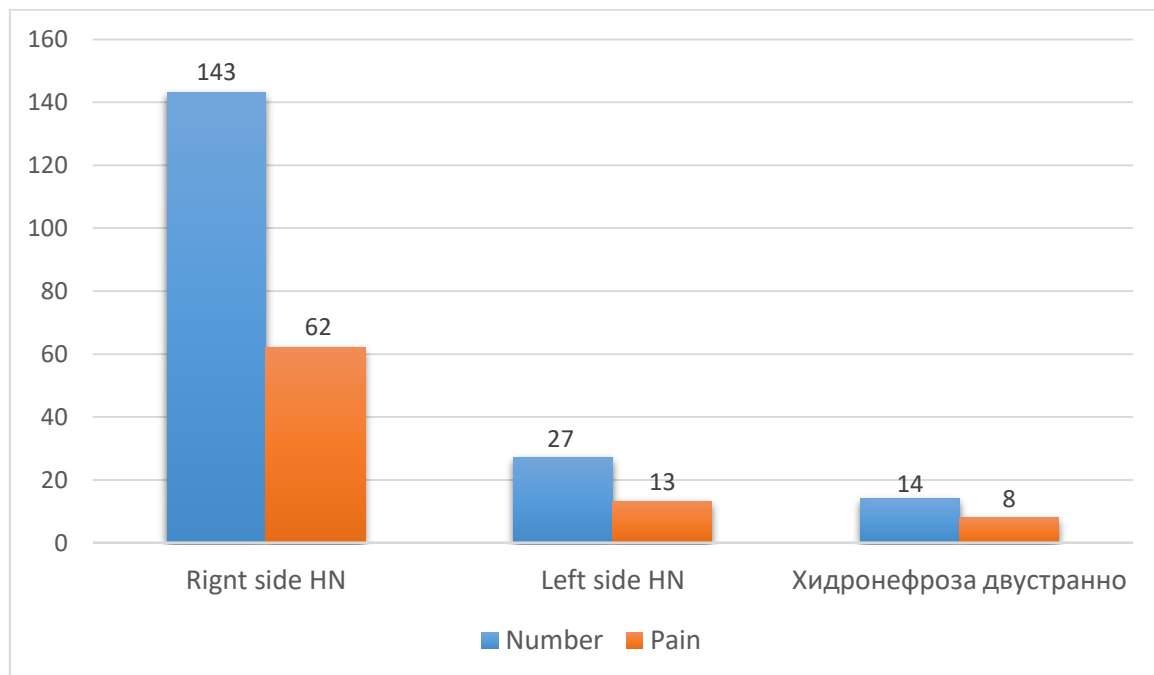


Fig. 7. Distribution of patients according to side of involvement and presence of pain syndrome

Depending on the side of the affected kidney, 43.36% (62 women) of patients with right-sided localization had pain symptoms, 48.14% (13 women) from left-sided hydronephrosis. We found the most pronounced pain syndrome in case of bilateral involvement 57.14% (8 women), (Fig. 7.).

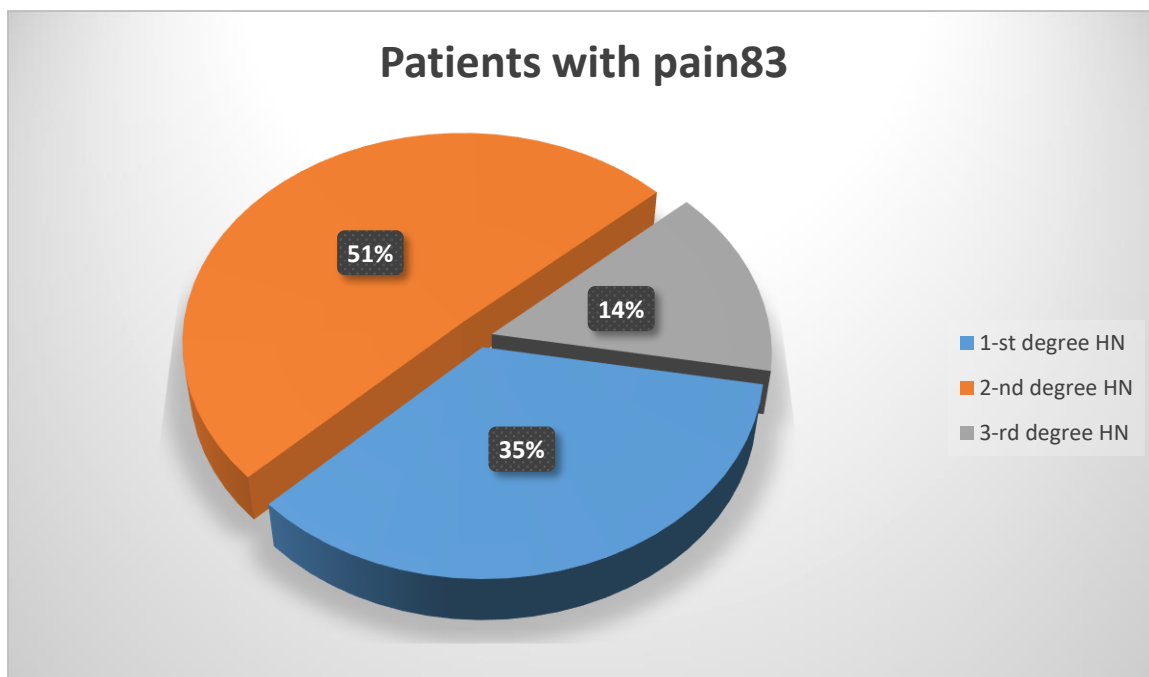


Fig. 8. Distribution depending on the degree of HN and the presence of pain

From figure 8 it is clear that of all patients with pain (83 women), according to the degree of hydronephrosis, the highest frequency of cases with the 2nd degree was observed - 50.66% (42 female patients), followed by the patients with 1- th degree and women with 3rd degree hydronephrosis have the third highest frequency of pain.

Table 5. Distribution of patients with fever from those with pain

	number	%
pain patients in general	83	-
patients with pain and elevated temperature > 37.0 0C	25	30.12%

The combination of pain syndrome and temperature > 37.0⁰ C was observed in 25 cases, i.e. in 30.12% of all pregnant women with pain. (Table 5.)

Table 6. Distribution of patients depending on the presence of pain and operative treatment

	Without pain	%	With pain	%
All	101	54,89	83	45,11%
Patients surgical treatment	0	0%	26	31,33% (14,13% of total number)

From Table 6, we found that the patients without pain (54.89%) did not require surgical treatment. In cases with pain symptoms (45.11%), 31.33% underwent surgical treatment (14.13% of the total number of examined).

2.2. Temperature

Temperature was a significant marker of complication. All 184 patients were examined at hospitalization and actively followed during the hospital stay.

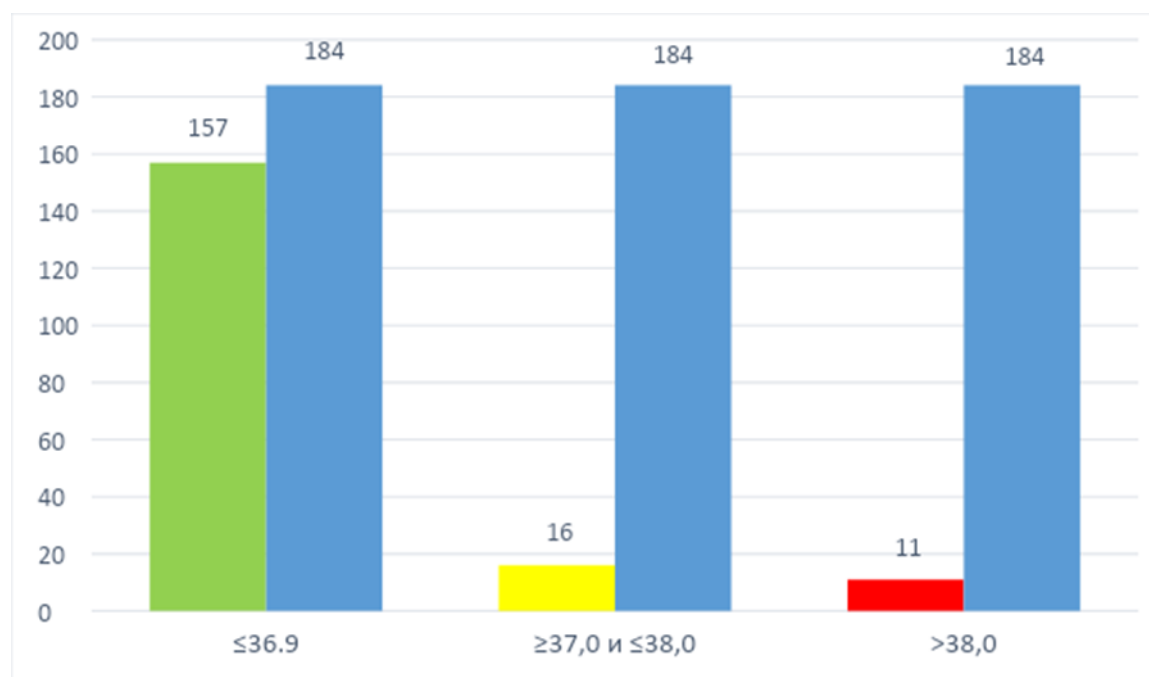


Fig. 9. Distribution of cases according to temperature values:

The study found that 14.67% had a temperature $\geq 37.0^{\circ}\text{C}$. We divided pregnant women into three groups: afebrile ($\leq 36^{\circ}\text{C}$), subfebrile (≥ 37.0 and $\leq 38.0^{\circ}\text{C}$) and febrile patients ($> 38.0^{\circ}\text{C}$). According to Figure 9, 157 pregnant women (85.33%) were in the first group, 16 women (8.7%) in the second group, and 11 febrile cases (5.98%).

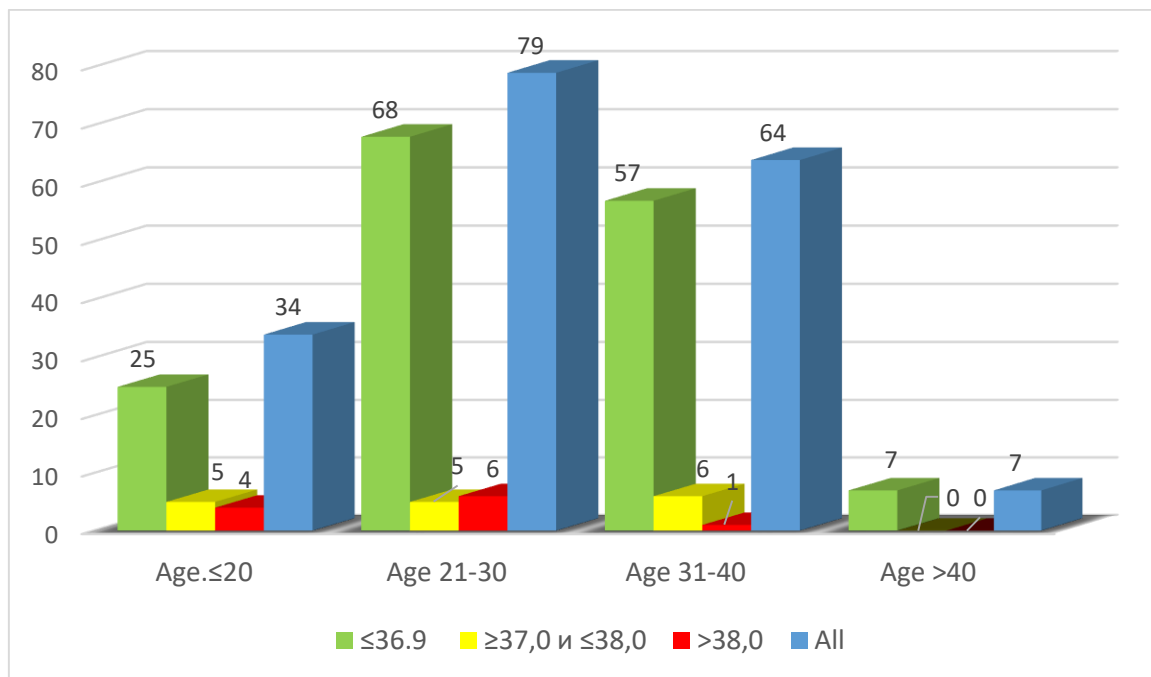


Fig. 10. Distribution of the temperature symptom according to age groups.

Table 7. Distribution of the temperature symptom according to age groups

	Age ≤20		Age 21-30		Age 31-40		Age > 40	
	number	%	number	%	numb	%	numbe	%
	34	100%	79	100%	64	100%	7	100%
≤36.9 °C	25	73.53%	68	86.08%	57	89.06%	7	100%
≥37,0°C и ≤38,0°C	5	14.71%	5	6.33%	6	9.38%	0	0%
>38,0°C	4	11.76%	6	7.59%	1	1.56%	0	0%

We analyzed the manifestation of the temperature symptom in the different age groups. From figure 10 and table 7, it is clear that subfebrile and febrile patients in the age range below 20 years predominate (14.71% and 11.76%), and all patients over 40 years are afebrile.

Table 8. Distribution of pregnant women according to the period of pregnancy and temperature >37.0 0C

	Up to 20 g.w.		After 20 g.w.	
	number	%	number	%
	35	19,02%	149	80,98%
fever>37.0 0C	1	2.85%	26	17.45%

Depending on the duration of the pregnancy, up to 20 g.w. only 1 patient had a temperature >37.0 0C (2.85%), and in the subgroup over 20 g.w., temperatures >37.0 0C (17.45%) were measured in 26 of the total number for the period. (Table 8)

2.3. Vomiting

Table 9. Distribution of patients with vegetative symptoms and applied treatment

	number	%
All patients with vegetative symptoms	13	7.07% of total number
Operative treatment	8	61.54%

Nausea and vomiting are autonomic symptoms observed in 13 patients (7.07% of the total number examined). In the analysis of the data, it was found that in more than half - 61.54%, operative treatment was necessary. (Table 9.)

Table 10. Distribution of cases with combined vegetative symptoms and pain referred to treatment

	number	%
Patients with vomiting and pain	12	6.52% of total number
Operative treatment	8	66.67%

From table 10, we deduced that in 6.52% of all examined we observed a combination of vomiting with pain symptoms. 66.67% of them underwent drainage manipulation.

2.4. Arterial hypertension

Table 11. Distribution of pregnant women with elevated BP values

	number	%
All patients with HN	184	-
Measured values of RR > 130/ 90 mmHg	25	13.59%

In 13.59% we observed elevated BP values above 130/90 mmHg. We did not find definitive data on the correlation of BP values and the presence of hydronephrosis (Table 11.).

3. Laboratory indicators

3.1. Leukocytes and "C" reactive protein

The study found that more than 60% of pregnant women did not have elevated acute-phase inflammatory markers. In the rest of the patients, there were elevated values of CRP >5 mg/L in about 40% and in more than half Leuc $\geq 10.109/L$ (Fig. 11. and Fig. 12.)

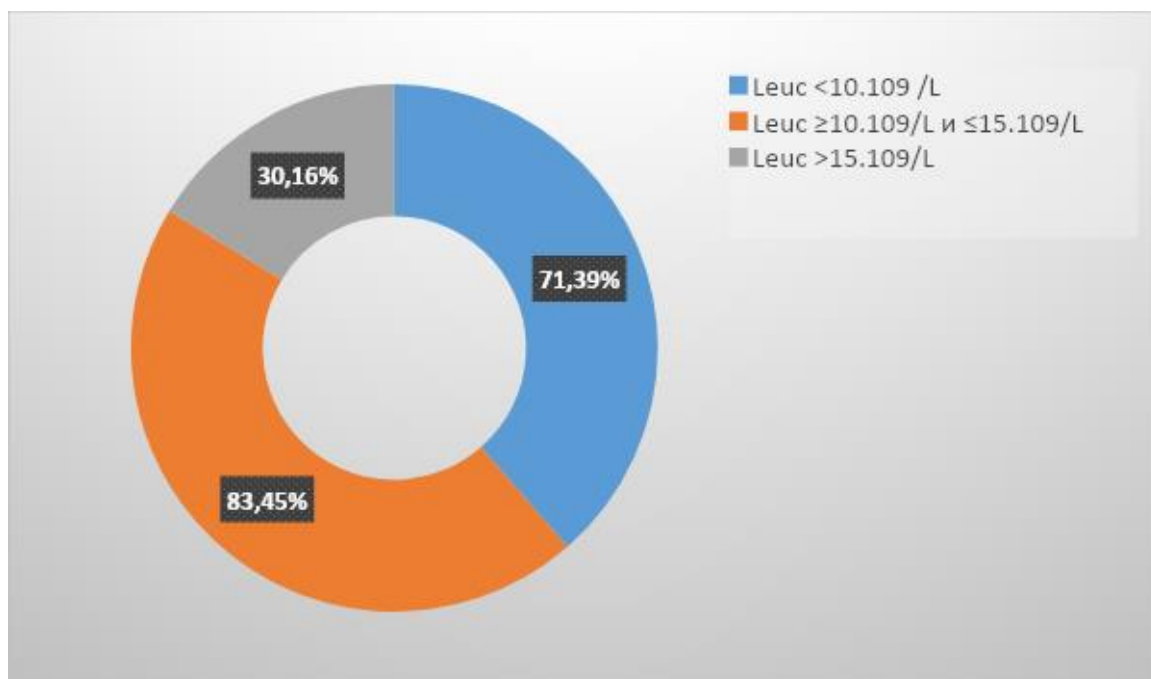


Fig. 11. Distribution of female patients according to the values of leukocytes from CBC

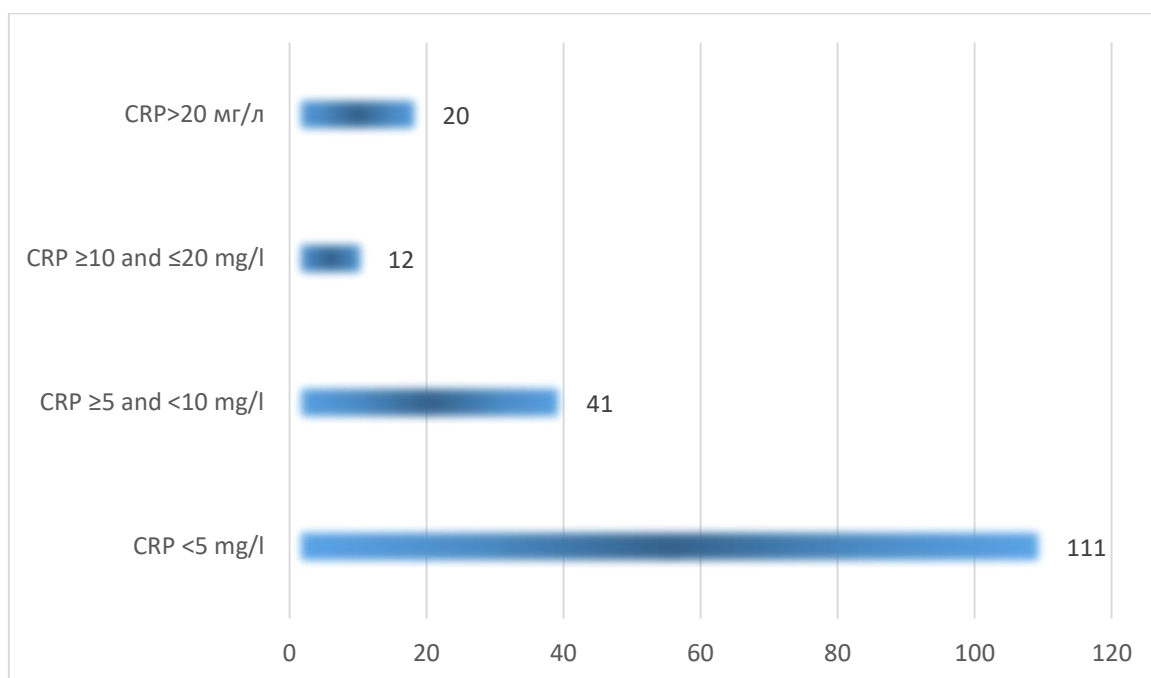


Fig. 12. Distribution of cases according to CRP values

Table 12. Distribution of patients with combination of acute phase markers

	Number	%
All	184	-
CRP>5 mg/l и	58	31.52%

Patients with elevated serum CRP values in combination with leukocytosis were studied. The data of the analysis indicate that in 31.52% (58 cases out of all) a combination of the acute-phase inflammatory markers was observed (Tab. 12.).

3.2. Creatinine

Another complication of HN is the manifestation of kidney failure. In our study, 1.63% of cases had elevated creatinine values above 97 $\mu\text{mol/L}$. At the same time, these patients had an increase in CRP above 5 mg/l and leukocytosis above $10 \cdot 10^9$ (Table 13.)

Table 13. Distribution of patients according to manifestation of renal failure.

	number	%
All with HN	184	-
Creatinine >97 $\mu\text{mol/l}$	3	1.63%
CRP>5 mg/l и Creatinine >97	3	1.63%
CRP>5, Leuc> $10 \cdot 10^9$, Creatinine >97	3	1.63%

Table 14. Distribution of pregnant women according to the "side of hydronephrosis" criterion and elevated serum creatinine values

	right sided HN		left sided HN		Bilateral HN	
	number	%	number	%	number	%
		77.71%		14.67%		7.61%
Creatinine >97 $\mu\text{mol/l}$	2	1.39%	0	0%	1	7.14%

Increased creatinine values were observed in 2 patients with unilateral right-sided HN (1.39% of right-sided) and in 1 pregnant woman with bilateral HN (7.14% of bilateral). (Table 14.)

3.3 Hemoglobin

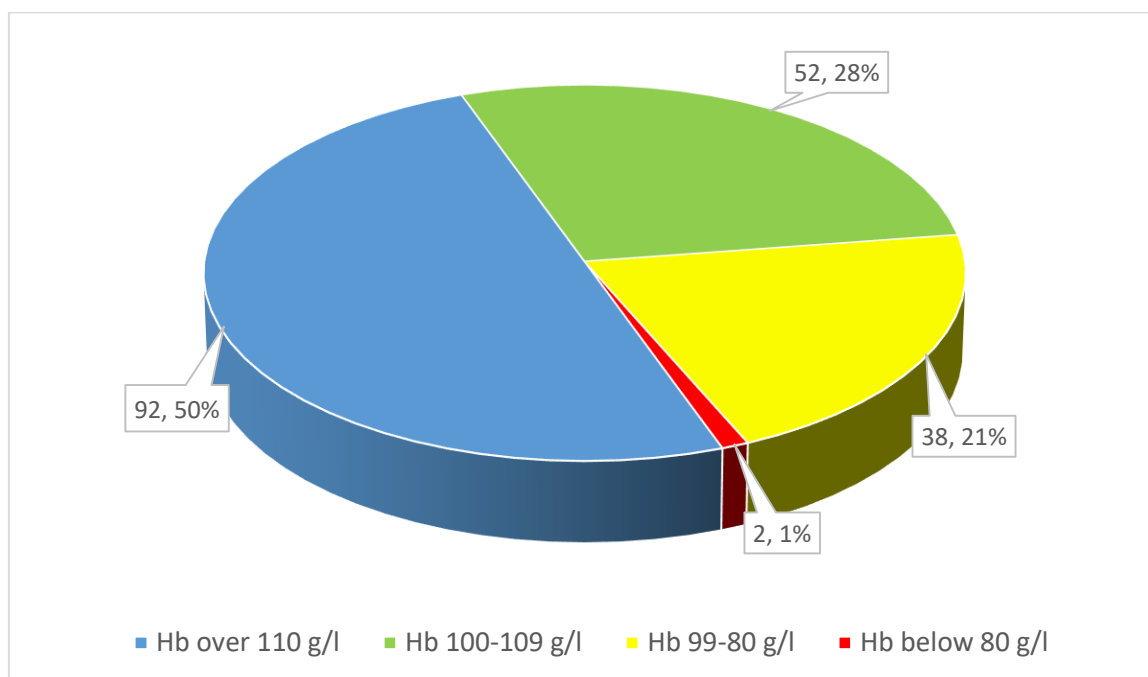


Fig. 13. Distribution of pregnant women according to the hemoglobin indicator

We examined the target group of female patients according to the hemoglobin indicator. From Fig. 13 it is evident that half of the examined have manifestations of anemia. Statistical methods proved a significant correlation between the period of pregnancy and manifestations of anemia.

3.4. Urine examination

3.4.1. Protein in urine and bacteriuria

When analyzing the data from the urine test, it was found that in 48.91% of the cases (90 women), the presence of protein in the urine was proven (Table 15.). Of all patients with

laboratory data for leukocytes above 10.10^9 /L, 36.28% of them had bacteriuria from the urine test.

Table 15. Distribution according to the indicator of proteinuria, leukocytosis and the presence of bacteriuria

	number	%
All pregnant women with HN	184	-
Presence of protein in the urine	90	48.91%
Patients with Leuc $>10.10^9$ /L	113	-
Presence of bacteriuria	41	36.28%

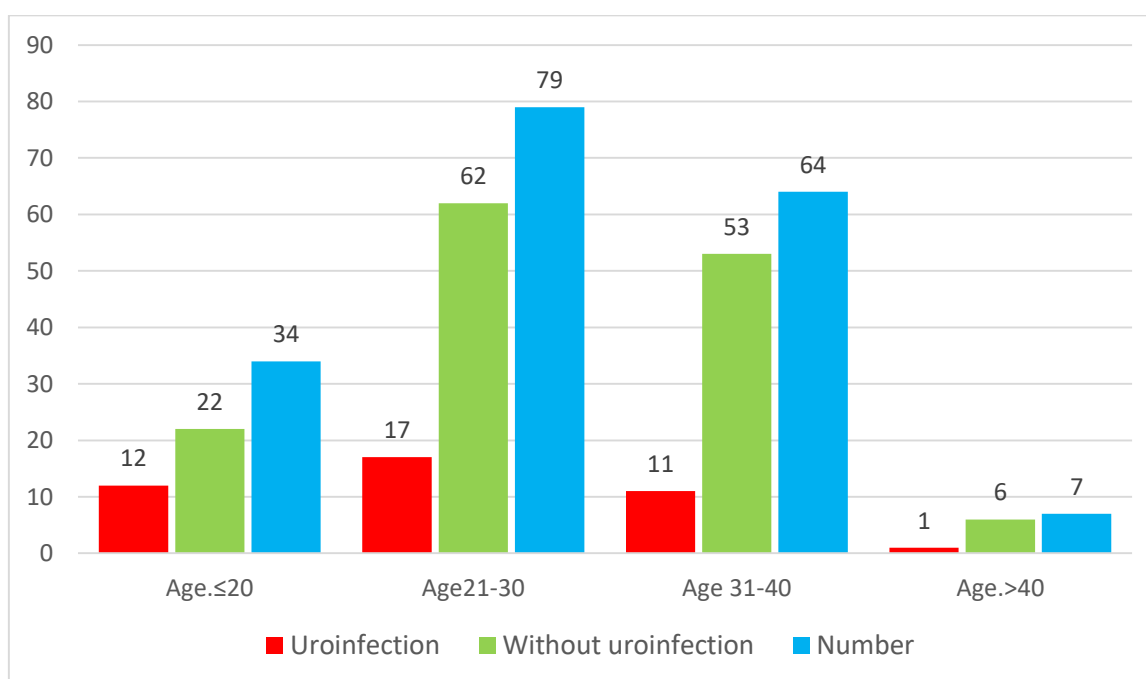


Fig. 14. Distribution by age and uroinfection criteria

When evaluating the distribution according to age and the presence of uroinfection, the data from our study indicate a tendency to decrease cases with increasing pregnancy. At the age of less than 20 years, we diagnosed uroinfection in 35.29%, while at the age of 31-40 years, in 17.19% of the cases. (Fig. 14.)

3.4.2. Microbiological studies

In the course of our study, patients with evidence of bacteriuria were subjected to a microbiological examination. We initially divided the results into three subgroups: Gram (-),

Gram (+) bacteria and mycoses. Further analysis supplemented the subgroups with the specific isolates.

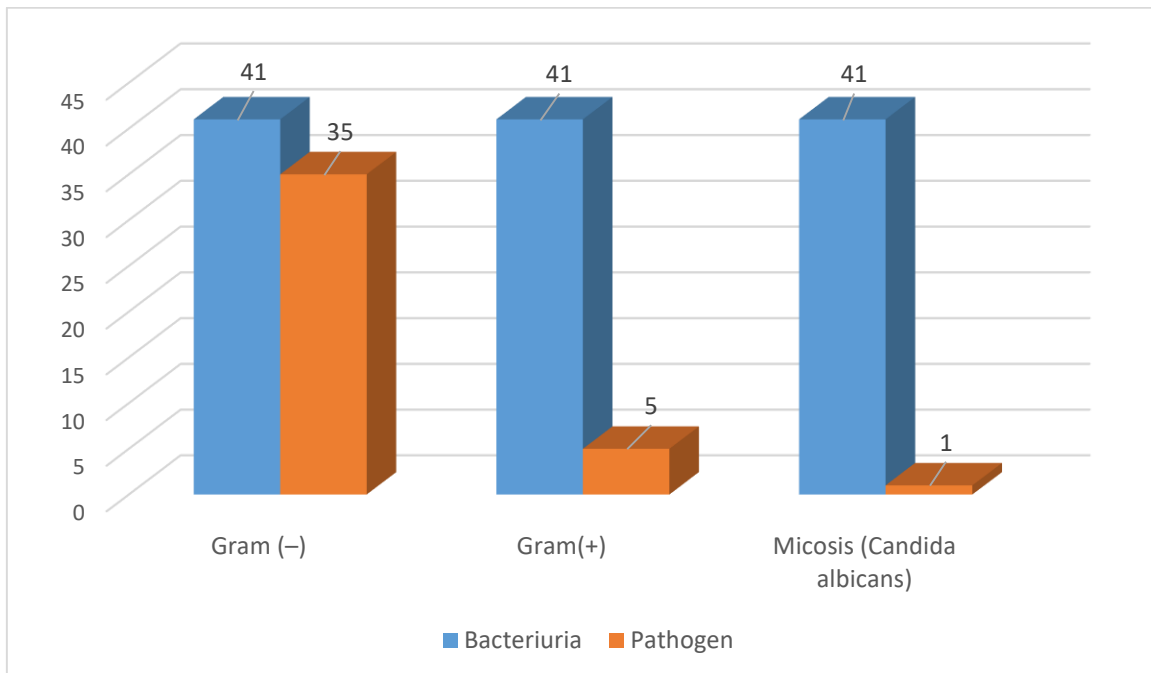


Fig. 15. Distribution of pregnant women according to microbiological isolates

Examining the cohort of 184 pregnant women and the available 41 bacteriurias, we found that Gram (-) strains prevailed in 19.02% of all, Gram (+) were 2.72% and in one patient mycosis - *Candida albicans* (0.54%) was isolated (Fig. 15).

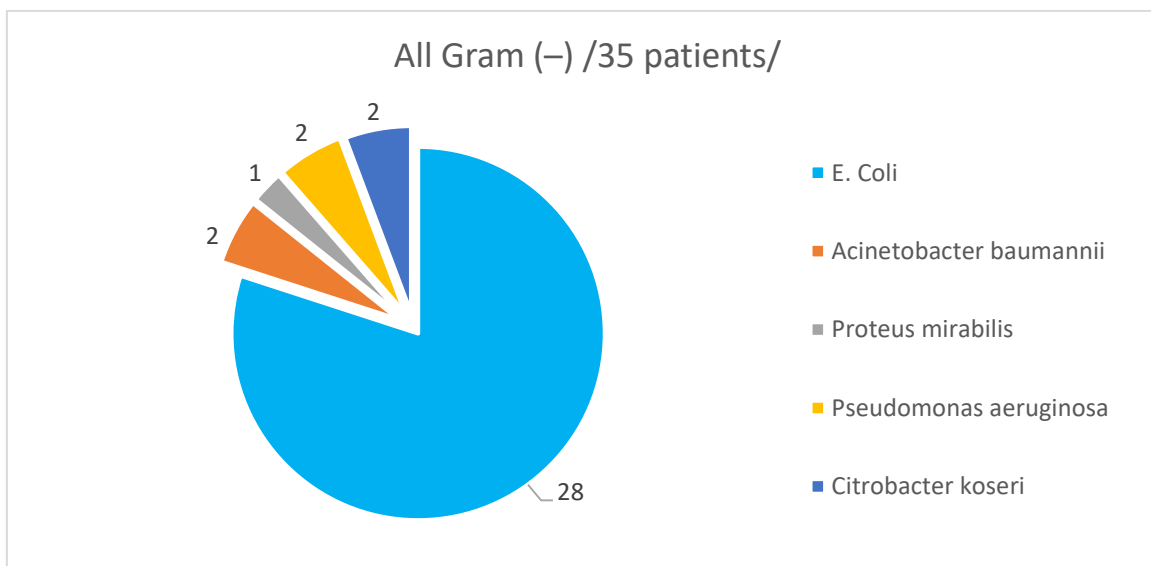


Fig. 16. Distribution of bacterial strains of all Gram (-) pathogens

From the analysis of Gram (-) agents, E.coli prevailed significantly - 80.0%, Acinetobacter baumannii, Pseudomonas aeruginosa and Citrobacter koseri - 5.71% of the cases and a single isolate of Proteus mirabilis were equally distributed (Fig. 16.).

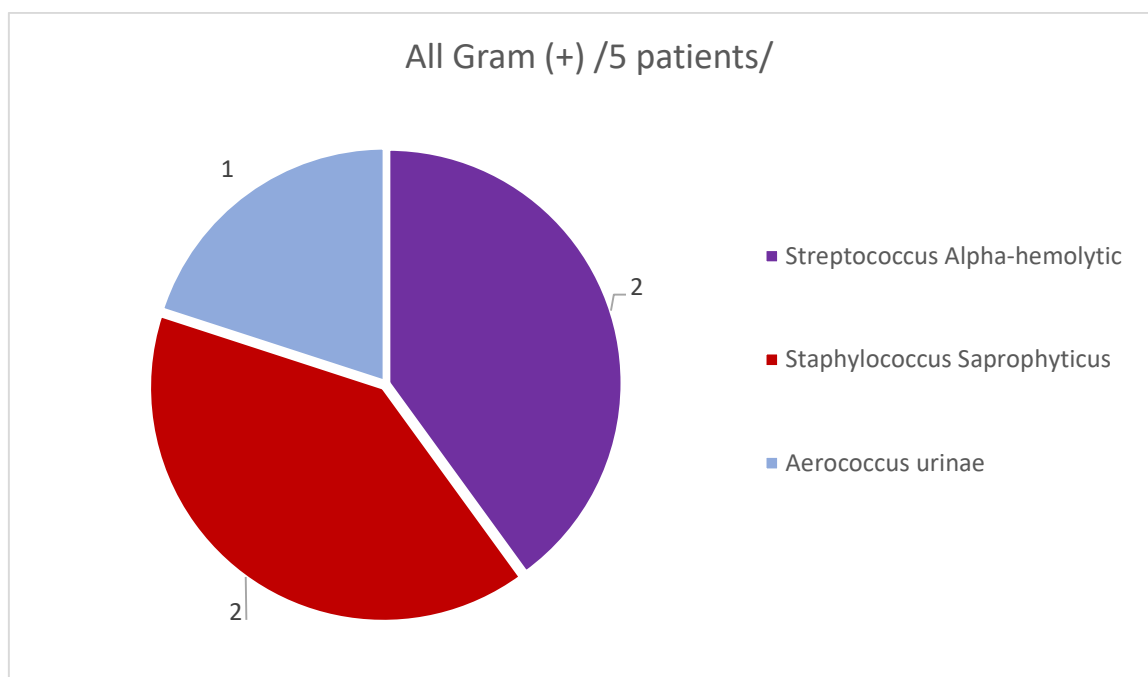


Fig. 17. Distribution of Gram (+) bacterial isolates

For Gram (+) microorganisms, we reported an equal distribution of Streptococcus Alpha-hemolytic and Staphylococcus Saprophyticus in 40.0% of the subgroup of Gram (+) microorganisms and one case of Aerococcus urinae ie. 20.0% (Fig. 17.).

4. Imaging methods

In the implementation of our study, all 184 patients underwent ultrasound of the UTS. Hydronephrosis was diagnosed by the method in 100% of pregnant women. One case additionally had MRI available (outpatient).

Table 16. Distribution of patients according to the degree of hydronephrosis.

	number	%
All	184	100%
1st degree HN	80	43.48%
2nd degree HN	90	48.91%
3rd degree HN	14	7.61%

From the obtained results when distributed according to the degree of HN, it is visible that the largest number of cases are with the second degree of hydronephrosis - 48.91% (90 female patients), and the smallest with the third degree - 7.61% (14 women), (Table .16.).

Table 17. Distribution of the degree of HN in relation to the duration of pregnancy

	All with HN up to 20 g.w.		All with HN after 20 g.w.	
	number	%	number	%
All	35	-	149	-
1st degree HN	25	71.43%	56	37.58%
2nd degree HN	9	26.47%	80	53.69%
3rd degree HN	1	2.94%	13	8.73%

From the ultrasound diagnosis, in addition to the presence of hydronephrosis, the distributions according to the degree of HN, as well as their correlation with the duration of pregnancy, were specified. (Plate 17.)

5. Treatment

In the Pathological Pregnancy Department of SBAGAL "Prof. Dr. D. Stamatov" Varna, we performed the conservative treatment. In case of indications or failure, after consultation with a urologist, the pregnant women continued their therapy in the Urology Clinic at the "St. Anna" in the city of Varna for the period 2019-2021. We managed to conservatively influence 85.87% of the cases (158 women) who were discharged and followed up. Urological manipulation was required in 26 patients (14.13%) (Fig. 18.).

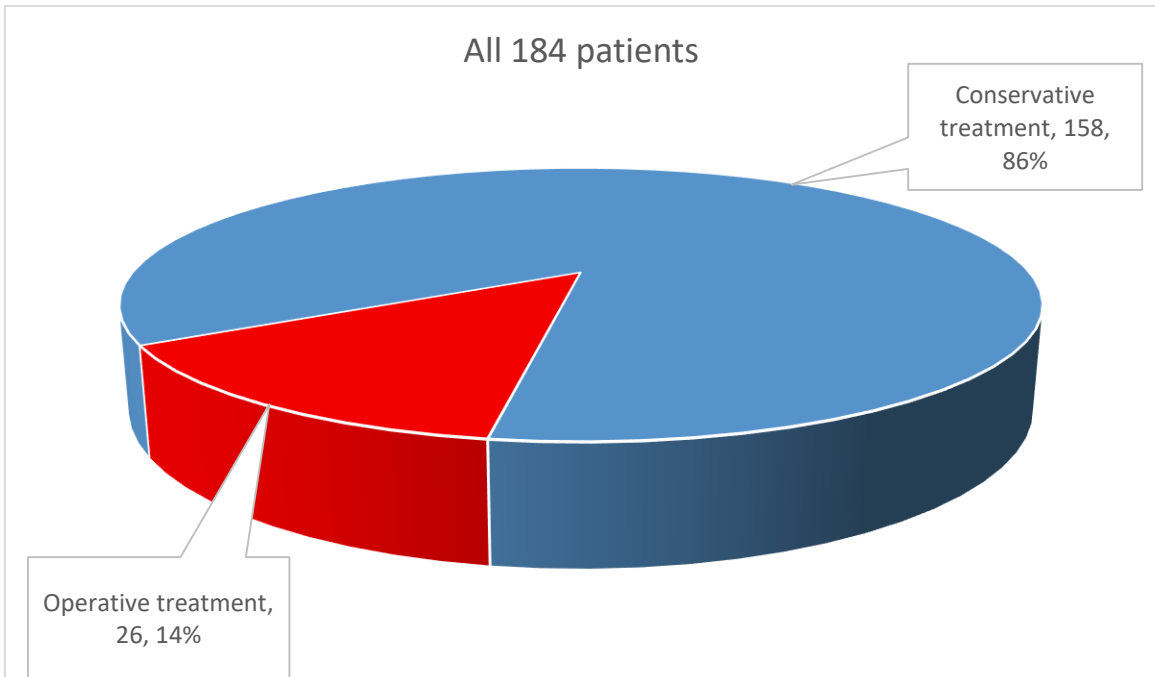


Fig. 18. Distribution by type of treatment

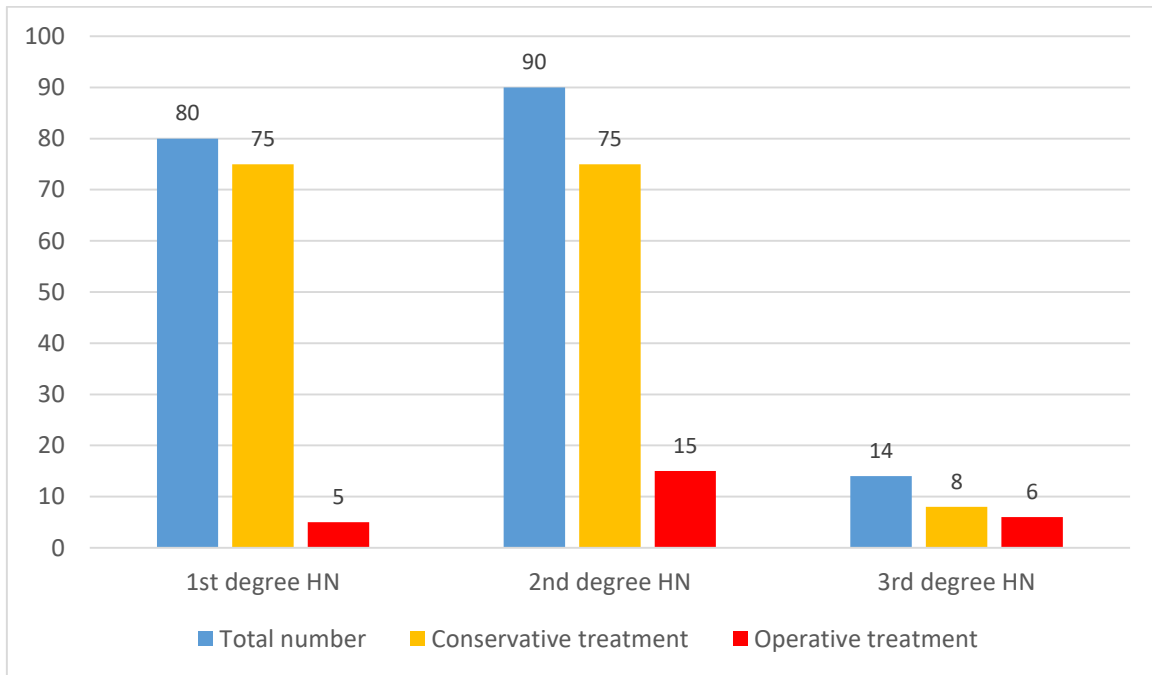


Fig. 19. Distribution of the type of applied treatment according to the degree of HN

We examined the diagnosed rate of HN at hospitalization and the subsequent treatment administered. The results of this showed that 93.75% of patients with 1st degree HN were

successfully treated conservatively, 83.33% with 2nd grade HN, and 57.14% of 3rd grade HN had a good conservative response. (Fig. 19.)

5.1 Conservative treatment

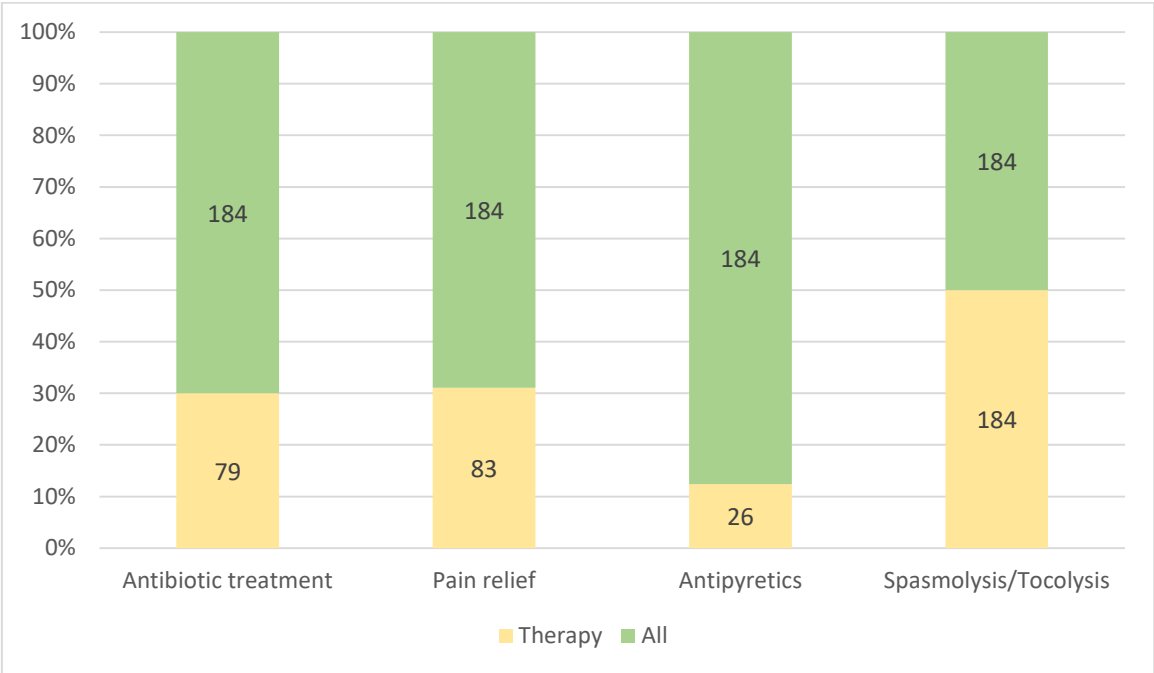


Fig. 20. Allocation according to the conservative approach

Antibiotic treatment was administered in 42.93%, analgesia in 45.11%, and antipyretics in 14.13%, and spasmolysis/tocolysis in 100% of cases. The total percentage exceeds 100%, because some pregnant women combine medical treatment (Fig. 20.).

Table 18. Distribution of pregnant women according to gestational age and antibiotic treatment

	All up to 20 g.w.		All after 20 g.w.	
	number	%	number	B%
	35	-	149	
Antibiotic treatment	11	31.43%	76	51.00%

When the pregnancy is up to 20 g.w. in 31.43% of cases an antibiotic was administered. There is a trend for an increased frequency of antibiotic treatment use after 20 g.w. (51.00%), (Table 18.).

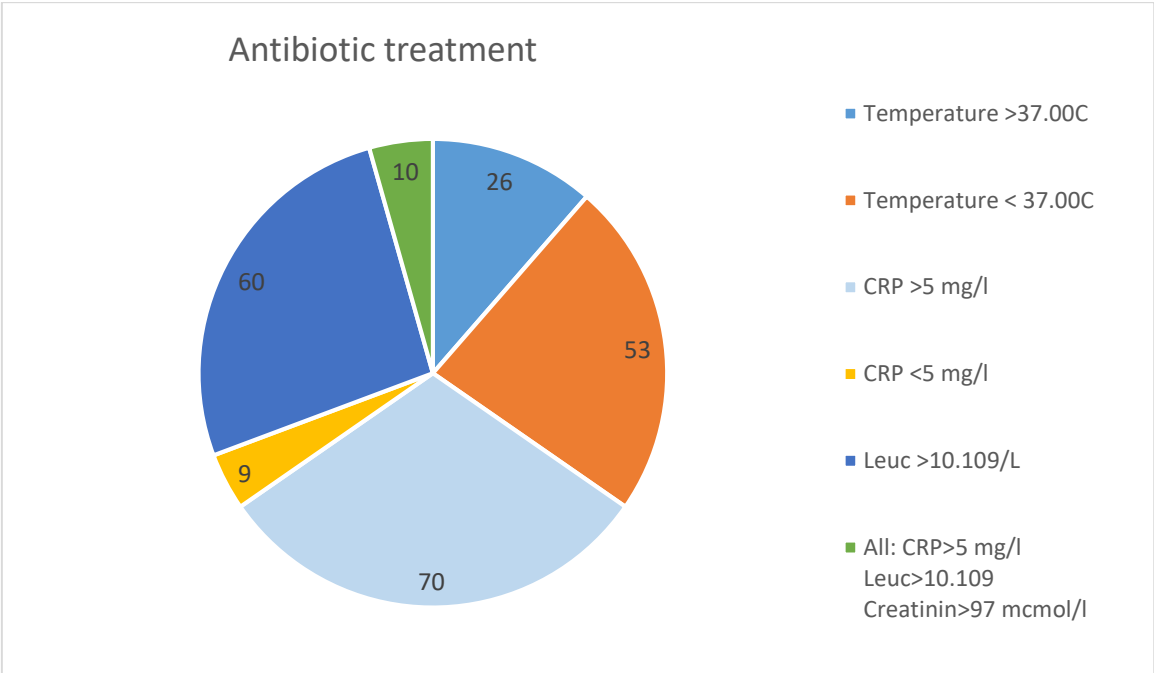


Fig. 21. Distribution of cases according to the need for an antibiotic and the presence of markers of inflammation.

When analyzing the criteria for applying antibiotic treatment, we found that in the presence of an acute phase marker, we resorted to empirical antibiotic treatment. With the most significant diagnostic value and the need to start AB treatment is CRP >5 mg/L in 88.61% of pregnant women, followed by Leuc >10.109/L in 75.95% (Fig. 21.).

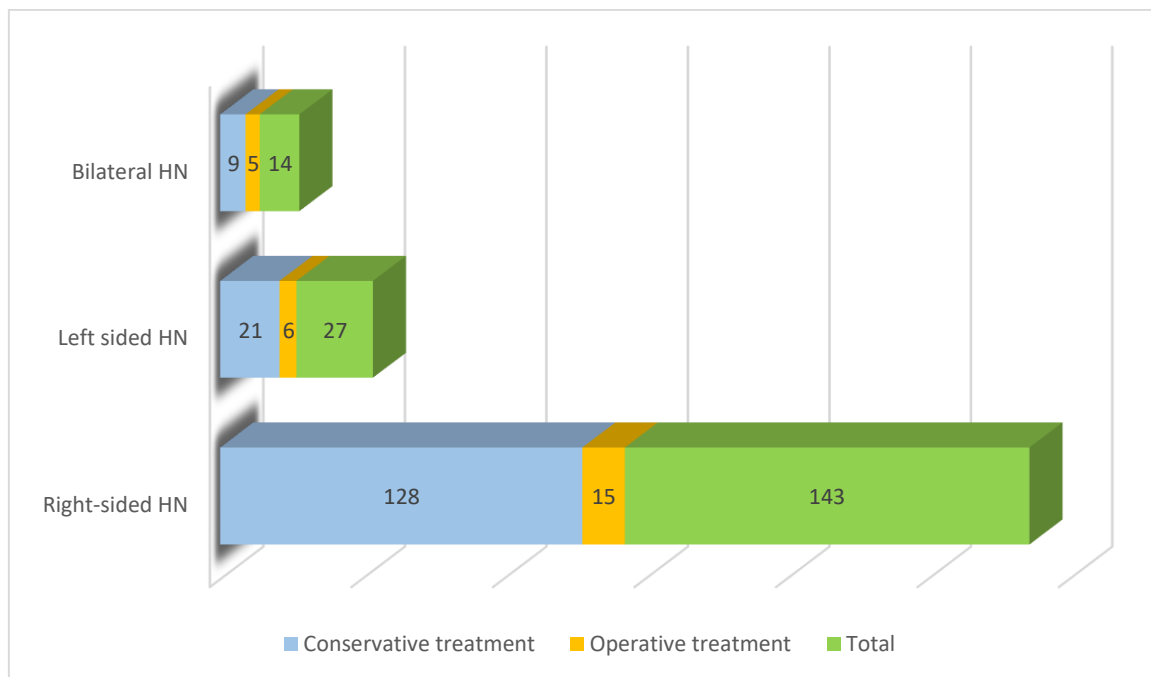


Fig. 22. Distribution of the method of treatment according to the country of HN

Table 19. Distribution of the method of treatment according to the country of HN

	Right-sided HN		Left sided HN		Bilateral HN	
	number	%	number	%	number	%
Conservative treatment	128	89.51%	21	77.78%	9	64.29%
Operative treatment	15	10.49%	6	22.22%	5	35.71%

In patients with right-sided HN (143 pregnant women), only 10.49% were surgically treated. For bilateral HNs, this share is 35.71%. And we observed significant improvement from drug therapy most often in right-sided patients - 89.51%, followed by left-sided patients in 77.78%. (Plate 19 and Fig. 22)

Table 20. Distribution of patients with pain and subsequent treatment

	number	%

All with pain symptoms	83	-
Conservative treatment	57	68.67%
Operative treatment	26	31.33%

Of all patients with pain symptoms, conservative treatment was applied to 68.67% and surgical treatment to the remaining 31.33% (Table 20).

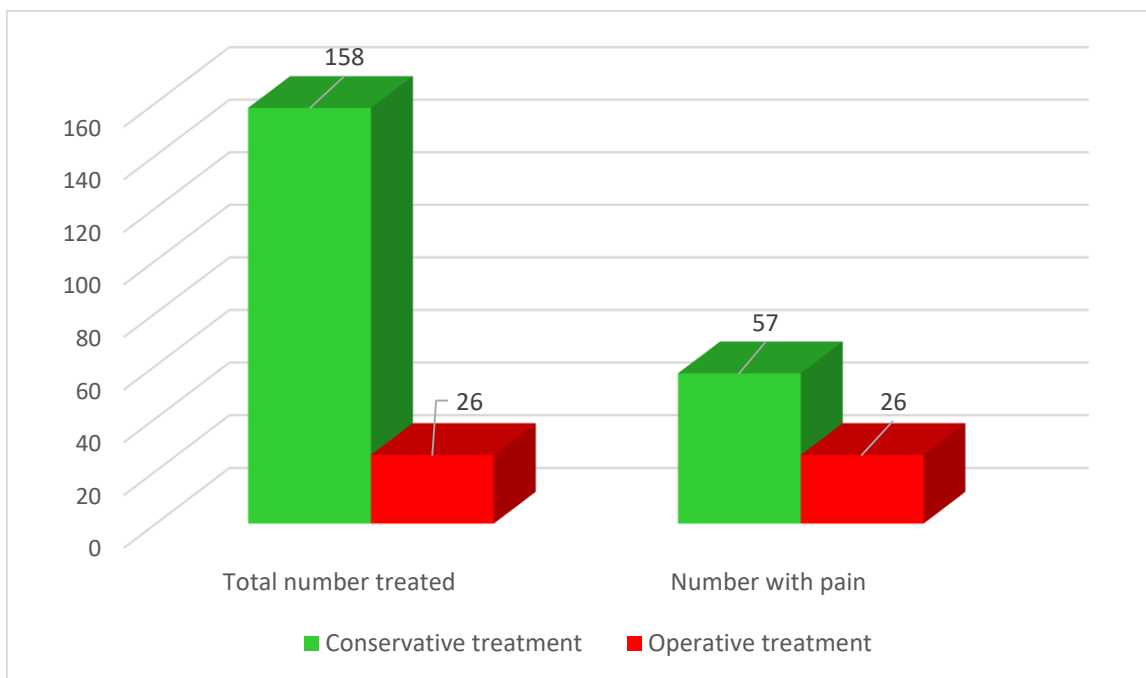


Fig. 23. Frequency distribution of conservatively and operatively treated pain symptoms

From the obtained results, we found that 100% of the surgically treated pregnant women had pain symptoms. And in 36.08% of conservatively applied treatment, pain is present as a complaint (Fig. 23.).

Table 21. Distribution of patients according to the presence of pain and the applied antibiotic treatment

	All with pain symptoms		All without pain	
	number	%	number	%
	83	45.11% от вс.	101	54.89% от вс
Antibiotic treatment	52	62.65%	27	26.73%

In pregnant women with pronounced pain symptoms, 62.65% had to include an antibiotic, compared to those without pain - only in 26.73% (these percentages include conservatively and operatively treated women) (Table 21.).

5.2. Surgery

Table 22. Distribution of the total number of patients and the type of surgical treatment applied

	number	%
All	184	-
DJ stent	25	13.59%
Nephrostomy	1	0.54%

The main methods that have been used for minimally invasive drainage are retrograde ureteral stenting (RUS) and percutaneous nephrostomy. In our study, a visible preference for RUS is found. Retrograde endoprotheses were placed in 25 pregnant women (13.59%). Only 1 patient had to have a PNS inserted (0.54%). (Plate 22.)

Table 23. Distribution of women according to the period of pregnancy and the need for operative urological treatment

	All up to 20 g.w.		All after 20 g.w.	
	number	%	number	%
Total number	34	-	149	
Operative treatment	0	0%	26	17.45%

In the analysis of women according to gestational age, it was found that up to 20 g.w.no operative treatment was performed. All patients with endourological treatment were after 20 g.w.. – 26 women out of 149 pregnant women (17.45%). (Table 23.)

Table 24. Distribution of surgical patients depending on body temperature

	T<37,0°C	T>37,0°C

	number	%	number	%
Total number of op. treatment	26	-	149	
Operative treatment	13	50%	26	17.45%

Retrogradely, it was estimated that operatively treated pregnant patients were equal to patients above 37.00C and those below 37.00C. (Table 24.)

Table 25. Distribution of female patients according to the leukocytosis symptom and subsequent type of treatment

	Conservative treatment		Operative treatment	
	number	%	number	%
Total number	158	-	26	-
Leuc > 10.10 ⁹ /L	92	58.23%	21	80.77%

Leukocytosis during pregnancy is a relative indicator of the presence of inflammation. An increase in Leuc > 10.109/L was observed in 58.23% of the examined group, and in 80.77% of the surgically treated subgroup. (Table 25.)

Table 26. Distribution according to the value of the CRP indicator and the applied urological treatment

	CRP <5 mg/l		CRP 5> mg/l	
	number	%	number	%
Total number	26	-	149	
Operative treatment	2	7.69%	26	17.45%

Table 26 reflects the relationship between the application of urological treatment and the value of CRP. Of the operated subgroup, only 2 patients had CRP <5 mg/L (7.69%).

Table 27. Distribution of cases with a combination of inflammatory markers – leukocytosis and elevated temperature, related to the type of treatment

	Conservative treatment		Operative treatment	
	number	%	number	%

Total number Leuc > 10.10 ⁹ /L и T>37,00C	3	18.75%	13	81.25%
Total number Leuc > 10.10 ⁹ /L и T>38,00C	2	18.18%	9	81.81%

When two of the inflammatory markers are combined, in more than 80% of the cases surgical treatment was necessary and less than 20% - conservative treatment (Table 27.).

Table 28. Comparative analysis of operated patients regarding acute-phase inflammatory markers

	Leuc > 10.10 ⁹ /L CRP <5.0 mg/l		Leuc > 10.10 ⁹ /L CRP > 5.0 -10.0mg/l		Leuc > 10.10 ⁹ /L CRP > 10.0-20.0 mg/l		Leuc > 10.10 ⁹ /L CRP > 20.0 mg/l	
	number	%	number	%	number	%	number	%
Total number	26	-	26	-	26	-	26	-
Operative treatment	2	7.69%	5	19.23%	3	11.54%	13	50%

Of the patients with surgical treatment, 50.0% of the cases had combined markers Leuc > 10.10⁹/L and CRP >20.0 mg/l, and 7.69% with Leuc > 10.10⁹/L and CRP <5.0 mg/l (Table. 28.)

Table 29. Comparative data in surgically treated patients regarding inflammatory markers

	Leuc <10.10 ⁹ /L CRP <5.0 mg/l T<37,0 ^o C		Leuc > 10.10 ⁹ /L CRP >5.0 mg/l T>37,0 ^o C	
	number	%	number	%
All op. treatment	26	-	26	-
Operative treatment	2	7.69%	13	50.0%

Of the urologically treated patients, it is evident that 50.0% had Leuc >10.10⁹/L, CRP>5.0 mg/l and T>37.0^oC and only 7.69% (only 2 women) had Leuc <10.10⁹/L, CRP <5.0 mg/l and T<37.0^oC (Table 29.).

Table 30. Frequency distribution of patients with Leuc > 10.10⁹/L, CRP>5.0 mg/l and T>37.0⁰C and the subsequent treatment

	Conservative treatment		Operative treatment	
	number	%	number	%
Leuc > 10.10 ⁹ /L CRP >5.0 mg/l T>37,0 ⁰ C	10	43.48%	13	56.52%

When analyzing the cases with three inflammatory markers and the subsequent treatment, those with surgical treatment predominate 56.52%. Regardless of the treatment approach, antibiotic therapy was applied to all patients - 100%, (Table 30.).

6. Statistical processing of the obtained results

6.1. Correlation analysis

For the needs of the analysis, we have 184 pregnant patients. The various indicators we have for them are presented on nominal, rank and interval statistical scales. For this purpose, we will use different single correlation coefficients, based on what scales each pair of correlated indicators is presented. We will present only the obtained statistically significant correlations where the limit indicator $\alpha < 0.05$.

We will interpret the obtained correlation coefficients based on table 31.

Table 31. Interpretation of correlation coefficients

Correlation coefficient value	Strength of the relationship
0.0	Missing connection
0.0 – 0.1	Very weak connection
0.1 – 0.3	Low connection
0.3 – 0.5	Moderate relationship
0.5 – 0.7	A significant relationship
0.7 – 0.9	A strong connection
0.9 – 1.0	A very strong connection
1.0	Functional link

1. Age category of pregnant women up to 20 years.

- correlation between the age of the pregnant woman up to 20 years and bacteriuria: $R = 0.561$ (significant relationship);

The result of statistical methods proves a significant relationship in the age group up to 20 years and the presence of bacteriuria from laboratory tests

- correlation between gestational age up to 20 years and antibiotic treatment: $R = 0.541$ (significant relationship);

The above results are also confirmed by the significant relationship of the need to apply antibiotic treatment in the same age category.

- correlation between gestational age up to 20 years and left hydronephrosis: $R = 0.506$ (significant relationship);

- correlation between the age of the pregnant woman up to 20 years and operative treatment: $R = 0.501$ (significant relationship).

We found a significant relationship in the subgroup up to 20 years of age and the presence of left-sided HN and the need for surgical treatment.

2. Age category of pregnant women 21 to 30 years:

- correlation between the age of the pregnant woman (21 to 30 years) and left hydronephrosis: $R = 0.823$ (strong relationship);

- correlation between the age of the pregnant woman (21 to 30 years) and right hydronephrosis: $R = 0.626$ (significant relationship);

- correlation between the age of the pregnant woman (21 to 30 years.) and bilateral hydronephrosis: $R = 0.585$ (significant relationship).

In the range of 21 to 30 years, we found a strong association in left-sided HN and significant in right-sided and bilateral localization.

- correlation between the age of the pregnant woman (21 to 30 years) and bacteriuria: $R = 0.761$ (strong relationship);

- correlation between the age of the pregnant woman (21 to 30 years) and antibiotic treatment: $R = 0.813$ (strong relationship);

- correlation between the age of the pregnant woman (21 to 30 years) and surgical treatment: $R = 0.724$ (strong relationship);

- correlation between the age of the pregnant woman (21 to 30 years) and the period of pregnancy (after the 20th week): $R = 0.721$ (strong relationship);

The result showing the strong correlation between these pregnant women and the presence of bacteriuria, antibiotic treatment and surgery is impressive.

- correlation between the age of the pregnant woman (21 to 30 years) and the period of pregnancy (up to the 20th week): $R = 0.636$ (significant relationship);

- correlation between gestational age (21 to 30 years) and CRP: $R = 0.602$ (significant relationship);

In relation to this age category and CRP, a significant relationship was proved, as well as a period up to 20 years.

3. Age of the pregnant woman (31 to 40 years)

- correlation between the age of the pregnant woman (31 to 40 years) and left hydronephrosis: $R = 0.767$ (strong relationship);

- correlation between the age of the pregnant woman (31 to 40 years) and the period of pregnancy (after the 20th week): $R = 0.732$ (strong relationship);

- correlation between the age of the pregnant woman (31 to 40 years) and bacteriuria: $R = 0.736$ (strong relationship);

- correlation between the age of the pregnant woman (31 to 40 years) and antibiotic treatment: $R = 0.781$ (strong relationship);

Mathematically, we proved strong relationships in the 31 to 40 age subgroup. Namely: in relation to left-sided HN, after 20 years, presence of bacteriuria and applied antibiotic treatment.

correlation between the age of the pregnant woman (31 to 40 years) and the period of pregnancy (up to the 20th week): $R = 0.683$ (significant relationship);

- correlation between gestational age (31 to 40 years) and right hydronephrosis: $R = 0.601$ (significant relationship);
- correlation between the age of the pregnant woman (31 to 40 years) and bilateral hydronephrosis: $R = 0.673$ (significant association).
- correlation between gestational age (31 to 40 years) and CRP: $R = 0.593$ (significant relationship);
- correlation between the age of the pregnant woman (31 to 40 years) and surgical treatment: $R = 0.666$ (significant relationship);

Significance of the relationships was proven for right-sided and bilateral HN, up to 20 g.w., elevated CRP values, surgical treatment and administered antibiotic.

4. Age of the pregnant woman over 40 years.

- correlation between the age of the pregnant woman over 40 years and left hydronephrosis: $R = 0.581$ (significant relationship);
- correlation between the age of the pregnant woman over 40 years and bacteriuria: $R = 0.573$ (significant relationship);
- correlation between the age of the pregnant woman over 40 years and antibiotic treatment: $R = 0.536$ (significant relationship);
- correlation between the age of the pregnant woman over 40 years and surgical treatment: $R = 0.526$ (significant relationship).

In pregnant women over 41 years of age, associations were significant with left-sided CNS involvement, antibiotic treatment, and applied surgical drainage manipulation.

5. Pregnancy period up to the 20th gestational week

- correlation between the period of pregnancy up to the 20th g.w. and the degree of hydronephrosis: $R = 0.801$ (strong relationship);
- correlation between the period of pregnancy up to the 20th g.w. and bacteriuria: $R = 0.571$ (significant relationship);
- correlation relationship between the period of pregnancy up to the 20thg.w. and hematocrit: $R = 0.559$ (significant relationship);

- correlation between the period of pregnancy up to the 20th g.w. and hemoglobin: $R = 0.526$ (significant relationship);
- correlation relationship between gestation period up to 20 g.w. and CRP: $R = 0.505$ (significant relationship).
- correlation between the period of pregnancy up to the 20th g.w. and surgical treatment: $R = 0.521$ (significant relationship);

According to the period of pregnancy up to 20g.w., we found a strong relationship with the degree of HN, and significant ones with the presence of bacteriuria, the values of hemoglobin, hematocrit and CRP.

6. Pregnancy period after the 20th week of gestation

- correlation between the period of pregnancy after the 20th g.w. and the degree of hydronephrosis: $R = 0.832$ (strong relationship);
- correlation between the period of pregnancy after the 20th g.w. and surgical treatment: $R = 0.726$ (strong relationship);
- correlation between the period of pregnancy after the 20th g.w. and hematocrit: $R = 0.661$ (significant relationship);
- correlation relationship between the period of pregnancy after the 20th g.w. and CRP: $R = 0.632$ (significant relationship);
- correlation between the period of pregnancy after the 20th g.w. and bacteriuria: $R = 0.626$ (significant relationship);
- correlation relationship between the period of pregnancy after the 20th g.w. and hemoglobin: $R = 0.583$ (significant relationship).

In the cohort after 20 g.w., two main relationships are clearly demonstrated, namely with respect to the degree of HN and operative treatment.

7. Leukocytes

- correlation between leukocytes and surgical treatment: $R = 0.733$ (strong relationship);
- correlation between leukocytes and antibiotic treatment: $R = 0.712$ (strong relationship);

As expected, a strong relationship was confirmed in the correlation between leukocytes - operative treatment and the need for an antibiotic.

8. CRP

- correlation between CRP and surgical treatment: $R = 0.621$ (significant relationship);
- correlation between CRP and antibiotic treatment: $R = 0.593$ (significant relationship).

The relationship is significant when comparing CRP and operative drainage manipulation and CRP-antibiotic treatment.

9. Pain symptoms

- correlation between pain symptoms and surgical treatment: $R = 0.736$ (strong relationship);
- correlation between pain symptoms and antibiotic treatment: $R = 0.707$ (strong relationship).

Regarding pain symptoms, we reported a strong correlation between pain symptoms versus surgery and antibiotic treatment.

6.2. Regression analysis

Regression analysis measures correlation-type relationships and examines the form of the relationship between two or more correlated phenomena. It is established by means of modeling. The chosen model for describing the studied relationship must necessarily have a certain analytical (mathematical) form.

Regression analysis solves the following tasks:

1. Determining the form of the dependence between the variables with graphical and analytical methods;
2. Determination of the regression function and estimation of its parameters;
3. Verification of statistical hypotheses about the reliability of regression models and their parameters.
4. The verification of statistical hypotheses about the significance of the regression models and their parameters takes place in the following sequence:
5. Statistical test for the adequacy of the regression model - based on Fisher's F-test.

6. Statistical test for the significance of parameters in the regression model - based on Student's t-test.

7. Statistical test for the presence of autocorrelation in the residual component - based on the Durbin-Watson test.

The theoretical values of F, t and DW criterion are:

1. Theor. = 3.841

2. theory. = 1.653

3. dL = 1.65; dU = 1.69

These values are for all univariate regression models and are at a 5% risk of error.

Statistical hypothesis testing is analogous for all univariate regression models.

We will consider univariate regression models in which the variables are represented by static variance (metered) series statistics. We will mark the result variable with Y, and the factor variable with X.

An important point in regression modeling is the selection of variables (factor and outcome) to be included in the models. They should be reduced to the smallest possible number, i.e. only those that can be quantified and express stable relationships.

6.3. One-factor regression models

After processing the information at our disposal, the following one-factor regression models were obtained, meeting the necessary statistical requirements (Table 32).

Table 32. One-factor regression models

Model №	regression models	R ² .100	t	F	d
1	^	17,64	50,749 -3,048	9,506	1,93
2	$\hat{Y} = 34,1136 - 0,699X$	27,49	20,146 -3,603	12,981	1,96
3	^	33,64	6,552 5,185	26,887	2,02
4	^	31,14	-3,917 4,587	21,045	2,01
5	^	46,24	-6,168 9,017	81,308	2,11

$$Y_i = -24,1356 + 2,886X_i$$

Based on the obtained one-factor regression models, we can make the following generalizations and conclusions:

1. Increasing the age of the pregnant woman by one year leads to a decrease in CRP by 0.16 mg/dl;
2. Increasing the age of the pregnant woman by one year leads to a decrease in leukocytes by $0.7 \times 10^9/l$;
3. An increase in the degree of hydronephrosis by one degree leads to an increase in leukocytes by $0.18 \times 10^9 /l$;
4. An increase in the degree of hydronephrosis by one degree leads to an increase in temperature by $0.6 \text{ }^\circ\text{C}$;
5. An increase in CRP by 1 mg/dl leads to an increase in leukocytes with $2.9 \times 10^9 /l$.

7. Discussion of the results

Pregnancy is a state with qualitative and quantitative changes in the female organism that occur simultaneously with the growing fetus. One of the essential changes that occurs concerns the dilatation of the pyelocalyx system. The dominant opinion is that this state is an invariable part of the reorganization of the mother's organism at this delicate moment. The question of how far the norm of "physiological" HN extends and at what point active medical intervention is necessary is still relevant, despite numerous large-scale studies and discussions.

There is a unanimous opinion on the need for an individualized approach, multidisciplinary coverage of the problem and active examination and follow-up of pregnant women with symptomatic HN.

Asymptomatic HN does not require conservative or operative treatment. This population is subject to control follow-up in order to take the necessary conservative and/or operative measures in case of signs of complications.

Active screening for HN is recommended during the second and third trimesters of pregnancy, due to the significantly higher frequency of the condition during this period. The dependence of age and the development of dilatation of the renal cavity system is described in the literature.

ART technologies are one of the fastest growing fields in human medicine. Egg donation in ART programs has been actively implemented in clinical practice in the last two decades. In Bulgaria, this procedure is legally regulated by regulation N28 ,Kovachev E 2020.

Thanks to the success of modern ART technologies and the frequent pregnancies over 40 years of age, the need arose to include them in the examined group.

7.1. Demographic characteristics

According to the data from our survey, the age distribution of pregnant women with HN is as follows: 18.48% are under 20 years, 20-29 years are 42.94%, 30-39 years are 34.78%, and over 40 years are 3.80%.

Similar are the results of Oriji, P et al.2022, surveying 400 pregnant patients, 7% were in the age range under 20 years, 49% - 20-29 years, and over 30 years 44%.

Relatively widely discussed by different authors are the sides of kidney involvement.

A research team of Ngai H Yet al. 2013, published that right-sided CN is diagnosed in 47%, left-sided in 37% and bilateral involvement in 17%.

Another author, Blanco LT al. 2017, published data for 90% right-sided and in 67% left-sided, being absent bilaterally.

Our results also indicate a right-sided predominance – in 77.71% of all symptomatic cases, in 14.65% we observed left-sided involvement and only in 7.61% bilaterally. The ratio between right-sided, left-sided and bilateral HN was maintained as in the above studies.

Of interest are the results of the study of gestational age and hydronephrosis. We divided the pregnant patients into two subgroups: up to 20 g.w. and over 20 g.w. Of all 184 patients, 19.02% were up to 20 g.w., and in 80.98% we observed HN over 20 g.w..

In the most recently published study by Oriji, P et al. 2022, pregnant women are divided into three groups according to gestational age: first trimester - 14.3%, second trimester - 30.4%, third trimester 48.6%.

Similar results were reported by a team of Bayraktar Z. et al. 2021: first trimester - 10.5%, second trimester - 47.6%, third trimester 41.8%.

In the analysis of the last two studies and grouping of pregnant women up to 20g.w. and after 20 g.w. results close to ours are obtained. The differences in the percentage ratios are due to the different way of separating the surveyed group.

According to the degree of PCS dilatation, the literature sources show conflicting data, depending on the ultrasound classification. Saylam

B. et al. 2021 published that of the group of patients examined, 58.8% had 1st degree HN, 2nd grade HN – 33.3%, and 3rd grade – 7.8%.

Oriji, P et al. 2022, subdivides HN into mild, moderate, and severe dilatation. They further specify that the mild degree corresponds to the 1st and 2nd degrees, the moderate degree corresponds to the 3rd degree, and the severe degree corresponds to the 4th grade according to the SFU classification. The data of the study indicate that a mild degree is observed in 45% (1st and 2nd degree), a moderate degree in 40%, and a severe degree in 13%

Our obtained results are close to those published by Saylam B. et al. 2021, namely 1st degree - 43.48%, 2nd degree - 48.91%, and we reported patients with 3rd degree in 7.61% of the examined pregnant women.

7.2. Pain

One of the most common symptoms for which a doctor's consultation is sought is pain. Its characteristics are different, determined by the cause, the speed of the changes that have occurred, and last but not least, due to the anatomical changes during pregnancy.

In cases with UUT obstruction, the pain is localized in the lumbar region ipsilateral to the obstructed kidney and is unilateral. Its strength and character depend on the degree and speed of the obstruction. Patients often define it as sharp, cutting, colicky, sudden onset or the type, weak, but for a short period reaching a high intensity. Irradiation is more commonly along the course of the ipsilateral ureter or may be parainguinal to the inner thigh and labia majora. Dysuric manifestations are also described by patients as pain.

Dell'Atti et al. 2014, described the pain as “flank pain” and reported a frequency in 63.0% of their patients.

According to another collective, the pain sensation was registered in 89.0% of pregnant women.

Ciciu et al. 2022, detailed pain symptomatology using a subjective complaint severity scale. In the presented data, severe pain is reported - 17.24%, moderate - 36.21% and weak lumbar pain in 13.79%. The total percentage of pregnant women with pain is 67.24%.

According to the results we obtained, we observed pain as a symptom in 45.11% of cases, or 83 patients. The percentage difference is probably due to the differentiation of the symptom from renal origin during the diagnostic process, with the aim of accurate assessment and subsequent treatment.

Over a one-year period and 51 observed singleton pregnancies Farr A. et al. report pain symptoms in 64.7% of right-sided HN, 13.7% - in left-sided involvement and in 21.6% of pregnant women with bilateral involvement.

Analysis of our results indicated that pain prevailed approximately equally in right- and left-sided HN, 43.36% and 48.14%, respectively, with a slight predominance for left-sided involvement. In bilateral HN, pain symptoms were present in 57.14%. Our reported results and their distribution according to the side of involvement confirm the conclusions drawn by other scientists that pain does not correlate with specific unilateral or bilateral involvement or the degree of manifestation. Therefore, in the presence of it, the main point is the initial ultrasound examination for evaluation and diagnostic confirmation of its origin.

Of interest is the fact that in some of the patients we observed, reporting a bilateral pain sensation, it was found unilateral by US, and vice versa, with US data of bilateral dilatation, a subjective sensation of unilateral pain or even a mention of mild lumbar discomfort. Even more impressive were the rare cases of pain sensation on the contralateral unaffected side. These exceptions are probably due to the radiating characteristic of flank pain, which at the acute moment of occurrence is difficult for some pregnant women to localize it in specifics. The subjectivity of pain as a complaint also influenced the results obtained. Similar reports were found in other studies that subjectivized the symptom present .

Depending on the degree of dilatation of the affected kidney and the presence of pain, we found that in 34.94% of the patients complained of pain in the 1st degree of HN, in the 2nd degree of HN - pain was defined in half of the pain subgroup ie. 50.60%, and in the 3rd one, only in 14.46% of cases.

Farr A et al. 2017 evaluated the pain on a 10-point scale and found that the intensity was 7.4 ± 2.5 for the 1st degree of HN, 7.7 ± 2.1 for the 2nd degree, and 7.6 ± 2.2 for the 3rd degree. The pain is of the highest intensity in patients with 2nd degree HN. Our data support the above opinion.

Our results are comparable to those reported by Farr A et al. 2017 that there is no correlation between the degree of maternal hydronephrosis and pain intensity. This fact makes diagnostic evaluation difficult. The conclusion we can also confirm is that in pregnant women with acute pain in the lumbar region, an ultrasound examination of the kidneys is recommended, regardless of the intensity of their pain.

7.3. Temperature

The fever index in these patients is also the subject of studies by many research teams. The data of M Mandal D et al. 2019 indicated that 33.33% of complicated hydronephrosis during pregnancy were febrile.

From the obtained results of those who passed through our treatment units, febrile over 38.0⁰C were 5.98%, and in the range $\geq 37.0^0\text{C}$ and $\leq 38.0^0\text{C}$ were 8.7%, afebrile were 85.33% of the cases.

The differences in the results obtained are based on the number of patients studied, in our study there were 184 compared to that of M Mandal D et al. 2019 – 33 "subjects".

Regarding the correlation of the body temperature value and the age characteristics of pregnant women, as well as a comparative analysis with the gestation period, we did not find literature data for comparison.

From the obtained results, we can summarize that the group of patients under 20 years of age with subfebrile and febrile episodes are the most frequent, respectively 14.71% and 11.76%, followed by the age range of 21-30 years subfebrile 6.33% and febrile in 7.59%. And the group without febrile data are over 40 years old. It is possible that the last result has a null value due to the small number of available pregnant women responding to our study. The general downward trend in this indicator is probably also due to the better follow-up of pregnant women over 30 years old due to the significant increase in the frequency of risky pregnancies. This, in turn, necessitates more frequent consultations and examinations, which may lower the risk of uroinfections and fever as a symptom.

Additionally examining pregnant women according to the period of pregnancy, we have proven an increase in body temperature above 37.0⁰C in only one patient up to 20 g.w. (2.85%) and in 17.45% of pregnancies over 20 g.w. The latter fact indicates an active search for markers of inflammation, one of which is febrility, preferentially in the second half of pregnancy.

Very often pain is combined with fever. Saylam B. et al. 2021 reported that 19.6% of 120 pregnant women examined had simultaneous pain and fever without mentioning the limits of fever. The results of our cohort of pregnant women for a similar period, regarding the combination of pain and temperature, indicate that in 30.12% we reported, in addition to the subjective sensation of pain, and increased temperature values above 37.0 C. We would summarize that the results are close in essence, and the available percentage difference is due to the subfebrile women entering our result. The latter were included with the aim of early detection of the presence of an inflammatory process of renal origin and timely treatment.

7.4. Vegetative symptoms

Vegetative symptoms have various manifestations and are among the main reasons leading pregnant women to a doctor's consultation. The most common manifestation is nausea and vomiting. A number of publications mention the presence of various autonomic symptoms, but without specifying correlations and frequency .

The data we received show that 7.07% of the total number - 184 pregnant women had evidence of vegetative symptoms, of which 6.52% of the same had both vomiting and pain. Following the course of their treatment, we found that in more than half (66.67%) operative treatment was applied in connection with the symptoms not affected by conservative therapy.

Thakur et al. 2020, published similar summary data regarding nausea and vomiting (9% autonomic symptoms).

This trend outlines the prediction of the course of treatment in the presence of the combination of symptoms, namely autonomic symptoms and pain.

7.5. Arterial hypertension

AH is a non-specific indicator of HN in pregnant women. Wanner C et al. 1987 reported arterial hypertension in 20% of CH cases, and Abbasi et al. 2020 reported a 35.1% incidence of AH (21,270).

Another team did not find a correlation between the values of AH and the presence of HN.

In processing our database, we found an overlap with Bayraktar Z data, as AH was present in 13.59% of cases. This fact correlates partly with the statistics of preeclampsia and it is difficult to differentiate whether the presence of HN is the cause of AH or the developing PE is concomitant with HN. In case of symptomatic HN and a violation of the filtration function of the kidneys with proteinuria, the doubts about the initial violations are even greater.

7.6. Laboratory results

Laboratory results were the next major component subjected to survey and statistical processing.

Since one of the most frequent complications of HN in pregnant women is the occurrence of uroinfection, the acute-phase inflammatory markers CRP and leukocytosis were the main parameters studied, due to their important clinical significance in terms of therapeutic behavior.

The reference limits of our laboratory for leukocytes are $4.0-10.0 \times 10^9/l$. We divided the patients into three subgroups, given the obtained results, to examine the dependence of leukocytes and the presence of UT inflammation. Given the physiological leukocytosis, which can be considered as an expression of physiological changes in the blood, in addition to the values of leukocytes, we also recorded the value of CRP (another sensitive marker for an inflammatory reaction in the body). The normal limit for CRP that we reported was below 5 mg/l.

From the obtained results, we found that 38.59% of all patients had Leuc $<10.10^9 /L$, nearly half or 45.11% Leuc $\geq 10.10^9/L$ and $\leq 15.10^9/L$, and Leuc $>15.10^9/L$ were 16.3% of the cases.

Mutiso et al. 2015 in a literature review with included clinical cases published values of leukocytes: in the first case of complicated CH and data on leukocytes in the norm, the second case with leukocytes $12.26 \times 10^9/l$ and the third with values $17.6 \times 10^9/l$, i.e. leukocytes as an independent indicator are not significant for existing complications.

DellAtti L at al. from 2014 over a 5-year period noted too wide limits of leukocytosis - $10.0 \times 10^9/l$ to $20.0 \times 10^9/l$ in 50% of patients with HN.

Exported data for leukocyte reference values from Abbassi-Ghanavati M. Et al. 2009 confirms our conclusion that during pregnancy, leukocytes as an independent marker are not sufficient for a definitive diagnosis.

Acute phase proteins, synthesized by the liver, are a protective mechanism of the body in case of an inflammatory incident, trauma or certain malignant diseases. CRP is a reagent of the acute phase and is significantly more sensitive than the other components of hematopoiesis.

Literature sources recommend its use alone to evaluate the response to the applied treatment and less to predict the type of therapy in symptomatic HN.

N'Gamba et al. found elevated CRP values in 31.7% of 82 pregnant women with symptomatic HN, which they rejected as a predictor of existing urolithiasis.

A study by Ercil H et al. 2017 published data that CRP levels were statistically significant in the second and third trimesters in the surgically treated group compared to the conservatively treated group. They prove significantly higher values of leukocytes and CRP in surgically treated pregnant women who terminated their pregnancies prematurely.

From the three-year study we conducted examining pregnant women with CH data, we found that 60.33% of women had CRP <5 mg/L, 22.28% had CRP values ≥ 5 and <10 mg/L, 6.52% of the cases were with CRP ≥ 10 and ≤ 20 mg/l, and 10.87% were with CRP >20 mg/l. Summarizing the latter, we found that nearly 40% have elevated values of the acute-phase marker CRP, which is close to the published values in the available database.

Based on the results obtained regarding the frequency of simultaneously elevated CRP and leukocytes (CRP >5 mg/l and Leuc >10.10⁹l), we found that 58 pregnant women (31.52%) had elevated values of both at the same time. Of this population group, nearly 50% were successfully treated conservatively, and the remaining half required surgical drainage. This confirms the finding of Tsai YL et al. that the laboratory constellation of elevation of leukocytes and CRP is more suitable for monitoring the adequacy of conservative therapy than the initial choice between conservative and operative treatment.

Another laboratory indicator that we studied was the value of nitrogen bodies and in particular creatinine. The reference values on which we are based are 44.0-97.0 $\mu\text{mol/l}$. The level of the latter directly correlates with UT function. A rise in creatinine values is a clear signal of impairment of renal function and initiation of renal failure. In the definition of acute kidney injury, it is precisely defined that, in addition to oliguria, with data on the rise of serum creatinine by more than 0.3 mg/dL in a 48-hour interval, we can definitively conclude the presence of HN. DellAtti L at al. from 2014 noted that in 36.11% of cases they reported an

increase in serum creatinine in the observed cohort, and in 50% a laboratory constellation for leukocytosis.

Our results demonstrate creatinine values above 97 $\mu\text{mol/L}$ in three patients, or 1.63% of the total population. It is noteworthy that these patients also had elevated CRP values and leukocytosis. In them, surgical drainage manipulation was applied, with the aim of improving kidney function and preserving the pregnancy close to term.

Although a small sample with a similar constellation, we can summarize that the presence of the triad: leukocytosis, increased CRP and creatinine, in pregnant women with HN and far from the term indicated for surgical treatment.

According to the distribution of cases with high creatinine values and side of HN, we found that in 1.39% we diagnosed right HN and in 7.14% with bilateral HN. These results are related to the reduction of the total renal function in the bilateral process.

The direct relationship between renal disorders and the manifestation of anemia has been extensively studied. We used the hemoglobin indicator as a baseline in the analysis of the constellation of the anemic syndrome. We take the generally accepted 110g/l as the lower limit of hemoglobin levels. Our results show evidence of anemia of varying severity in 50% of all 184 pregnant women. In 28.26%, Hb levels were in the range of 100-10⁹ g/l, 20.65% had a pronounced anemic syndrome, and 1.09% had Hb levels below 80 g/l.

Abbasi et al. 2020 published data on the presence of anemia in over 80% of the examined pregnant women, with more than half of them having a moderate to severe form.

Wing DA compared pregnant women with pyelonephritis and those without pyelonephritis and found that women with evidence of pyelonephritis were more likely to develop anemia 26.3% of the time, and healthy women at a dramatically lower rate of 11.4%.

In the studied group of patients, the occurrence of anemic syndrome can be explained by the disorders in erythropoietin synthesis. Recent facts prove the role of the kidneys in maintaining hematopoiesis during pregnancy.

In addition, statistical methods proved a significant correlation between the period of pregnancy, the presence of HN and manifestations of anemia.

The analysis of the literature data and the obtained results shows the significance and importance to screen, diagnose and treat UT disorders in a timely manner, in order to prevent complications for both the mother and the fetus.

Urinalysis is the other key laboratory parameter that we monitored in patients with symptomatic HN. Urinalysis is a basic test in the diagnosis of both asymptomatic bacteriurias and those associated with an active inflammatory process. Their control is extremely important regarding the outcome of the pregnancy and the well-being of the mother and fetus. All patients with bacteriuria or pyuria must undergo a microbiological analysis of the causative agent and an antibiogram reflecting its sensitivity.

The patients examined by us were tested for the presence of protein in the urine using test strips. Nearly half of the cohort group tested positive, or 48.91%. To differentiate the quantitative loss, the positive ones were subjected to a quantitative study at 24 hours. urine, in order to distinguish physiological proteinuria, the upper limit of which is 300 mg/24h. Recent results have deepened the differential diagnosis regarding cases with preeclampsia.

A number of studies recommend screening for proteinuria from early pregnancy in order to differentiate groups with renal impairment from those with developing preeclampsia. For more accurate criteria for the advance of preeclampsia, the ratio of protein:creatinine is taken as a pathological value above 30 mg/mmol.

The latter data were used by us to select the group with renal disease, but not the women with preeclampsia and concomitant HF. According to this criterion, we do not find a correlation with HN due to difficulties in selecting the diagnostic groups and a combination of pathological entities.

The presence of bacteria in the urine is an indicator for deepening the urine tests, regardless of clinical symptoms. Urostatics during pregnancy increases the capacity of the urinary tract by about 200-300 ml, which increases the risk of infection. Urine culture is the diagnostic test of choice.

In our study, all patients with bacteriuria and/or pyuria underwent microbiological tests to evaluate the microorganism and its antibiotic sensitivity. Out of all 184, there were 41 with data on bacteriuria, i.e. 22.28%.

We analyzed the group with leukocytes $>10 \cdot 10^9 /L$ and the data on the presence of bacteriuria, where we found that 36.28% of patients with elevated leukocytes also had bacteria in their urine. With data on uroinfection were 22.28% of the total cohort.

According to the age characteristics, we found that uroinfection is most often observed in the group under 20 years of age, and with increasing age, the frequency decreases - 21.52% in the range of 21-30 years, 17.19% in pregnant women 31-40 years old and is the lowest in pregnant women over 40 years. -14.29%.

The results of our study, according to the microbiological constellation, indicate that the highest percentage of Gram (-) isolates is 19.02% of all 184 women, the second most frequent are Gram (+) - 2.72% and 0.54% of the total group is isolated *Candida albicans*.

E.coli prevails in 80.0% of our bacteriuric patients. *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Citrobacter koseri* were equally distributed at just over 17% and a single isolate of *Proteus mirabilis*.

Gram (+) bacteria were demonstrated in 12.20% of the 41 bacteriurias present. The following pathogens of uroinfection were confirmed from this subspecies: *Streptococcus Alpha-hemolytic*, *Staphylococcus Saprophyticus* and *Aerococcus urinae*.

When processing the information, we excluded cases of contamination that were either insignificant or their cultures remained sterile.

From the analysis of the received information and the studied literature, we confirmed the predominance of Gram (-) microorganisms inflaming the urinary tract of pregnant women, with a predominance of *E.coli*.

Of interest is the comparison with isolates from cervical secretions in 2018, according to data from the Bulgarian Association of Microbiologists, in which *E.coli* predominates in 27.13%. Whether these results are due to contamination from the urinary tract or are the primary focus of the microorganism is a matter of further study and analysis.

Kalinderi K et al. 2018 reported *Escherichia coli* isolates in up to 86% of cases of symptomatic and asymptomatic pregnant women, and the remaining approximately 14% reported the presence of *Staphylococcus saprophyticus*, *Klebsiella* spp, *Enterobacter* spp, *Proteus* spp, *Enterococcus* spp, group B *Streptococcus* from urine culture studies. The team clearly defined the risk factors associated with bacteriuria, namely: previous urinary tract infections,

anatomical variations of OS, functional abnormalities (HN), diabetes mellitus, sickle cell anemia, low socioeconomic status .

The prevalence of asymptomatic bacteriuria during pregnancy is about 10%, and according to our data, it is 7% of the total group. Lower serum levels of interleukin-6 and serum antibody responses to E. coli antigens that occur during pregnancy are associated with an increased incidence of asymptomatic bacteriuria during pregnancy .

The conclusion we made was that with increasing age, perinatal care and the responsibility of patients regarding pregnancy increase. From the latest data available, over 7,000 pregnant women per year are unmonitored. A large percentage of them are from socially vulnerable communities with difficult access to health care. Data from NSI for 2019 indicate a continuing trend for a prematurity rate of 10.01% associated with perinatal and postnatal morbidity and mortality. The latter are directly related to congenital infection, which in no small percentage is due to urinary pathology.

7.7. Imaging methods of research

Abdominal ultrasound is the most common imaging test used during pregnancy. In addition to pregnancy assessment, ultrasound is also a basic method for OS screening. Its routine use provides important information about the kidneys - their anatomical changes, location of HN, degree of echogenicity of the renal parenchyma, presence of tumor masses, inflammatory component, stones in the kidneys and ureter. Other imaging methods, such as MRI, can be used, but ultrasound is the most widely used due to the fact that there is no radiation for both the mother and the fetus. An important factor driving its frequent use is its wide availability and low cost .

Some authors, before performing the ultrasound examination, recommend qualitative evaluation of the urine by means of test strips, in order to confirm or reject proteinuria and glycosuria .

According to the various literature sources, the specificity of ultrasound of the UTS in pregnancy is between 86% and 90%, and the sensitivity of the method is significantly lower - between 24% and 34%. The authors report a lower diagnostic value in patients with accompanying calculus, especially in the middle third of the ureter. Emphasize difficulties in distinguishing between physiological HN and that due to existing calculus. Scientists have repeatedly emphasized that the results of abdominal sonography can be limited both by the

pregnancy and the habitus of the patient, by adjacent intestinal gases, and also by the experience of the sonographer .

In the present study, we performed ultrasound in all 184 pregnant women. This was a selection factor, including them in the study. In 100% of cases, we found HN in varying degree and side of involvement. One patient presented with an MRI that was performed in an outpatient setting and confirmed the ultrasound finding of HN.

The data regarding the period of pregnancy proved the data from the literature that HN is more frequent over 20 g.w., in our case 80.97% against 19.03% for HN before 20 g.w.. More frequent right-sided involvement was also confirmed.

To determine the degree of HN, we used the Ultrasound classification system –SFU, modified in 2007 by Onen (1993), which defines changes in four degrees.

When analyzing the results in relation to the duration and degree of HN, we found that the 1st degree HN is observed more often up to 20 g.w.. - 71.43%, while in the second half of pregnancy it is 37.58%. The second degree of HN dominates after 20 g.w.. in 53.69%. The third degree was reported in fewer cases, with those in the second half of pregnancy again prevailing.

The available data correlate with those reported in multiple studies regarding the degree of HN and are confirmatory.

Given the significantly higher number of pregnant women with HN in the second half and the greater frequency of significant CH, we concluded that screening for the presence or absence of CH is appropriate to be performed in the period around 20 g.w.. i.e. in the period of fetal morphology 18-22 g.w..

7.8. Treatment

All symptomatic HN in pregnant women, regardless of the onset, age and duration of pregnancy, are subject to treatment. Due to the increased risk of pregnancy and its outcome, they are subject to hospitalization. The main methods of treatment are conservative and/or operative.

Conservative therapy includes saline solutions, analgesics and antibiotics. In the case of ARF, septic condition, shock or unresponsiveness to medical treatment, operative methods are resorted to. These most commonly include DJ stenting or percutaneous nephrostomy.

In pregnant patients who present with pain and hydronephrosis, it is very important to distinguish physiologic from pathologic hydronephrosis in terms of providing appropriate treatment .

The specific treatment method for symptomatic hydronephrosis during pregnancy is still debatable .

In pregnant women with evidence of symptomatic HN, the first method of choice in determining the therapeutic plan is conservative treatment. The main components are pain medication, rehydration and, if indicated, antibiotic therapy. Depending on the general condition of the patient, the presence of vegetative symptoms, fever, contractions and/or an increased risk of premature birth, the therapeutic plan is supplemented with medications suitable for the period of pregnancy.

Saylam B. et al. 2021 report success from conservative therapy in over 96% of cases, and 3.9% of patients had a symptom complex of acute pyelonephritis up to urosepsis. They recommend ureteral catheterization with a DJ stent in therapy-refractory cases and emphasize its effectiveness and safety .

Another study from 2021. of Demir et al. advise prompt surgical treatment, in all cases of refractoriness to conservative treatment and/or existing renal damage. The authors emphasize that urethral drainage manipulation is indicated for the degree of HN 3 and 4. The data of the study determined the parameters of the clinical indicators according to which they determined the conservative and operative method of treatment. From the analysis of their results, they reported a positive correlation with surgical intervention (DJ stent) and the degree of HN, the anterior-posterior diameter of the pyelocalyx system especially in the second and third trimester, creatinine values, the strength of pain sensation, positivity of urocultures .

Ercil H et al. 2017 determine pain and kidney damage as leading factors in the choice of treatment. In the study, they observed an increase in CRP, leukocytes, a high immediate pain rating, and preterm birth in the group treated with DJ urethral catheterization and percutaneous nephrostomy .

A study by Fainaru et al. reported that 73% of patients with maternal hydronephrosis had mild hydronephrosis and responded well to conservative treatment. They also highlighted good perinatal outcomes as a pregnancy outcome, but also that 7.1% of symptomatic patients with moderate or severe hydronephrosis did not respond to conservative treatment .

Damir Pus`kar's co-authors observed symptom regression after an average of 5 days of drug treatment in symptomatic pregnant HN .

A Fainaru, 2002 reported that in 92.9% of the pregnant women with HN observed by them, within 2-5 days they observed a remission of symptoms after conservative therapy .

Fluctuations of conservative influence according to the literature review are in the range of 70% to 96%. The latter results are due to the fact that some studies excluded low-grade HN and their therapeutic effect .

A study conducted by Angulo et al. published data indicating significant parameters: urolithiasis and renal colic in pregnant women requiring ureteral drainage manipulation.

And Ercil et al. add antibiotic resistance in pyelonephritis and HN as an indication converting the medical approach to operative .

About 20-30% of ureteral calculi are not expelled spontaneously and require active medical intervention. Method of choice is ureteral DJ stent or percutaneous nephrostomy. Both approaches aim for rapid decompression of the UTS.

When conducting our research in the Department of Pathological Pregnancy of SBAGAL "Prof. Dr. D. Stamatov" Varna, we performed the conservative treatment. If the symptoms were not affected, after consultation with a urologist, the pregnant women continued their therapy at the Urology Clinic at the "St. Anna" city of Varna. Clinical and statistical data indicate that we were able to conservatively influence 85.87% of cases (158 women) who were discharged and followed up to the delivery period and in the early postpartum period. Urological manipulation was required in 26 patients (14.13%). The average period for reporting effectiveness from the applied conservative treatment was 2-5 days.

The results we obtained are comparable to those reported by the literature sources and are of a confirmatory nature.

We examined the diagnosed extent of HN and subsequent medical treatment. The analysis shows that 93.75% of patients with 1st degree HN were successfully treated conservatively,

83.33% with 2nd grade HN, and 57.14% with 3rd grade HN. These data correlate with the general opinion of a number of researchers, one of which is Fainaru O et al. 2002, namely in the 1st degree - 73.2%, in the 2nd degree - 19.2%, and in the 3rd degree - 7.6% . Therefore, the higher degree of HN is less responsive to medication and surgical interventions are more often required.

The data on the relatively smaller percentage of pregnant women with high-grade HN are encouraging, but the severe clinical course and therapeutic difficulties should be well known.

We deepened the study in the drug therapy we administered. We found that in almost half we administered antibiotic treatment and analgesia (42.93%; 45.11%), we administered antipyretics in 14.13% of cases, and the entire cohort administered antispasmodic and tocolytic treatment in parallel with rehydration. Puskar D et al. published data on a 94% response to combined antibiotic and analgesic treatment. From the data thus presented, the conclusions that followed are: antibiotic treatment covers almost half of the group, which, based on the antipyretic and the available bacteriuria (41 patients), is required more often. To evaluate the indications, we used, in addition to the clinical picture and the urine test, the acute-phase inflammation markers.

During pregnancy, antispasmodic/tocolytic treatment plays a major role in both conservative and operative approaches.

In order to differentiate the period of pregnancy in which AB treatment is more often required, we compared the cases up to 20 g.w. and after 20 g.w.. Given the results for uroinfection up to 20 g .w.and after 20 g.w., it was proven that AB treatment is more often indicated in the second half of pregnancy (51.00%). This fact is due to the frequent appearance of HN after 20 g.w.. and the resulting conditions for uroinfection - symptomatic or asymptomatic.

The summarized literature data and our frequency distribution results are identical to those regarding UTIs and gestational age.

The reference points from the clinical-laboratory constellation, on which we included AB-treatment, were temperature $>37.0^{\circ}\text{C}$ - 32.91%, CRP >5 mg/l - 88.61%, Leuc $>10.10^9/\text{L}$ - 75.95%. From the indicated data, it is clear that the most significant are the presence of leukocytosis and elevated CRP, which correlates with the presented data of Ercil H et al 2017.

Analyzing the pain symptoms and AB therapy, it was proven that in patients with pain in 62.65% it is necessary to include it.

The percentage result when combining the following parameters is impressive: CRP>5 mg/l, Leuc>10.10⁹, creatinine>97 μmol/l and the cases with AB treatment - 43.48%. This raises new questions about the presence of CH and associated infection, along with laboratory evidence of impaired renal function. Due to the relatively small number of cases (10 pregnant), we could not draw a conclusion specifically regarding the conservative treatment, since some of these patients were converted to the operatively treated group.

From the published literature data on the type of treatment according to the side of symptomatic HN, our results confirmed the opinions and proved that conservative treatment is more often required for right-sided localization - 89.51, and for left-sided involvement in 77.78%, the lowest (64.29%) is success rate in bilateral HN. A counterpoint to the above are the results in the subgroup of those treated surgically, i.e. most often with bilateral involvement 35.71%, and the lowest percentage with right-sided HN - 10.49%. In support of this, Fainaru O. et al. also described that 86.5% of right-sided HN responded to conservative treatment, 13.5% of left-sided HN also responded well to medication, and all 100% of bilateral ones underwent surgical drainage manipulation .

This is probably due to an underlying undiagnosed pre-pregnancy pathology, such as calculi of the UT, abnormalities of the UTS , etc. combined with HN.

Frequency distribution of conservatively and operatively treated pain in relation to the symptom also has its important role in the analysis of the method and efficiency in the compilation of the therapeutic algorithm. A number of studies have used a recent pain rating system and strongly state its importance. Our results support the above. According to Ngai et al. In 2013, lumbar pain prevailed in 23.77% of pregnant women who required surgical treatment.

And Tsai YL et al. 2007 reported the need for surgery in 16% of patients with pain.

Our analysis shows that of all examined pregnant women, 14.13% underwent surgery, and compared to the subgroup with pain symptoms - in 31.33%. Given the lack of specification in the literary sources of the control groups and the reported results, we can conclude that the data we obtained are completely comparable to the above. The data are conclusive that 100% of the surgically treated pregnant women were in pain, against 36.08% of those from the conservative group.

The latter results could be used for prognostic purposes even during the taking of the anamnestic data, ultrasound and establishing the country and degree of HN. We would expect refractoriness to conservative treatment in complicated (pain symptoms) high-grade bilateral HN.

From the analyzed data, it was repeatedly emphasized that the method of choice for surgical treatment is ureteral stenting - antegrade or retrograde. Tsai YL et al reviewed the effectiveness of DJ drainage intervention and proved it as the method of choice . They explicitly emphasize the importance of conservative approaches, due to the available complications of manipulation, the postoperative period and the need for anesthesia.

Bulgarian authors collective 2022 also reported that the main methods of emergency decompression are retrograde ureteral stenting and percutaneous nephrostomy, emphasizing that the choice of operative treatment method depends on the etiological factor and the general condition of the patient .

An African study on the effectiveness of treatment of renal colic in pregnancy, mainly due to BCC, reviewed nine studies on the topic in detail. They report the advantages and disadvantages of temporary drainage, namely:

Advantages: minimal invasiveness, rapidity, ability to perform under local anesthesia, without exposure to radiation, reduction of pain, effectiveness in relief of obstruction and protection of renal functions. Ureteral stents and percutaneous nephrostomy are safe and effective during pregnancy. Timing of DJ stenting or PCN placement should consider gestational age, patient preference, and tolerability .

Disadvantages: Temporary drainage includes frequent replacement, multiple procedures, high cost, poor tolerance, dislocation, migration, risk of urinary infection, if replacement is necessary, the pregnancy is at risk and last but not least, these manipulations in some pregnant women are not definitive treatment, i.e. require surgery after birth. Other rare complications include hematuria, preterm birth, and sepsis .

RUS vs nephrostomy, which should be preferred? This question is always up for debate. Both have well-defined advantages and disadvantages and are equally effective for urinary tract decompression. In terms of infection, one study showed them to be equivalent . Recent findings suggest that both procedures are equivalent in terms of patient outcomes .

The clinical scenario for the operative approach directly depends on the availability of resources, experienced doctors and last but not least on the informed decision of the patient, given the delicate period of her life.

Utku Can et al. 2018 published data regarding the frequency of DJ stenting versus PNS in pregnant women with CKD. The results indicated a predominant preference for the DJ stent in 81% and in only 2% PN.

The main methods that we used for the surgical treatment of symptomatic HN are also RUS and percutaneous nephrostomy. Out of all 26 pregnant women undergoing invasive treatment, 25 of them, i.e. 96.15% underwent RUS and only in one case percutaneous nephrostomy was required. DJ stenting was preferred due to its advantages, namely placing it under ultrasound control ie. lack of radiation, ease of implementation in the second and third trimester of pregnancy and lack of need for an external collector system. The isolated case of percutaneous nephrostomy limits the possibility of comparing the two groups.

The data regarding the period of pregnancy and the surgical treatment that was carried out are categorical that in 100% of our patients, drainage manipulation was carried out in the second half of the pregnancy. The temperature indicator has equal weight and we do not observe a statistical difference in the subgroups above and below 37.00C. Leukocytosis prevailed in the surgically treated group compared to the conservative therapy group - 80.77% versus 58.23%. The total percentage exceeds 100%, as some of those managed conservatively converted to an invasive surgical method of treatment.

The results of the CRP values are particularly impressive. According to the obtained data, more than 92% of surgically treated pregnant women had CRP > 5 mg/l.

Ercil H et al., 2017. in the table of his study, he indicates an average value of Leuc=11.7x10⁹L in pregnant women treated conservatively and Leuc=15.0x10⁹L for those treated surgically.

The mean values of CRP are also corroborating – 12.2 mg/l for the conservative group and 19.6 mg/l for the operatively treated group (99). These data are comparable to those presented by us above and support the conclusion that with an increase in leukocytes and/or CRP, the number of operative interventions concerning HN increases. This places these markers as highly sensitive and treatment-specific.

We illustrated this trend with a deeper analysis of the data. Half (50%) of urologically operated pregnant women have Leuc > 10.10⁹/L and CRP >20.0 mg/l, which confirmed the analyzes presented in the scientific community about the significance of the indicators.

Summarizing the facts presented above, in 56.52% of the cohort we found the following confirmatory clinical-laboratory constellation for the imposition of operative manipulation: Leuc > 10.10⁹/L, CRP >5.0 mg/L and body temperature >37.0⁰C.

Ercil H et al., 2017. comparing two subgroups of conservative and operative treatment, reported that those treated surgically had Leuc > 15.10⁹/L, CRP > 18 mg/L and body temperature > 37.0⁰C in over 28%. The authors summarized the confirmatory nature of leukocyte and CRP and leukocyte values regarding the need for urological drainage manipulation.

CONCLUSION

In our practice, the most common reason pregnant women with symptomatic HN are hospitalized is pain. Along with uterine contractions, they are a serious diagnostic challenge.

The "sickness" often described by patients has too wide limits and tolerability. Localization does not definitively define the renal origin of the condition. Reflex excitability of the uterus is also a cause of pain.

The frequency of HN is clearly higher in reproductive age, namely 20-40 years. Physiological HNs are not a clinical problem until they become complicated. Data from the available literature confirmed that the right-sided localization is predominant, compared to the left-sided and bilateral ones. First degree of HN prevails in the first half of pregnancy, and second and third degree after 20 g.w.. Urine stasis is a serious prerequisite for the occurrence of infection. Its presence complicates pregnancy. In the largest proportion, the microbiological isolates are from Gram (-) microorganisms with a predominance of E.coli. Symptomatic or asymptomatic UTI requires active medical treatment. The constellation of fever and elevated inflammatory markers correlates with failure of conservative treatment, and often these pregnant women are referred for surgical intervention. Vegetative symptoms complement the symptom complex of kidney pathology.

The method of choice and of primary importance for the diagnosis of HN is ultrasound. Harmless, affordable and sufficiently informative means to prove the presence of UT dilatation.

The improvement of modern ultrasound devices, with the advent of digital technologies, allow a significant increase in image resolution.

Laboratory methods are the basis of the diagnostic approach. In addition to clarifying the condition, they are also used for follow-up and control during conservative treatment.

We determined the individualized therapeutic approach for each pregnant woman with symptomatic HN based on the following indicators:

- Information from medical records
- History and general condition data
- Duration of pregnancy and data on complications
- Age factor
- Accompanying diseases
- US – results by degree and side of involvement
- MRI results
- Laboratory parameters: PKC, CRP, biochemistry, blood sugar, ionogram, CAS, total protein, albumin, coagulation status, standard urine-sediment
- Microbiological examination of urine

Based on the above listed indicators and the available results, we observed the following therapeutic behavior.

1. In all pregnant women with symptomatic HN, we started conservative treatment:

- pain symptoms – analgesics
- uterine contractions - tocolysis, spasmolysis
- high pelvic score and risk of prematurity - corticosteroid prophylaxis of the fetus
- vegetative symptoms - antiemetics
- fever - antipyretics
- uroinfection – antibiotics

- anemia - iron preparations
- hypoproteinemia – FFP, human albumin
- for all – rehydration with water-salt solutions, vitamin therapy, phytotherapy
- AH – antihypertensive therapy

Reporting the results of the treatment between the second and fifth day!

2. We offered patients with an unsatisfactory response to the above treatment for surgical urological treatment. (ARF, threatening sepsis, 3-4th degree HN, bilateral HN, single functioning kidney) Methods of operative intervention:

- RUS – method of selection
- PNS

3. Definitive treatment for obstructive pathology after childbirth.

The correct treatment decision is a complex process and would hardly fit into the absolute framework of algorithms. In Figure 24, we have schematically illustrated the general principles that we followed in our daily practice for the diagnosis and treatment of pregnant women with symptomatic HN.

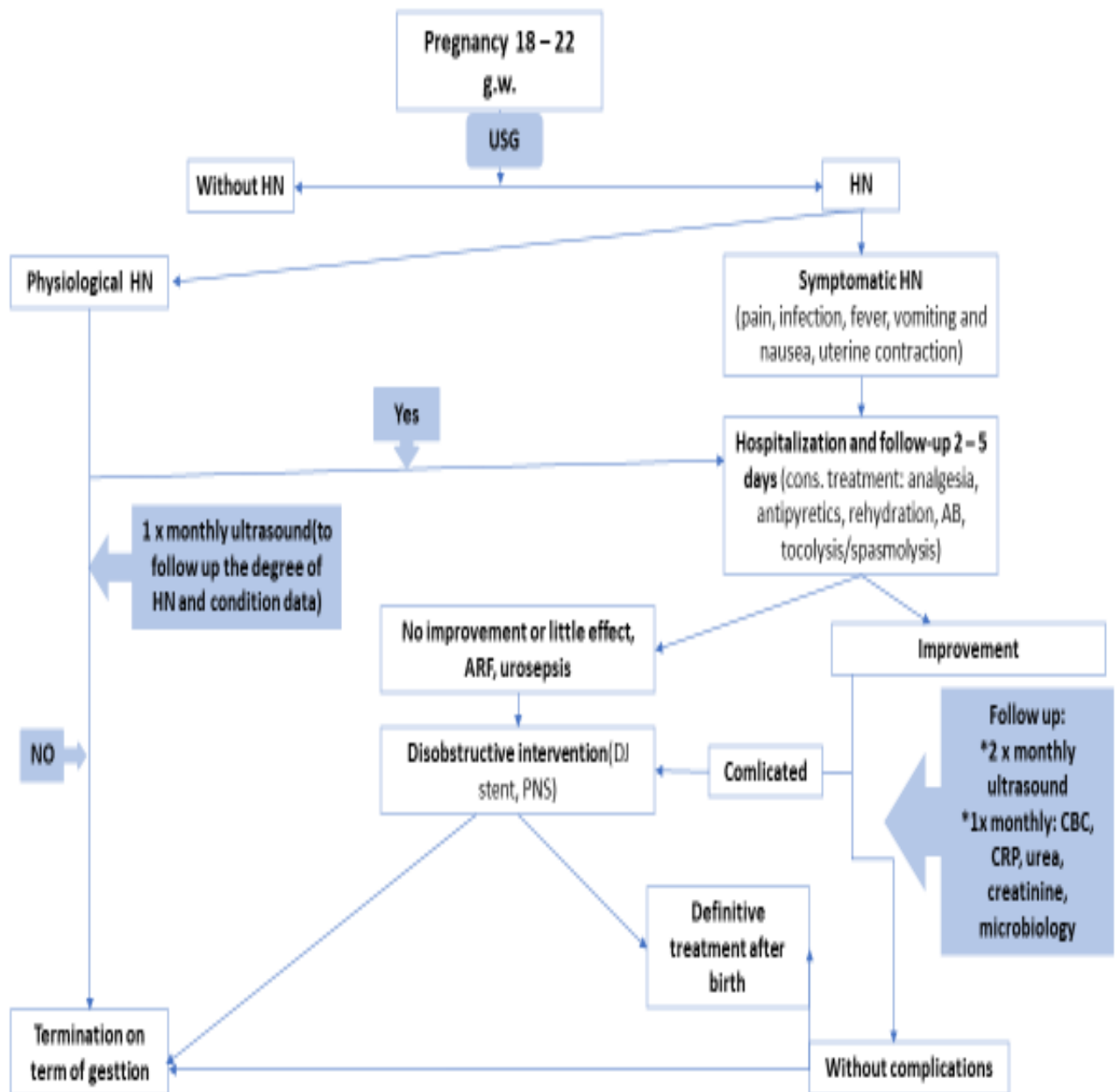


Fig. 24. Algorithm of behavior in pregnant women with HN

CONCLUSIONS

1. Screening and follow-up of pregnant women for UUT obstruction is recommended between 18-22 gestational age, to reduce the frequency of complications of both hydronephrosis and pregnancy.
2. Symptomatic hydronephrosis should be treated promptly and urgently. If the treatment is started on time, the conservative treatment is successful more than 85% of pregnant women cases. After discharge from the hospital, follow-up of the changes in the upper urinary tract should be continued.
3. The most common cause of complication of physiological dilatations of UUT in pregnant women, which necessitates hospitalization and active treatment, is infection of the urinary tract. The most common reason that pregnant women seek consultation is pain.
4. In the diagnostic plan, apart from the clinical data, the results of the laboratory tests CBC, CRP and nitrogen bodies are important, in combination with ultrasound they are the main guide for choosing the appropriate type of treatment.
5. The conservative treatment include the use of analgesics and antibiotics and it is most often required, in one with tocolysis/spasmolysis. The operative treatment demonstrate that the retrograde ureteral stenting is the method of choice.
6. The conservative method of treatment has a higher success rate in unilateral hydronephrosis compared to bilateral.
7. Operative treatment is necessary after consultation with a urologist in the case of: no effect/deterioration of the condition after 2-5 days of conservative treatment, severe general condition and threatening or developing urosepsis, septic condition, evidence of aggravated CRF and/or ARF. The relative indications are acute obstructive pyelonephritis with elevated two or more acute-phase inflammatory markers and bilateral symptomatic hydronephrosis.
8. Operative treatment is more likely to be applied in the second half of pregnancy and in bilateral high-grade hydronephrosis.
9. The analysis of our data proved the success of the proposed algorithm, according to which we carried out the hospitalization, diagnosis and treatment of pregnant women with symptomatic hydronephrosis.

DISSERTATION CONTRIBUTIONS

1. Original scientific and applied contributions

1. Symptomatic hydronephrosis in pregnant women was studied and analyzed for the first time in Bulgaria.
2. An original diagnostic and treatment algorithm for pregnant women with HN has been developed with the possibility of wide application in medical practice.

2. Contributions of a confirmatory nature

1. Analyzing the literature data and our own results, we confirmed that symptomatic HN during pregnancy is more common after 20 g.w.. and requires more frequent treatment.
2. It is confirmed that right-sided localization of HN in pregnant women is more common compared to left-sided and bilateral.
3. We proved that the main imaging tool for the diagnosis and follow-up of HN, regardless of the gestational period of the pregnancy, is the ultrasound examination.
4. It is confirmed that the most common causative agent isolated from urine, of complication with uroinfection hydronephrosis, is *Esherichia coli*.
5. We proved that in pregnant women with evidence of symptomatic XH, the presence of bilateral high-grade HN is associated with a higher incidence of ARF.

DISSERTATION RELATED PUBLICATIONS

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Kuchovski, Renal colic and pregnancy-risks and complications, journal Obstetrics and Gynecology, Vol 57, issue 5, 23-27, 2018

2. Dimitrova Z., E. Kovachev, K. Tsvetkov, T. Ganev, A. Sandulov,

Hydronephrosis during pregnancy, Journal of Obstetrics and Gynecology, Vol 58, Issue 4, 18-21, 2019

3. Sandulov A., D. Anakievski, Z. Dimitrova, PNS or ureteral stent for emergency deobstruction in hydronephrosis associated with gynecological malignancies, Sp "Urology and endourology", Voll27 issue 3, 55-63, 2021

4. Dimitrova Z., T. Ganev, A. Sandulov, Pregnant woman with hydronephrosis - a challenge in obstetric and urological practice, Sp "Urology and endourology", Voll 28 issue 2, 26-31, 202

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