

Algorithm for the Early Diagnosis and Management of Pregnant Women with Renal Pathology

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Abstract

The studies on the structure and dynamics of morbidity of kidneys in pregnant women performed in Baku in the period from 2009 to 2011 found that the following conditions had leading positions: chronic pyelonephritis (27.2%), renal hydronephrosis (14.8%) and eclampsia (12.0%). Specific weight of cystitis was 4.8%, urolithiasis - 3.2%, renal colic - 2.4%, renal malformations - 0.8%. The leading risk factors for the development of renal pathology in pregnant women of Baku were the following: burdened hereditary nephrologic pathology (48.0%), moderate pre-eclampsia (42.0%), bacterial and viral infections (38.0%), unsatisfactory housing conditions (35.6%), anemia (32.0%), severe pre-eclampsia of pregnant women (28.0%), and diseases of cardiovascular system (14.8%). The results of the obtained research data made it possible to develop proposals for the early diagnosis and further prognosis of renal pathology in pregnant women, which consist of:

- the algorithm of measures for medical surveillance of pregnant women with renal pathology by nephrologist (urologist); these measures must include organization of the mandatory registration of all pregnant women who have a history of clinical and laboratory manifestations of inflammatory chronic pathology of the urinary tract, or were previously diagnosed with kidney disease;

- the prognosis for exacerbations of renal pathology in pregnant women by using a prognostic scale that involves an assessment of the risk factors for exacerbation of renal pathology during pregnancy with subsequent attribution to the medical surveillance group.

Keywords: *prevalence of renal disease, pregnancy, prevention*

1. INTRODUCTION

Urogenital pathology still remains an urgent problem of modern healthcare due to its prevalence among population, the diversity of spectrum of their pathogenic effects on the body, and serious medical and social consequences [1, 2]. Kidney diseases in pregnant women pose a serious threat to the normal development of gestation and fetus, since the pathology of these organs leads to violation of many vital functions of the body, while pregnancy significantly increases the burden on kidneys [3,4,5,6]. In recent years, we have seen an increase in the incidence of renal pathology among pregnant women, especially in those with chronic forms of renal pathology characterized by prolonged clinical course and frequent exacerbations [7,8,9]. Without taking into account social and behavioral features of life of pregnant women, the ongoing fight against renal pathology does not bring the desired success. As a result, renal pathology continues to be the most massive and most significant medical and social problem [10, 11].

One needs to study epidemiological aspects, improve an algorithm for early diagnosis and management of pregnant women with the purpose of developing scientifically grounded set of measures to reduce losses in health status of pregnant women from renal pathology and their complications. In this regard, the study of a number of important epidemiological issues of prevention of renal pathology among pregnant women predetermined the purpose of our studies.

Objective is to study the structure of renal pathology in pregnant women with the development of an algorithm for early diagnosis and management of pregnancy.

2. MATERIALS AND METHODS

To achieve the purpose of the study, in our paper based on the clinical and laboratory criteria developed, in the period from 2009 to 2011 we examined 250 women aged from 17 to 39 years (the mean age was 27.98 ± 5.3) with renal pathology, being in the period of 16-40 weeks of pregnancy. Patients were followed up on the basis of the Department of Obstetrics and Gynecology of the II Azerbaijan Medical University and Maternity Hospital No. 5 named after Sh. Aleskerova. In the paper we used methods of retrospective epidemiological analysis of the prevalence of renal pathology of pregnant women in Baku city. The prevalence and incidence of renal pathology in pregnant women depending on the nosological form was studied during the analysis of medical case histories over the three-year period. It included the analysis of clinical characteristics, characteristics of the course of pregnancy, childbirth, postpartum period, condition of fetus and newborn in 250 women. These women constituted the main group of subjects with renal pathology; in addition, 80 pregnant women aged from 18 to 34 (the mean age was 24.57 ± 0.7) without renal pathology and clinical manifestations in the history were used as the control group.

The inclusion criteria were the following: the presence of pregnancy and renal pathology, age of patients from 17 to 39 years, and informed consent of pregnant women to participate in the study.

The exclusion criteria were the following: diabetes mellitus, stage 5 of chronic kidney disease, grade 3 arterial hypertension, ischemic heart disease, local neoplasms, systemic diseases of blood and connective tissue, withdrawal from study participation. Gestation period was established based on the date of the last menstrual period, beginning of fetal movement, first appearance in the

antenatal clinic, and the data of ultrasonic fetometry. The methods of retrospective epidemiological analysis of the spread of renal pathology of pregnant women in Baku city were used in the study. The prevalence and incidence of renal pathology of pregnant women depending on the nosological form were studied during the analysis of case histories over a three-year period. Evaluation of the functional state of the mother-placenta-fetus system was performed by using ultrasonography, Doppler study and cardiocography. Ultrasonic and dopplerometric studies were carried out on the device manufactured by Aloka SSD-2000 (Japan). For cardiocography we used an automated antenatal monitor (AAM-04) created by Unicos (Russia). Particular attention in patients with gestational age of 10-11 weeks was paid to the comparative evaluation of blood levels of such growth factors (GFs) as: vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), insulin-like growth factor (IGF), transforming growth factor (TGF-β) and epidermal growth factor (EGF), tumor necrosis factor (TNF), which were examined by using the method of solid-phase enzyme immunoassay with "R&D systems" kits (USA) (specific for GFs and intended for their quantitative study in blood serum).

Statistical processing of the obtained results was carried out by using the computer software Microsoft Excel 2007. In the comparative evaluation of two values, Student's reliability criterion was calculated. Differences were considered significant at $p < 0.05$.

3. RESULTS AND DISCUSSION

Study of the structure and dynamics of the registered pathologies of the urinary system in pregnant women in the period from 2009 to 2011 in Baku showed the prevalence of chronic pyelonephritis (22.7±0.8%) compared with renal hydronephrosis (14.8±0.6%) and preeclampsia (12.0±0.5%). The specific weight of cystitis did not exceed 4.8%, urolithiasis was 3.2%, renal colic was 2.4%, and kidney anomalies constituted only 0.8%. Urolithiasis was 3.2%, cystitis was 4.8%, chronic glomerulonephritis was 9.6% ($p < 0.05$). No statistically significant differences were found (6.4% and 5.2%) during the analysis of the incidence of asymptomatic bacteriuria and tubulointerstitial nephritis (Fig. 1).

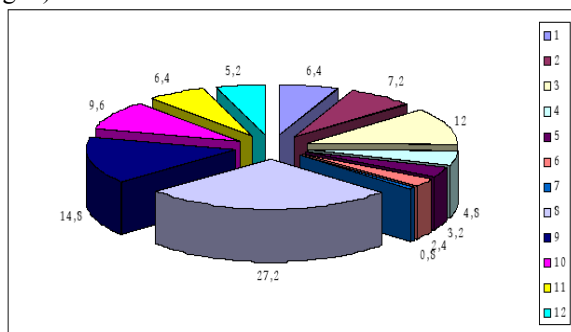


Fig. 1. Structure of morbidity of renal pathology in the examined pregnant women of Baku in the period from 2009 to 2011: 1 - acute pyelonephritis; 2 - gestational pyelonephritis; 3 - pre-eclampsia; 4 - cystitis; 5 - urolithiasis; 6 - renal colic; 7 - kidney anomalies; 8 - chronic pyelonephritis; 9 - kidney hydronephrosis; 10 - chronic glomerulonephritis; 11 - asymptomatic bacteriuria; 12 - tubulointerstitial nephritis

In epidemiological terms, it is also important to identify the seasonality of infectious diseases, as it allows for the implementation of targeted preventive measures. According to the curve of intra-annual dynamics of morbidity in renal pathology, two periods of seasonal increase in morbidity were observed in pregnant women. They were registered in February and July (Fig. 2).

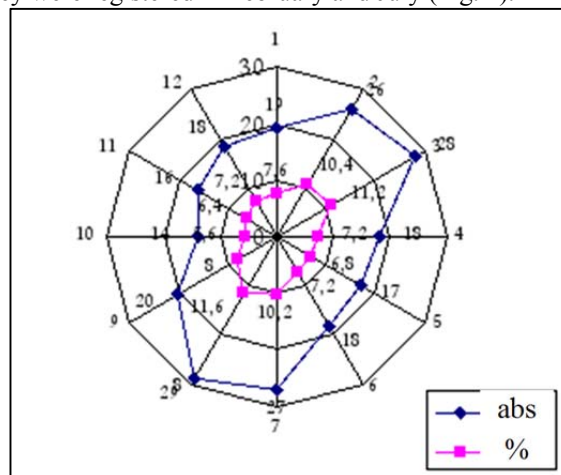


Fig. 2 Intra-annual dynamics of seasonal morbidity of renal pathology in pregnant women in Baku in the period from 2009 to 2011 (%).

All the examined patients in the course of the studies were managed prospectively. Age of the pregnant women in group I and II ranged from 17 to 39 years, and the mean age was 27.98±5.3 years in group I, and 24.5±3.7 years - in group II. Age characteristics of patients are presented in Table 1.

As it turned out, the most numerous group consisted of pregnant women in the age group of 20-29 years - 160 women in group I (64.0±3.9%), and 29 pregnant women in group II - 58.0±6.9%. First and repeated deliveries in 30 years and older (in group I - 75 subjects, and in group II - 19 subjects) made up 30.0±3.7% and 38.0±6.7%, respectively. Pregnancy under the age of 18 years was observed in 15 (6.0±1.9%) and in 2 (4.0±1.6%) subjects in groups I and II ($p > 0.05$), respectively.

Questionnaire made it possible to identify a number of epidemiological facts explaining patterns of the spread of renal pathology among pregnant women in Baku city. Therefore, based on comprehensive analysis of the questionnaire data, we considered it important to determine to what extent the complex of social factors inherent in 250 pregnant women with renal pathology observed by us affected the level of prevalence of renal pathology.

An observational analytical epidemiological control case study was conducted with the study of obstetric, biological and social anamnesis of pregnant women with renal pathology (n = 250, main study group) in order to identify risk factors for the formation of renal pathology in pregnant women of Baku city (Table 2). At the same time, the dependence of kidney diseases associated with socio-hygienic factors on the state of maternal health, course of the pregnancy and childbirth, hereditary complications, and viral and bacterial infections was noted.

Table 1. Age characteristics of the pregnant women

Age (years) Groups	≤ 18		20 - 29		≥ 30	
	N	%	N	%	N	%
Group I (n = 250)	15	6.0 ± 1.9	160	64.0 ± 3.9	75	30.0 ± 3.7
Group II (n = 80)	2	4.0 ± 1.6	29	58.0 ± 6.9	19	38.0 ± 6.7

Table 2. Risk factors for the formation of renal pathology in pregnant women of Baku

Symptom	Main group (n = 250)		Control group (n = 80)		P
	Abs.	%	Abs.	%	
Burdened heredity (nephrologic pathology)	120	48.0	7	8.8	P <0.001
Anemia in pregnant women	80	32.0	9	11.3	P <0.05
Preeclampsia of varying severity	105	42.0	14	17.5	P <0.05
Previous viral and bacterial infections	95	38.0	13	16.8	P <0.05
Supercooling	57	22.0	8	10.0	P <0.05
Concomitant diseases of cardiovascular system	37	14.8	5	6.2	P <0.05
Concomitant diseases of gastrointestinal tract	20	8.0	2	2.5	P <0.05
Non-adherence to the dietary pattern	35	14.0	7	8.8	P <0.05
Influence of stress factors	30	12.0	7	8.8	P <0.05
Unsatisfactory housing conditions	95	38.0	17	21.3	P <0.05
Eating protein food	30	12.0	5	6.2	P <0.05
Eating lots of salt	37	14.8	6	7.5	P <0.05

Table 3. The level of GFs in the serum of the examined patients in the I trimester of gestation (M ± m)

Parameters	Clinical groups		
	Group 1 (IUGR), n = 23	Group 2 (FPI), n = 37	Control group, n = 20
VEGF, ng/mL	17.27±1.66*	12.30±1.28*	8.81±0.68
TGF-β, pg/mL	194.42±16.61*	232.68±15.58*	131.96±7.14
EGF, pg/mL	544.00±37.07*	651.00±42.44*	424.23±23.68
IGFR, ng/mL	66.02±5.63*	138.24±22.63	164.78±15.6
FFR, ng/mL	6.94±0.88	1.61±0.39*	6.31±0.88
TNF, pg/mL	89.27±12.87*	44.41±7.90	39.98±4.92

Note * - reliability of differences relative to the parameters in the control group.

Main risk factor for the formation of renal pathology in pregnant women of Baku city was the following: burdened heredity for nephrologic pathology, which was observed in 48.0% of pregnant women in the main group. In the control group, the hereditary burden of kidney disease was significantly lower - 8.8% (p <0.001). According to the pathology of cardiovascular system, heredity was burdened in 14.8% of pregnant women with renal pathology and in comparison with those in the control group (6.2%). During pregnancy, the following conditions were registered: preeclampsia (42.0% in the main group, 7.5% in the control group, p <0.05); anemia (32.0% in the main group, 11.3% in the control group, p <0.05). The presence of concomitant chronic diseases of the cardiovascular system in pregnant women with renal pathology was revealed in 14.8% cases (6.2% in the control group, p <0.05). It is important to note that when examining pregnant women with renal pathology changes in electrocardiogram were recorded in 34.8% of cases, mainly in form of violation of repolarization processes.

In the recent years, it has been established that GFs play an important role in pregnancy during the formation of the valuable hemodynamic system of fetus.

With the development of the theory of GFs, with the help of which individual features of the placenta development are determined, a new trend has emerged in the doctrine of placental insufficiency. Most attention today is deserved by such GFs as VEGF, FGF, IGF, TGF-β and EGF, TNF. Interest in the study of the above-noted factors is caused by their active participation in the processes of growth, placentation and fetal development.

The comparative study of the content of some GFs in pregnant women with renal pathology revealed a certain number of patterns and differences in their production in case of complicated and physiological pregnancy. In accordance with the study tasks, we conducted the survey of 60 women of the main group, conditionally divided into 2 clinical groups:

group 1 - pregnant women with renal pathology complicated by fetoplacental insufficiency (FPI) and intrauterine growth restriction (IUGR) - n = 23;

group 2 - pregnant women with renal pathology complicated by FPI only - n = 37. The control group consisted of 20 women with physiological pregnancy.

In patients with IUGR syndrome, concentration of vascular endothelial, transforming and epidermal GFs was

2.1, 1.6 and 1.2 times higher, respectively, than similar indicators in pregnant women with physiological pregnancy. The same data were obtained in the examined pregnant women with FPI. In contrast to healthy pregnant women, in FPI patients these indicators of the studied GFs were 1.3, 1.7 and 1.4 times higher, respectively, than in similar ones (table 3).

The obtained data on the violation of production of these factors (VEGF, TGF- β and EGF) demonstrated the complicated course of pregnancy in these women with renal pathology. Along with the high expression of all the above-mentioned GFs typical for pregnant women with renal pathology, we had also noted multidirectional nature of changes in the production of such GFs as IGF, FGF and TNF in pregnant women from the control group and patients with FPI of both groups.

CONCLUSION

When studying the structure and dynamics of kidney morbidity in pregnant women for the period from 2009 to 2011 in Baku city we found that the leading positions were the following: chronic pyelonephritis (27.2%), renal hydronephrosis (14.8%), and eclampsia (12.0%). The specific weight of cystitis was 4.8%, urolithiasis - 3.2%, renal colic - 2.4%, and renal anomalies - 0.8%. The leading risk factors for the development of renal pathology in the pregnant women of Baku city were the following: burdened hereditary nephrologic pathology (48.0%), moderate pre-eclampsia (42.0%), bacterial and viral infections (38.0%), unsatisfactory housing conditions (35.6%), anemia (32.0%), severe pre-eclampsia of pregnant women (28.0%), and diseases of the cardiovascular system (14.8%).

The unfavorable financial situation of families, as a rule coincides with unsatisfactory housing conditions. Therefore, these two factors have a comprehensive negative impact on health components. It is no accident that pregnant women with renal pathology are more often detected in families with poor housing conditions than those in the control group: 35.6 ± 3.0 and $27.3 \pm 5.0\%$ ($t = 3.02$, $p < 0.01$). And vice versa, their number is lower in comparison with the latter ones living in families with favorable housing conditions - 14.0 ± 2.2 and $21.2 \pm 4.5\%$ ($t = 3.46$, $p < 0.001$).

Differences in the content of FGF, IGF, and TNF in the blood serum of patients of groups 1 and 2 allowed us to identify specific criteria for differential diagnosis of early FPI formation with fetal hypotrophy and without it. A considerable decrease in FFR and maintenance of normal TNF and IGFR levels was recorded in the serum of pregnant women with FPI associated with increased production of angiogenesis regulation factors (EGF, VEGF, and TGF- β) without fetal hypotrophy. The decrease in the production of IGF and the increase in the expression of TNF in the serum of pregnant women during an early gestation proved the development of FGR syndrome. Comparing the obtained data, one can ascertain that the detection of hemodynamic disorders in the early stages of pregnancy in the basin of uterine arteries, with the assessment of levels of GFs in the serum of pregnant

women suffering from renal pathology allows to diagnose the development of pathological placentation and the degree of functional placental insufficiency long before the formation of clinical symptoms.

Results of the conducted studies allowed us to establish epidemiological characteristics of renal pathology in pregnant women (morbidity, structure, dynamics) in Baku city for the period from 2009 to 2011. The conducted studies convince of the social confinement of renal pathology among pregnant women and the role of a number of social and epidemiological prerequisites in their widespread prevalence among the pregnant women in Baku city. Apparently, elimination of the identified social and epidemiological prerequisites opens up broad prospects in the organization and conduction of rational measures on prevention of renal pathology among pregnant women.

The results of the obtained research data allowed us to develop proposals for early diagnosis and further prognosis of renal pathology in pregnant women, which consist of the following:

- an algorithm of measures for medical surveillance of pregnant women with renal pathology, which includes organization of the mandatory consultation by nephrologist (urologist) of all pregnant women with a history of clinical and laboratory manifestations of chronic inflammatory pathology of the urinary tract, or previously diagnosed with kidney disease;

- giving a prognosis for exacerbations of renal pathology in pregnant women by using a prognostic scale which involves an assessment of the risk factors for exacerbation of renal pathology during the pregnancy, with subsequent attribution to the medical surveillance group.

Thus, a control system for renal pathology in the pregnant women of Baku city has been developed with justification for monitoring kidney disease in pregnant women for an objective assessment of the epidemiological situation, determining the frequency of pathology, its structure, dynamics, risk factors for the occurrence of renal pathology. Diagnostic informative value of all risk factors was identified with allocation among them of the leading risk factors for the development of renal pathology in the pregnant women of Baku city.

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