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SELECTED PARAMETERS OF RENAL FUNCTION AND HYDRO-ELECTROLYTE BALANCE IN PREGNANT GOATS*

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ABSTRACT

The experiment was carried out on 4 pregnant goats at age 2–3 years. Changes in basic indices of renal function were analysed in the scope of hydro–electrolyte management in the consecutive five months of gestation. Blood and urea samples were collected fortnightly during the first three months of gestation, and weekly during the remaining two months. The analyses included urea volume and glomerular filtration rate, as well as blood plasma concentration, clearance, tubular reabsorption and excretion of sodium, potassium, chlorides and total osmotically active substances.

Glomerular filtration rate did not increase in the organisms of the studied goats, and hydro–electrolyte management was very efficient throughout gestation. Intensive reabsorption of free water occurred in renal tubules, and fractional excretion of sodium did not exceed 0.55%. The most extensive retention of water and sodium occurred in the 3^{rd} and 4^{th} months of gestation, which was demonstrated by diuresis and Na renal clearance being the lowest of the entire period of the experiment. A decrease in blood plasma molality was observed as late as in the 3^{rd} month, and resulted from a decrease in sodium concentration. Changes in potassium and chloride concentrations were of little importance in this process.

Key words: pregnancy, goats, renal function parameters, hydro–electrolyte balance.

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INTRODUCTION

The maintenance of constant internal milieu is the basic physiological law that rules in the organism of a complex metazoan. Homeostasis and functional integration of all the cells, tissues and systems of the organism are controlled by the neural and endocrine systems. These coordinate and integrate the functioning of all the organs and other systems; therefore the functional unity of the organism can be maintained in physiological conditions.

Pregnancy and the resulting necessity to assure optimal growth and development conditions for the foetus mobilise the maternal organism for unusual tasks. It is a time of substantial changes in metabolism and neurohumoral regulation and of increased functional load of most organs and systems, which requires high efficiency of the organism homeostatic mechanisms.

Kidneys play the key role in the maintenance of constant internal milieu and are the main organs that actively regulate the volume of organism fluids, their ionic composition and osmotic pressure. Therefore, efficient functioning of kidneys during pregnancy is undoubtedly one of the factors of the mother's health, normal pregnancy development and delivery of live and healthy offspring.

In the course of gestation, the activity of many organs and systems, as well as the functioning of regulatory mechanisms, undergo functional modifications. The most evident changes occur in the cardiovascular, urogenital, neural, and hormonal systems. These changes are manifested through clearly different values of some parameters, as compared to pre–pregnancy period, including hydro–electrolyte balance indices, acid–base balance parameters, and the concentration of many hormones and metabolites in blood serum [12, 14, 41, 42].

In available literature, any reports on functional changes in kidneys and in hydro–electrolyte balance regulatory mechanisms in pregnant farm animals are scarce. Studies on the changes in those "indices" during pregnancy were carried out mainly for women and rats, and those are the only source of information in this domain.

It has been known that total body water content (TBW) increases in pregnancy [9, 10, 11, 37, 47]. For women, as much as approx. 70% of overall weight gain during pregnancy is attributable to water. Both extracellular fluid (ECF) and intracellular fluid (ICF) increase in volume [9, 13, 22, 44]. The volume of circulating blood increases by approx. 30% [31, 44, 47]. As a result of a disproportionate increase in the volume of blood plasma in relation to that of blood cells, the blood becomes thinner, the plasma molality decreases, and so does the plasma concentration of electrolytes and albumins [5, 9, 10, 11, 13, 22, 44]. A consequence of such extensive growth in circulating blood volume is that the heart stroke volume increases, which is observable as early as in the first trimester of gestation [3, 31]. Systemic vascular resistance (SVR) and blood pressure decrease, whereas renal blood flow (RBF) and glomerular filtration rate (GFR) increase [20, 21].

Sodium–water balance in pregnancy is clearly positive, however it does not seem to be governed by the usual physiological rules, and its regulatory mechanisms have not been fully explained so far. It has even been suggested that a "new" sodium–water balance appears with pregnancy, being regulated by the already known factors, yet undoubtedly also by those still unknown [3, 7, 30].

There are no reports on the hydro–electrolyte homeostasis regulation in pregnant goats, and our knowledge on renal function indices in this species is very low. According to Ketz [19], glomerular filtration rate, as measured with inulin clearance, is 51 $ml \cdot min^{-1} \cdot m^{-2}$ in adult goats, whereas Vogel (48) observed it to be 55 $ml \cdot min^{-1} \cdot m^{-2}$. Muszczyński [33] stated that glomerular filtration rate in goats amounted to an average of 62 $ml \cdot min^{-1} \cdot m^{-2}$ during the day and 47 $ml \cdot min^{-1} \cdot m^{-2}$ during the night. Ketz [19] and Vogel [48] reported for goats that renal plasma clearances of sodium, potassium, and chlorides were, respectively, 0.1, 25.0, and 1.1 $ml \cdot min^{-1} \cdot m^{-2}$. According to Muszczyński [33], the clearances of sodium, potassium, and chlorides display clear diel fluctuations in goats, with the diurnal maximum values 0.95, 14.40, and 1.25 $ml \cdot min^{-1} \cdot m^{-2}$ respectively, and the nocturnal maximum values 0.08, 7.86, and 0.65 $ml \cdot min^{-1} \cdot m^{-2}$ respectively.
The aim of this study was to determine and analyse the changes in selected renal function indices and hydro–electrolyte balance parameters in goats during pregnancy.

MATERIALS AND METHODS

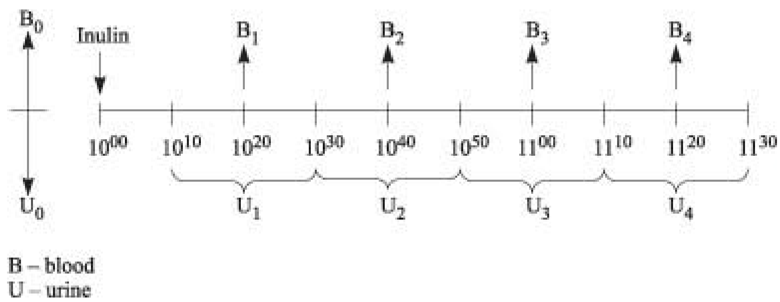
The analyses were carried out on 4 pregnant White Improved goats at age 2–3 years. The animals were healthy over the period of the experiment, showing no clinical symptoms of any disease. The goats were housed at the menagerie of the Department of Animal Physiology, kept in individual stalls, and fed according to feeding standards for small ruminants. The animals were fed 3 times per day (at 8^{00}, 13^{00}, and 18^{00} hrs), with daily ration including meadow hay, wheat bran, and sugar beet pulp. The goats were provided with water and straw ad libitum.

The animals were serviced in the second oestrus (mid October), and the kidding took place within the normal period of time. Blood and urine samplings (n = 8) were done fortnightly during the first 3 months of gestation, and weekly (n = 16) during the last 2 months.

The samplings required prior preparation of the goats. About an hour before an analysis, the animals were weighed, and the external jugular vein was catheterised, which allowed quick and gentle collection of 5 blood samples in short time intervals, as well as intravenous administration of strictly specified dose of inulin [2]. A Foley balloon catheter was placed in the urinary bladder for the complete drainage of urine and for the determination of per–minute diuresis rate.

As soon as so–called zero blood and urine samples (B_0 and U_0) had been collected, at 10^{00} hrs, the animals were intravenously administered 20 cm^3 of 10% inulin solution (2 g of inulin). After another ten minutes, four 20–minute periods of urine collection began (U_1, U_2, U_3, and U_4). In the middle of each urine–sampling period, a blood sample (B_1, B_2, B_3, and B_4) was collected as well (Fig. 1).

Fig. 1. Scheme of experiment - timing of blood sampling and urine collection



The collected blood was centrifuged, and both the samples of plasma and urine were frozen and stored at –20°C. The following were assayed in blood plasma and urine:

- Inulin concentration (resorcinol method)
- Sodium and potassium concentration (flame photometry)
- Chloride concentration (potentiometric titration)
- Osmotic pressure (cryoscopic method)

The results of laboratory analyses were used to calculate the clearance of inulin (C_{in} = GFR), sodium (C_{Na}), potassium (C_K), and chlorides (C_{Cl}), as well as that of osmotically active substances (C_{Osm}). Filtered load (F) and excreted load (UV), as well as tubular reabsorption (TR, expressed as percentage of filtered load) were calculated for the analysed components of plasma and urine. All the renal function indices were expressed per 1 m^2 of body surface area.

The obtained results were structured by consecutive months of gestation (I, II, III, IV, and V); mean values ($\overline{x}$) and standard deviations (SD) were calculated. The significance of differences for the studied renal function indices was estimated with one–way analysis of variance and Duncan's multiple range test (Statgraphics 5.0 software).

RESULTS

The results of the experiment are presented in Tables 1–5.

Diuresis volume (V) for pregnant goats ranged between 0.46 and 0.71 $ml \cdot min^{-1} \cdot m^{-2}$ (Table 1). The largest volume of urea excretion was observed in the 2^{nd} month of gestation, whereas the lowest level was in the 3^{rd} and the 4^{th} month (differences statistically significant at $p \leq 0.01$).

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Table 1. Urine volume (V) and glomerular filtration rate (GFR) in pregnant goats

Month of pregnancy		V	GFR
		[ml·min^{-1}·m^{-2}]	
I	n	8	8
	$\bar{x}$	0.57	51.74
	SD	0.12	7.00
II	n	8	8
	$\bar{x}$	0.71	53.65
	SD	0.41	6.26
III	n	8	8
	$\bar{x}$	0.46	54.38
	SD	0.16	4.52
IV	n	16	16
	$\bar{x}$	0.46	51.03
	SD	0.23	4.70
V	n	16	16
	$\bar{x}$	0.53	48.10
	SD	0.24	3.87
Statistically significant differences ($p \leq 0.01$)		II – III, IV	V – II, III

n – number of repetitions; – arithmetic mean; SD – standard deviation.

The goat glomerular filtration rate (GFR, Table 1) did not show significant changes from the 1st through the 3rd month of pregnancy, however a slight yet gradual rising trend was observed, from 51.74 to 54.38 ml·min^{-1}·m^{-2}. After the "peak" GFR, observed in the 3rd month, glomerular secretion declined to 48.10 ml·min^{-1}·m^{-2} (in the 5th month of gestation). Primary urine volume per 1 minute for the goats in the 5th month of gestation did not actually differ from that observed in the 1st month, however it was significantly lower than those recorded in the 2nd and 3rd months.

Plasma sodium concentration (P_{Na}, Table 2) displayed clear and statistically confirmed falling trend over the entire period of the study; from 141.2 mmol·dm^{-3} in the 1st month to 135.1 and 135.2 mmol·dm^{-3} respectively in the 4th and the 5th month of gestation.

Table 2. Sodium concentration in blood plasma (P), clearance (C), glomerular filtration (F), tubular reabsorption (TR), and excretion with urine (UV) in pregnant goats

Month of pregnancy		P_{Na} [mmol·dm^{-3}]	C_{Na} [ml·min^{-1}·m^{-2}]	F_{Na} [mmol·min^{-1}·m^{-2}]	TR_{Na} [%]	UV_{Na} [mmol·min^{-1}·m^{-2}]
I	n	8	8	8	8	8
	$\bar{x}$	141.2	0.216	7.244	99.69	0.031
	SD	4.7	0.206	0.945	0.38	0.031
II	n	8	8	8	8	8
	$\bar{x}$	140.8	0.205	7.538	99.56	0.029
	SD	4.8	0.203	0.752	0.71	0.027
III	n	8	8	8	8	8
	$\bar{x}$	138.0	0.140	7.488	99.49	0.019
	SD	7.8	0.115	0.540	0.45	0.016
IV	n	16	16	16	16	16
	$\bar{x}$	135.1	0.097	6.902	99.81	0.013
	SD	9.0	0.091	0.905	0.20	0.013
V	n	16	16	16	16	16
	$\bar{x}$	135.2	0.160	6.506	99.67	0.022
	SD	9.1	0.127	0.775	0.26	0.018
Statistically significant differences ($p \leq 0.01$)		I – IV, V, II – IV,V	I – III, IV, II – III, IV			I – III, IV, II – III, IV

Explanations as in Table 1.

Sodium clearance (C_{Na}) significantly decreased between the 1st and 4th month, from 0.216 to 0.097 ml·min^{-1}·m^{-2}. In the 5th month of gestation, the sodium renal clearance actually increased to 0.160 ml·min^{-1}·m^{-2}, however it did not exceed the values observed in the first two months. As demonstrated by the presented results, the highest sodium retention took place in the 3rd and 4th months of gestation.

The changes in primary urine filtered sodium load (F_{Na}) observed in the goats corresponded with the changes in GFR, though being statistically insignificant. During the first 3 months of gestation, F_{Na} was relatively steady and amounted to, respectively, 7.244, 7.538, and 7.488 mmol·min^{-1}·m^{-2}, while in the next two months it decreased to 6.902 and 6.516 mmol·min^{-1}·m^{-2}.

The tubular reabsorption of sodium (TR_{Na}), expressed as percentage of filtered load, did not demonstrate significant changes over the experiment. It remained high throughout the gestation, ranging between 99.49–99.81%, with the lowest values in the 2nd and 3rd month, and the highest in the 4th month.

The sodium load excreted with urine (UV_{Na}) systematically decreased from the 1st through the 4th month of gestation, reaching 0.031, 0.029, 0.019, and 0.013 mmol·min^{-1}·m^{-2} respectively. In the last, 5th month, the sodium urine excretion increased to 0.022 mmol·min^{-1}·m^{-2}, however it was lower (yet insignificantly) than that observed in the first two months.

Plasma potassium concentration (P_K, Table 3) during the first four months of gestation did not undergo any significant changes, ranging between 4.1 and 4.4 mmol·dm^{-3}. In the last month of gestation, however, a significant increase in plasma potassium level occurred, to 5.1 mmol·dm^{-3}.

Table 3. Potassium concentration in blood plasma (P) and clearance (C), glomerular filtration (F), tubular reabsorption (TR), and excretion with urine (UV) in pregnant goats

Month of pregnancy		P_K [mmol·dm^{-3}]	C_K [ml·min^{-1}·m^{-2}]	F_K [mmol·min^{-1}·m^{-2}]	TR_K [%]	UV_K [mmol·min^{-1}·m^{-2}]
I	n	8	8	8	8	8
	$\bar{x}$	4.1	27.734	0.213	45.76	0.115
	SD	0.4	6.815	0.027	11.82	0.023
II	n	8	8	8	8	8
	$\bar{x}$	4.4	25.262	0.230	54.62	0.103
	SD	0.8	13.806	0.035	22.86	0.052
III	n	8	8	8	8	8
	$\bar{x}$	4.4	27.573	0.237	48.50	0.121
	SD	0.5	7.046	0.041	10.47	0.038
IV	n	16	16	16	16	16
	$\bar{x}$	4.2	25.506	0.214	50.53	0.106
	SD	0.6	12.199	0.045	21.85	0.053
V	n	16	16	16	16	16
	$\bar{x}$	5.1	16.916	0.252	62.03	0.087
	SD	0.6	7.418	0.042	18.38	0.035
Statistically significant differences ($p \leq 0.01$)		V– I, II, III, IV	V – I, II, III, IV	V – I, IV	I – V	

Explanations as in Table 1.

The clearance of potassium (C_K), similarly to its plasma concentration, did not display any significant fluctuations over the first four months, remaining within the range of 25.262 to 27.734 ml·min^{-1}·m^{-2}, however in the last 5th month, potassium renal clearance considerably declined, as much as to 16.919 ml·min^{-1}·m^{-2}.

Potassium load secreted in renal glomeruli (F_K) in the 1st, 2nd, 3rd, and 4th month of gestation was 0.213, 0.230, 0.237, and 0.214 mmol·min^{-1}·m^{-2} respectively (differences statistically insignificant). The changes in the amount of potassium filtered to primary urine were corresponding with the fluctuation of GFR and potassium plasma concentration during that period of time. In the 5th month, despite a considerable decrease in GFR, the excreted potassium load significantly increased to 0.252 mmol·min^{-1}·m^{-2}, which was a direct result of its increased concentration in the blood plasma.

During the first four months of gestation, the potassium tubular reabsorption (TR_K), expressed as a percentage of filtrated load, demonstrated only statistically insignificant changes in the range 45.76–54.62%. In the last month of gestation however, TR_K rose considerably to 62.03%, and consequently exceeded the values of this index observed in the beginning of gestation.

Potassium excretion with urine (UV_K) remained relatively stable throughout the experiment, at the level of 0.087 to 0.121 $mmol \cdot min^{-1} \cdot m^{-2}$.

Chloride plasma concentration (P_{Cl}, Table 4) in the 1st month of gestation was 109.2 $mmol \cdot dm^{-3}$ on average. In the second month, the concentration of Cl^- decreased, temporarily yet significantly, to 103.2 $mmol \cdot dm^{-3}$, and, after its growth in the 3rd month, it remained relatively stable until the end of the experiment: 108.6–110.2 $mmol \cdot dm^{-3}$.

Table 4. Chlorides concentration in blood plasma (P), clearance (C), glomerular filtration (F), tubular reabsorption (TR), and excretion with urine (UV) in pregnant goats

Month of pregnancy		P_{Cl} [$mmol \cdot dm^{-3}$]	C_{Cl} [$ml \cdot min^{-1} \cdot m^{-2}$]	F_{Cl} [$mmol \cdot min^{-1} \cdot m^{-2}$]	TR_{Cl} [%]	UV_{Cl} [$mmol \cdot min^{-1} \cdot m^{-2}$]
I	n	8	8	8	8	8
	$\bar{x}$	109.2	0.698	5.661	98.64	0.076
	SD	5.5	0.285	0.861	0.56	0.031
II	n	8	8	8	8	8
	$\bar{x}$	103.2	1.113	5.528	98.12	0.100
	SD	11.7	0.494	0.837	0.90	0.061
III	n	8	8	8	8	8
	$\bar{x}$	108.6	0.814	5.904	98.49	0.088
	SD	2.9	0.370	0.484	0.73	0.040
IV	n	16	16	16	16	16
	$\bar{x}$	110.3	0.870	5.628	98.27	0.094
	SD	6.0	0.408	0.632	0.84	0.046
V	n	16	16	16	16	16
	$\bar{x}$	108.7	0.893	5.228	98.13	0.094
	SD	6.4	0.398	0.521	0.83	0.054
Statistically significant differences ($p \leq 0.01$)		II – IV	I – II	III – V		

Explanations as in Table 1.

Chloride renal clearance (C_{Cl}) significantly increased between the 1st and the 2nd month of gestation – from 0.698 to 1.113 $ml \cdot min^{-1} \cdot m^{-2}$ – than it dropped and “stabilised” in the range of 0.814–0.893 $ml \cdot min^{-1} \cdot m^{-2}$.

In the first two months of gestation, the load of chlorides filtered (F_{Cl}) to primary urine did not show any significant changes, being 5.661 and 5.528 $mmol \cdot min^{-1} \cdot m^{-2}$. In the 3rd month, there was a significant increase in F_{Cl} to 5.904 $mmol \cdot min^{-1} \cdot m^{-2}$, then a gradual falling trend was observed over the subsequent two months (5.628 and 5.228 $mmol \cdot min^{-1} \cdot m^{-2}$).

Chloride tubular reabsorption (TR_{Cl}) did not show significant changes, remaining in the range 98.12–98.64 % over the period of the study.

Similar to tubular reabsorption, chloride excretion with urine (UV_{Cl}) remained relatively stable throughout the gestation, ranging between 0.076–0.100 $mmol \cdot min^{-1} \cdot m^{-2}$.

Blood plasma osmotic pressure (P_{Osm}, Table 5) slightly increased between the 1st and the 2nd month of gestation, from 297.2 to 300.4 $mmol \cdot kg^{-1}$ H_2O. However, the increase was only temporary, and the plasma molality gradually and significantly decreased during the subsequent period, being 294.0, 293.8, and 289.6 $mmol \cdot kg^{-1}$ H_2O in the 1st, 2nd, and 3rd month of gestation respectively.

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Table 5. Blood plasma molality (P), osmotic clearance (C), glomerular filtration (F), and excretion with urine (UV) of osmotically active substances in pregnant goats

Month of pregnancy		P_{Osm} [$mmol \cdot dm^{-3}$]	C_{Osm} [$ml \cdot min^{-1} \cdot m^{-2}$]	F_{Osm} [$mmol \cdot min^{-1} \cdot m^{-2}$]	UV_{Osm} [$mmol \cdot min^{-1} \cdot m^{-2}$]
I	n	8	8	8	8
	$\bar{x}$	297.2	1.498	15.312	0.446
	SD	6.5	0.423	1.896	0.129
II	n	8	8	8	8
	$\bar{x}$	300.4	1.434	16.109	0.435
	SD	8.9	0.437	1.931	0.124
III	n	8	8	8	8
	$\bar{x}$	294.0	1.711	15.977	0.494
	SD	4.6	0.633	1.480	0.373
IV	n	16	16	16	16
	$\bar{x}$	293.8	1.178	15.000	0.348
	SD	9.2	0.319	1.545	0.095
V	n	16	16	16	16
	$\bar{x}$	289.6	1.360	13.939	0.378
	SD	6.4	0.560	1.229	0.171
Statistically significant differences ($p \leq 0.01$)		II – III, IV, V	III – IV, V	II – V	III – IV, V

Explanations as in Table 1.

The renal clearance of osmotically active substances (C_{Osm}) did not change significantly during the first three months of gestation, and was 1.498, 1.434, and 1.711 ml/min/m^2 respectively, however it decreased considerably in the last two months, to 1.178 and 1.360 $ml \cdot min^{-1} \cdot m^{-2}$.

The quantitative changes in osmotically active substances secreted in renal glomeruli (F_{Osm}) were proportional to the changes observed in GFR over the entire period of the study. In the 1st, 2nd, 3rd, 4th, and 5th month of gestation, the filtered load of osmotically active substances amounted to, respectively, 15.312, 16.109, 15.977, 15.000, and 13.939 $mmol \cdot min^{-1} \cdot m^{-2}$; a significant difference in F_{Osm} occurred only between the values observed in the 2nd and the 5th month.

The load of osmotically active substances excreted with urine (UV_{Osm}) in the first three months of gestation was 0.446, 0.435, and 0.494 $mmol \cdot min^{-1} \cdot m^{-2}$ respectively (differences statistically insignificant). After the “peak” excretion, which was observed in the 3rd month, UV_{Osm} decreased significantly in the subsequent two months, to 0.348 and 0.378 $mmol \cdot min^{-1} \cdot m^{-2}$.

DISCUSSION

The diuresis changes in goats that were observed in the experiment were most probably caused by varied secretion of an antidiuretic hormone (ADH) – vasopressin (AVP). This has been demonstrated by the changes in plasma molality observed in respective periods of time. ADH is a hormone that makes the membranes of distal and collective tubules permeable to water; therefore, water reabsorption is achievable from the tubular fluid into the hypertonic renal core intraparenchyma. As a result of ADH activity, concentration–dependent reduction in diuresis occurs and excreted urine becomes concentrated [11, 22, 35, 47]. In all the studied periods, the osmotic clearance in the pregnant goats was higher than diuresis volume, which explicitly demonstrates the tubular absorption of free water. The enhanced excretion of vasopressin during pregnancy was observed by many authors [1, 4, 16, 23, 24]. Higher ADH concentration in pregnancy, and also consequent enhanced water absorption in renal tubules, contributes to the growth in blood plasma volume and stabilises its molality at lower levels, as compared to the pre–pregnancy period, all the more that both thirst threshold and vasopressin secretion threshold decrease considerably during pregnancy, by about 5 $mmol \cdot kg^{-1}$ H_2O [10, 11, 46, 49, 50].

GFR increase is a physiological state in pregnancy, observable both in women and laboratory animals. It is mainly caused by an increase in extracellular fluid volume (including intravascular fluid) and by a decrease in blood plasma oncotic pressure (which leads to an increase in both filtration pressure and filtrating surface area) [3, 45]. In women, the increase in glomerular filtration rate begins as early as in the second month of gestation.

Towards the end of pregnancy, i.e. around the 36th week, GFR is by more than 50% higher than that observed in the non–pregnant [20, 21, 27, 45]. In rats, glomerular filtration rate rises from the 5th day of gestation. The peak values, by approx. 30% higher than those for non–pregnant females, are observed between 12 and 16 days, when GFR gradually yet significantly decreases [7, 27]. The increase in GFR is one of the main factors that play a role in enhanced water and sodium excretion with urine. Even a slight growth or decline in GFR leads to some changes in sodium and water excretion in the same direction. A growth in glomerular filtration during pregnancy in women or in rats must be "recompensed" with an enhanced activity of the mechanisms that shape the reverse absorption of water and sodium in renal tubules, as it has been known that their balance during pregnancy is clearly positive [22, 27, 40]. As the results presented here demonstrate, the increase in GFR in pregnant goats was very small, as compared to that in pregnant women, and only temporary. This appears to be a simple yet efficient mechanism of water and sodium retention during pregnancy, which is of special importance as plant feeds contain little sodium [39]. No increase in GFR, or even its decrease in cows in the 7th, 8th, and 9th month of gestation, was indicated by a steady, relatively high concentration of endogenous creatinine in blood plasma, 135–138 $\mu mol \cdot dm^{-3}$, as reported by Madej *et al.* [26]. In women, GFR enhancement results in reduction of creatinine concentration in plasma, to approx. 44.2 $\mu mol \cdot dm^{-3}$, in the third trimester of gestation [45]. The creatinine concentrations that are physiological for non–pregnant women (70.72–88.4 $\mu mol \cdot dm^{-3}$), if recorded in the 2nd or 3rd trimester of gestation, become a basic symptom for the diagnosis of renal failure [25].

Positive balance of both sodium and water is a typical fact in normal pregnancy of women and many animal species [7, 10, 11, 30, 35, 37]. For women, the positive sodium balance reaches 900–950 mmol throughout gestation [9]. However, the sodium and water retention, especially in the latter half of gestation, does not seem to be controlled by the "usual" physiological rules, which are in control in a non–pregnant female organism [3, 27, 30]. This is additionally "complicated" by increased concentration and activity of both natriuretic mechanisms (e.g. increased ERBF, GFR, progesterone, dopamine, ANP, prostaglandin) and antinatriuretic mechanisms (e.g. increased level of angiotensin II, aldosterone, deoxycorticosterone, glucocorticoids, and estrogens) [6, 7, 10, 14, 35, 40, 44]. One of the possible explanations for the enhanced sodium and water retention in the organism of a pregnant female is a local or general decline of renal tubules response to the activity of natriuretic factors, in which case the antinatriuretic stimulation prevails [27, 29]. Studies conducted on rats revealed that renal tubules are "resistant" to many natriuretic factors, especially during the latter half of gestation. In consequence, e.g. exogenous administration of atrial natriuretic peptide does not detectably influence the functioning of distal or collective tubules of nephrons, while its effects on the haemodynamics of circulation remain [27, 37]. In pregnancy, extracellular fluid volume increases by nearly 50%. The intravascular compartment grows larger, and the plasma volume increases by approx. 40%. This promotes better blood supply to organs, including the pregnant uterus [3, 9, 13, 22, 44]. However, renal retention of water is slightly higher than that of sodium, which results in lower sodium concentration in blood plasma with its higher overall contents in the organism [3, 5, 10, 11]. For pregnant women, a significant decrease in blood plasma sodium concentration is observable from the 5th week of gestation [9, 10, 11, 44]. As demonstrated with the results of this study, sodium concentration in goats actually decreased steadily throughout the gestation, however it was not until the 4th month when its significant changes were observed. On the other hand, the most extensive retentions of sodium ions and water were recorded in the 3rd and 4th month of gestation, as demonstrated with diuresis and Na clearance – both being the lowest during this period. Over the entire period of gestation, sodium metabolism in the studied animals was very efficient, which has been best demonstrated with over 99.5–percent absorption of the Na load filtered to primary urine. Some deviations in GFR and consequently in F_{Na} were "recompensed" by proportional changes in tubular reabsorption. This might demonstrate the full efficiency of glomerular–tubular balance "mechanism". Micropuncture examinations of pregnant rats demonstrated that sodium reabsorption increased both in the ascending limb of the nephron loop and in collecting tubules, whereas the proximal reabsorption increased only slightly [27]. According to Lindheimer and Ketz [25], the sodium retention in the organism of a pregnant female is associated with the increase in quantity and activity of Na^+–K^+–ATPase in cellular membranes of renal tubules.

The maintenance of appropriate potassium concentration in the extracellular fluid in physiological conditions depends an efficient, simultaneous action of both renal and extra–renal regulatory mechanisms [8, 28]. The renal mechanism, regulating urine excretion of potassium in line with its amount absorbed from food, controls the equalized balance of the element. Theoretically, pregnant females should dispose of potassium surplus with urine through high plasma concentration of aldosterone and other mineralocorticoids (e.g. ANP, deoxycorticosterone, glucocorticoids) [6, 12, 14, 15, 51], along with reduced distal and collecting tubules sensitivity to natriuretic hormones (e.g. ANP, progesterone) [27, 29, 30, 32, 37, 41, 42]. During pregnancy, enhanced retention of potassium and its accumulation occurs mainly in the foetal space and in reproductive organs [25]. Pregnant females are resistant to kaliuresis, which in non–pregnant females is caused by exogenous mineralocorticoids and by increased potassium supply in diet, and cyetic "hyperaldosteronism" in not accompanied by

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hypocalaemia [25, 27, 29]. This has been confirmed by the results of this study, as in the pregnant goats neither hypocalaemia nor increased potassium excretion with urine were observed. On the contrary, during the last two months of gestation, a clear decrease in potassium renal clearance was recorded, whereas in the last, 5th month, a significantly increased level tubular absorption and blood plasma concentration of the ion was observed. It was presumably an effect of increased progesterone concentration. Biosynthesis of progesterone during pregnancy is strongly enhanced [41, 42]. According to Lindheimer and Ketz [25], the ability to retain potassium in pregnancy, despite a high concentration of potential mineralocorticoids (e.g. aldosterone, deoxycorticosterone, cortisol) and a large supply of sodium to distal segments of the nephron, results from the antimineralocorticoid activity of progesterone. The activity of progesterone is similar to that of spironolactone, a potassium–sparing diuretic [18]. As a consequence of the activity, the quantity of excreted potassium is reduced, which is usually convertible to an increase of the electrolyte in blood plasma. Thus, progesterone has clearly antimineralocorticoid properties in the scope of potassium metabolism, however, on the on the hand, the increase of the element during pregnancy is responsible for the "resistance" of glomerular zone cells in the adrenal cortex against the hindrance of aldosterone biosynthesis by ANP [32]. The increase in blood plasma potassium concentration, observed in this experiment during the last month of gestation, might have also been a consequence of metabolic acidosis, developing at a low degree of intensity.

Up to now the processes regulating the chloride renal excretion have not been fully explained. Chloride ions are referred to as the anions that accompany the cations of sodium and potassium, which are excreted with urine. Blood plasma chloride concentration usually corresponds with its sodium concentration, being subject to the same regulatory mechanisms [18]. The results of this study demonstrate however that chloride ion cannot be considered just as an "acid anion" that is equivalent to sodium cations in extracellular fluid. Chloride, hydrocarbon, potassium, and hydrogen ions migrate between the intra– and extracellular fluids, maintaining the equilibrium between anions and cations (electroneutrality), in this way regulating the state of acid–base balance.

Reduced molality of goat blood plasma during the last three months of gestation was caused mainly by reduced sodium concentration. A decrease in osmotic pressure is a physiological state in pregnancy [1, 24, 25, 27, 50]. Plasma molality changes in pregnant woman's organism are observable as early as in the 5th week. In the 10th week of gestation, the osmotic pressure of extracellular fluid is by about 10 $mmol \cdot kg^{-1}$ H_2O lower compared to the period before pregnancy. Such difference remains until the parturition [9, 10, 11, 25, 37, 45]. The lowering of maternal extracellular fluid molality has an important physiological implication, as it stimulates water transport through the placenta [13, 17, 25, 43]. As it has been demonstrated, lack of both observable reduction in osmotic pressure of extracellular fluid and lack of increase in blood plasma volume may lead to the diagnosis of pathological pregnancy – the preeclampsia state in women. Such conditions go together with low body weight gain of the pregnant woman and considerable hindrance in growth and development of the foetus [15, 38, 44]. One of the factors responsible for the reduction of plasma molality in pregnancy is the enhanced biosynthesis and secretion of vasopressin. For both pregnant and non–pregnant females, an explicit relationship exists between osmotic pressure variations and antidiuretic hormone concentration in blood plasma; however, as it was mentioned before, the threshold of ADH secretion is much lower in pregnancy. It has also been suggested that blood pressure changes are the main factor responsible for regulation of both biosynthesis and secretion of vasopressin, whereas the plasma molality changes are of lesser importance [10]. A reduction in sodium concentration and plasma osmotic pressure may also, to some extent, explain the enhanced activity of renin–angiotensin–aldosterone system, which is observable in pregnancy [36].

Comparing the results of the described experiment with the literature data, one may state that the reduction in blood plasma molality in pregnant goats is noticeably delayed, as compared to that in pregnant women. This becomes especially evident, should the pregnancy duration of both species be taken into account.

CONCLUSIONS

1. No significant increase in glomerular filtration rate is observable in pregnant goats, which promotes retention of water and sodium in the organism.
2. Throughout the gestation, intensive absorption of free water occurs in renal tubules, and the fractional sodium excretion does not exceed 0.55%. This demonstrates both efficient and sparing water–sodium metabolism.
3. The most extensive sodium and water retention in pregnant goats takes place in the latter half of gestation.
4. Blood plasma molality reduction in pregnant goats does not occur until the 3rd month of gestation, and results mainly from decreased sodium concentration, whereas the changes in potassium and chloride concentration are of minor importance for this process.

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