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PARTICIPATION OF STRUCTURE PARTS OF A FETAL KIDNEY IN ITS VOLUME AND THEIR AGE-RELATED CHANGES

SUMMARY

Regardless of considerably grow and develope of fetal kidney and his structure parts, they are very modestly studied. The process of growing continues as well in postnatal life, but under more attention by the scientists. Thus, stereological research of fetal kidney is important for us to fully comprehend normal development of its structures. Aim of this study was to establish the measure of participation of three macroscopic structure parts of human fetal kidney: cortex, medulla and sinus, by the factor of gestational age. We tried to determine the periods of their maximal and minimal participation and to compare them during different gestational ages. We analysed 45 pairs of human fetal kidneys, aged from fourth to tenth lunar month. Kidneys were divided into nine groups according to their gestational age. The volume densities of the cortex, medulla and sinus were determined using the stereological methods. The results were statistically elaborated and periods of maximal and minimal participation of these structures were observed. Cortex has its maximal participation in fetal kidney's volume in X lunar month and minimal in V lunar month. On the other hand, medulla has its maximal participation in V and minimal in X lunar month. Renal sinus has the highest percentage in the period of decrease of medulla's participation and slow increase of cortex participation. It is useful to know periods of maximal participation of kidney structures because the function of fetal kidney possibly depends on the prevalent portion of cortical or medullar components of the nephron. This study is an effort to provide some parameters which can help in future investigation of the human fetal kidney development.

Key words: **fetal kidney, cortex, medulla, sinus, volume, stereology**

INTRODUCTION

Fetal research, in particular fetal growth and development, attract much less attention than they deserve. Misconceptions about the proportional growth of fetal organs and about the periods without special characteristics and differences in its development are, once for all, eliminated. Thanks to the progress of modern diagnostic procedures, especially ultrasound fetal assays, we are able to draw conclusions about the growth and development of fetal organs, kidneys included. Prenatal diagnostics of kidney anomalies, especially in its size and shape, has enormous importance regarding timely diagnose and institution of the so-called "fetal therapy" (1).

Charasteristics of adult kidney are well known. Regarding the kidney in prenatal age, one may observe that its embryonal period attracted more attention compared to its fetal period. If observing a fetal kidney, there are some questions which are not well elucidated: How do particular structures of the kidney (cortex, medulla, pyelo-calix system), definitely formed in embryogenesis, grow and develop onwards? Which structure parts take the initiative in growth and in which months? What is the ratio: "their individual volume versus the whole kidney volume". Reviewing the available literature we may easily observe that stereological, quantification methods are much more utilized in adult kidney studies than in studying fetal kidney.

Aim of this work was to determine volume densities of the fetal kidney structural parts, as relative stereological variabilities and, at the same time, to determine their participation in a kidney volume. Evaluating their periodical changes we tried to discover the periods of maximal and minimal participation of these structural parts in a kidney volume.

MATERIAL AND METHODS

In this study, 45 fetuses were analyzed divided according to lunar months based upon temple to crown-rump length (CRL) (2). On the basis of literature facts, preliminary research and due to intensive growth of examined structural parts of the kidney during these months, IV and V lunar months were divided into two subgroups, the first and second half. All fetuses were fixed in 10% formaldehyde for a period of at least 30 days. Macrodissection was used to extract both kidneys en block and separate them from the surrounding tissue.

For stereological analysis two test systems were used. For kidneys in the IV, V and VI months D64 system was used and for kidneys in VII, VIII, IX and X months M42 system was used. Different test systems were used because of different cut sizes. D64 system has more points than M42 system and it was important to use it for smaller fetal kidneys. Consequently, approximately equal number of points fell upon the surface of the cut. Test systems were photocopied on a transparent paper and reduced to an adequate analytical size. With nonius distance "d" was measured and, according to the general formulae, characteristics of testing systems were established. The kidneys were cut perpendicular to their length axis with spacing t=2.5 mm for the IV, V and VI months and t=5 mm for the VII, VIII, IX and X months. The cuts clearly showed renal sinus and parenchyme. Cortex and medulla could be distinguished by colour. Testing system was directly placed on the surface of the cut (figure 1) and then points which fell upon the cortex, medulla and sinus of the kidney were counted with operational microscope or magnifying glass (3). Volume density was determined according to the formula:

$$V_{Vf} = P_f / P_t,$$

"V_{Vf}" is the volume density of the examined structure (phasis); "P_f" is the number of points falling upon the examined phasis and "P_t" is the number of points of used test system (4,5).

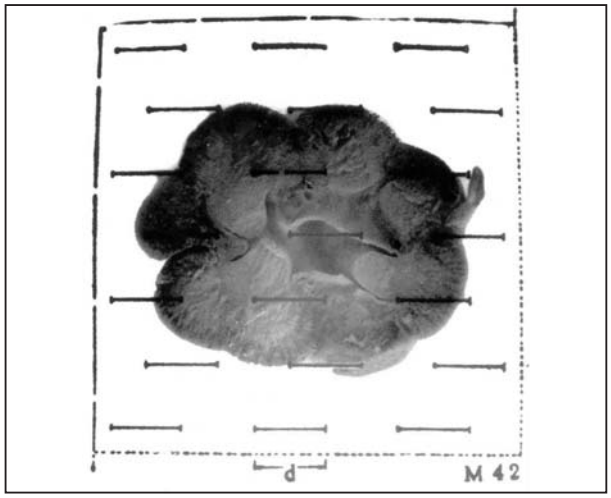

Figure 1. Test system M42 placed on the cross section of the fetal kidney

All of these parameters were statistically processed (6) and graphically presented.

RESULTS

Table 1, figure 2 and figure 3 show the participation of structure parts of kidney in its volume (expressed in percentage). This participation is equal to the volume density of these parts. Renal cortex has its maximal participation in IV and even more in IX and X lunar month, namely, it has its maximal volume immediately before birth. Medulla has the maximal participation in V lunar month and from that time until birth its proportion decreases. Renal sinus is mostly represented from the second half of V until VIII lunar month.

DISCUSSION

Stereological methods are precise instruments for obtaining the quantitative data about three-dimensional structures. Irregular shape of different human organs was in many cases a big problem for determination of their size and dimensions of their structures. From XVII century, when Italian mathe-

Table 1. Participation (volume density) of kidney's structure parts in its volume, expressed in percentage

Fetal age	N	CORTEX				MEDULLA				SINUS			
		Left kidney		Right kidney		Left kidney		Right kidney		Left kidney		Right kidney	
		Participation	SD	Participation	SD	Participation	SD	Participation	SD	Participation	SD	Participation	SD
IV a	5	0.545 54.5%	0.02	0.522 52.2%	0.02	0.424 42.4%	0.01	0.446 44.6%	0.02	0.031 3.1%	0.01	0.032 3.2%	0.01
IV b	5	0.512 51.2%	0.16	0.530 53.0	0.09	0.427 42.7%	0.13	0.431 43.1%	0.07	0,061 6.1%	0.03	0,039 3.9%	0.01
V a	5	0.449 44.9%	0.06	0.448 44.8%	0.07	0,480 48.0%	0.06	0.484 48.4%	0.06	0.071 7.1%	0.03	0.068 6.8%	0.02
V b	5	0.454 45.4%	0.02	0.431 43.1%	0.03	0.449 44.9%	0.02	0,453 45.3%	0.03	0.097 9.7%	0.02	0,116 11.6%	0.02
VI	5	0.503 50.3%	0.03	0.463 46.3%	0.02	0.414 41.4%	0.03	0.444 44.4%	0.02	0.083 8.3%	0.02	0.093 9.3%	0.03
VII	5	0.503 50.3%	0.04	0.471 47.1%	0.07	0.421 42.1%	0.04	0.424 42.4%	0.07	0.076 7.6%	0.01	0.105 10.5%	0.01
VIII	5	0,496 49.6%	0.03	0.509 50.9%	0.02	0.402 40.2%	0.03	0.383 38.3%	0.04	0.102 10.2%	0.01	0.108 10.8%	0.05
IX	5	0,555 55.5%	0.09	0.566 56.6%	0.03	0.351 35.1%	0.04	0.335 33.5%	0.04	0.094 9.4%	0.08	0.099 9.9%	0.03
X	5	0.589 58.9%	0.08	0.641 64.1%	0.13	0.331 33.1%	0.07	0.282 28.2%	0.12	0,080 8.0%	0.01	0.077 7.0%	0.02

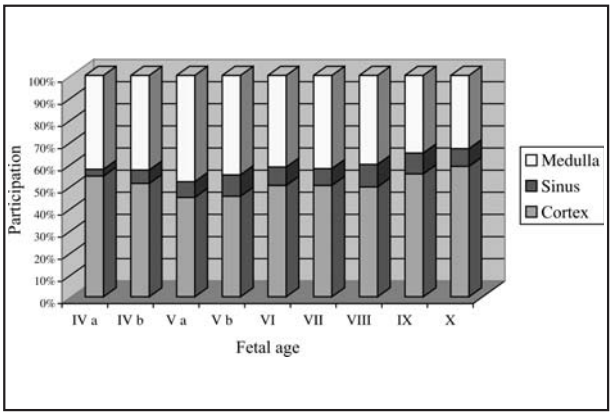

Figure 2. Participation of left kidney's strcture parts

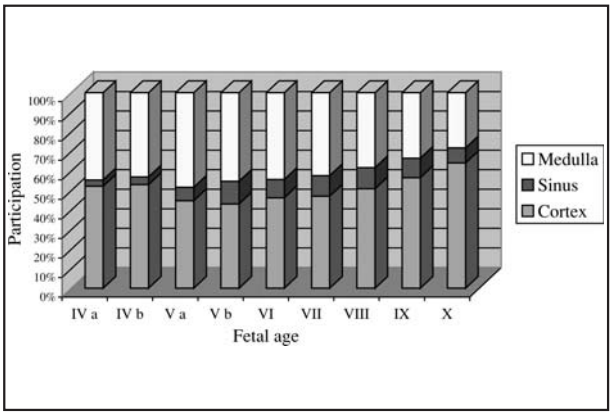

Figure 3. Participation of right kidney's strcuture parts

matician Kavalieri had established the first principles of mathematical calculation of the volume of definite structures, stereological methods have been permanently developed and improved in quality, but equipment, measuring and calculations have remained relatively simple (4,7).

An important stereological parameter of the kidney is the fractional volume, namely the percentage of a certain component in an organ volume (8).

Our results demonstrated that the participation of renal cortex is minimal in the second half of V lunar month, gradually increasing onwards. At the end of intrauterine life it increases more rapidly and, immediately before birth, it achieves the highest value (64%). These results are logical, because it is well known that nephrogenesis runs centrifugally, towards the renal capsule until birth and, for this reason, the cortex of a fetal kidney has its maximal growth and development in that time (9). This trend of percental growth of the renal cortex continues after birth, when in some cases, especially in the third and fourth decade of life, the cortex achieves the percentage of even 70% of the kidney volume (10).

The results of the study show that maximal participation of the renal medulla occurs in V lunar month and further on, with ageing of the fetus, it de-

creases continually. That is the reason why we may conclude that in V lunar month there is the most intensive development of juxtamedullar nephrons whose straight parts with collecting tubules, vasa recta and intersticial tissue make up the structure of the medulla.

Renal sinus has its maximal percentage from the second half of V until VIII lunar month. This period is characterized by the decrease of medullar participation and a low grade increase of cortex participation in the kidney volume.

Such results may be associated with the fetal kidney functional consequences. The control of liquid volume and retention of electrolytes mainly depends on medullar elements of the nephron, while filtration, selective secretion and reabsorption depend on the cortical components of the nephron (11). For this reason, it is necessary to be well acquainted with the basic results of this study in order to better understand the fetal kidney functioning.

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UČEŠĆE STRUKTURNIH DELOVA FETALNOG BUBREGA U NJEGOVOJ ZAPREMINI I NJIHOVE UZRASNE PROMENE

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SAŽETAK

Bez obzira na znatan rast i razviće, fetusni bubreg i njegove strukture su veoma slabo proučavani. Proces rasta se kontinuirano nastavlja u postnatalnom životu, ali uz značajniju pažnju naučnika. Zbog gore navedenog, stereološka istraživanja fetusnog bubrega su veoma značajna za razumevanje normalnog razvića njegovih struktura. Cilj ovog rada bio je da utvrdi udeo tri makroskopske strukture bubrega humanog fetusa: kore, srži i šupljine, u odnosu na gestacijsku starost. Autori su pokušali da odrede periode njihovog najvećeg i najmanjeg udela u zapremini bubrega i da ih uporede kroz različita gestacijska doba. Analizirano je 45 pari bubrega humanih fetusa, starosti od četvrtog do desetog lunarnog meseca. Bubrezi su podeljeni u devet grupa, u zavisnosti od njihove gestacijske starosti. Korišćenjem stereoloških metoda određivane su zapreminske gustine kore, srži i šupljine bubrega. Rezultati su statistički obrađeni, a periodi najvećeg i najmanjeg zapreminskog udela zabeleženi. Kora ima najveći procentualni udeo u zapremini fetusnog bubrega u X lunarnom mesecu, a najmanji u V lunarnom mesecu. Na drugoj strani, bubrežna srž svoj najveći udeo ima u V, a najmanji u X lunarnom mesecu. Bubrežna šupljina je najprisutnija u periodu smanjivanja udela srži i periodu laganog rasta udela kore. Veoma je značajno poznavati periode najvećeg učešća pojedinih bubrežnih struktura zato što funkcija fetusnog bubrega najverovatnije zavisi od dominantnog udela kortikalne ili medularne komponente nefrona. Ova studija je pokušaj da se odrede neki parametri koji mogu biti od pomoći u daljim istraživanjima razvića bubrega humanog fetusa.

***Ključne reči*: fetusni bubreg, kora, srž, šupljina, zapremina, stereologija**