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Review

Fetal biometry: Relevance in obstetrical practice

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ABSTRACT

Ultrasound imaging in obstetrics and gynecology dates back to 1958 when The Lancet published the first article about the use of ultrasonography for fetal and gynecological assessments. It is now almost inconceivable, 60 years later, to think of effective performance in obstetrics and gynecology without the variety of ultrasound, for example, real time imaging, power and color Doppler, 3D/4D ultrasonography, etc. Such examinations facilitate the assessment of intrauterine fetal growth and development during pregnancy, provide alerts about the risk of pre-eclampsia and preterm birth, help identify anatomic reasons for infertility, diagnose ectopic pregnancies, uterine, ovary and tubal pathology. Ultrasonography is also used for diagnostic and treatment procedures during pregnancy or for the treatment of infertility. This article is an overview of the development of fetal ultrasound, the methodology and interpretation of ultrasound in the assessment of intrauterine fetal growth and fetal biometry standards both worldwide and in Lithuania.

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1. History of fetal ultrasound biometry

Lack of data or contradictory facts often make it difficult to trace back the precise date of a large number of medical inventions. This is not the case in terms of the history of ultrasound in obstetrics and gynecology.

The use of ultrasound equipment in medicine began in the 1950s (until then it was only used in the military industry). The first medical A-mode (amplitude-mode is a one-dimensional imaging which represents the time required for the ultrasound

beam to strike a tissue interface and return its signal to the transducer, the greater the reflection at the tissue interface, the larger the signal amplitude [1]) equipment was created in Japan in 1949, and the first B-mode (brightness-mode is a two-dimensional ultrasound presentation display composed of the bright dots representing the ultrasound echoes, the position of the echo is determined from the position of the transducer and the transit time of the acoustical pulse [2]) ultrasound transducers introduced in 1951 allowed obtaining more accurate anatomic information compared with the earlier equipment and made interpretation of the images easier [3–5].

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Several years later, in 1958, *The Lancet* published the paper 'Investigation of abdominal masses by pulsed ultrasound' by obstetrician-gynecologist I. Donald, engineer T. Brown and registrar J. MacVicar. This paper is considered to be the reference point in the history of ultrasound use in the practice of obstetrics and gynecology (Fig. 1) [4,6]. In this paper the scholars presented the world's first contact 2D ultrasound Diasonograph scanning machine, which they had developed, and described the opportunities for using B-mode ultrasound in obstetrics and gynecology; they also published the first ultrasound images of the fetus and gynecological formations [6]. Furthermore, this paper detailed the physical characteristics and safety of ultrasound scanning machines, their use for the assessment of prenatal fetal growth and gynecological diseases and outlined further development of these examinations.

In the mid-1960s other companies – Kretztechnic in Austria and Aloka in Japan – developed commercial transvaginal transducers but the potential of transvaginal scanning was not realized until the advent of real time imaging [4,5]. In Germany, R. Soldner, an engineer who worked for Siemens, developed the first (almost) real time scanner [4,5]. Compared to the Diasonograph, the image resolution was poor yet this machine was purchased widely in German-speaking countries and by the late 1960s was probably the most commonly used machine in Europe [4,5].

I. Donald and the scholars led by him continued their intensive research of ultrasound after the development of the Diasonograph and in 1963 described the early diagnosis of the hydatid mole (in its characteristic snowstorm appearance), identified fetal development anomalies in the period of early pregnancy, offered guidelines for assessment of the growth of the gestation sac (by ultrasound when the bladder of the pregnant woman is full) [4,5,7]. J. Willocks, a colleague of I. Donald, published an article in 1964 about the use of A-mode ultrasound to identify differences in biparietal diameter (BPD) in the third trimester of pregnancy between normal growth and restricted growth fetuses [8]. This publication may be considered as the beginning of fetal ultrasound biometry. Unfortunately, due to the lack of precision, the idea brought forward in 1968 by S. Campbell, another member of I. Donald's team, to use B-mode ultrasound machines for fetal biometry measurements surpassed the A-mode ultrasound transducers several years later [9]. S. Campbell also announced that the midline echo of the fetus could be seen clearly from the thirteenth week of pregnancy and that the second trimester cephalometry of the fetus was a reliable method to identify pregnancy [9]. This introduced a new concept into prenatal medicine – “determination of gestational age by ultrasound”. S. Campbell developed the first fetal growth chart in the world that showed changes in the BPD of the fetus between gestation weeks 13 and 40 [9]. Later similar charts were developed by M. Hansmann, A. Kratochwil, R. Sabbagha and many others and they are, with certain corrections, still used [4,5].

The scientists, aware that the brain is the last structure affected in the case of fetal growth restriction, understood that the use of BPD alone to assess fetal growth restriction was not sufficiently accurate as a method. Thus, in 1971, H. Thompson and E. Makowsky also introduced the thoracic circumference (TC) measurement, to be used along with BPD, into fetal growth assessments [4,5]. In 1975 these examinations were supplemented by M. Hansmann with abdominal circumference (AC) measurement [10]. Several years later, L. Grennert and P. Persson demonstrated for the first time, with reference to long-term results of the research that covered the detection of gestational age and twin gestations during the early prenatal period, that routine ultrasound screening was necessary during pregnancy [4].

With further investigations, in 1967 A. Kratochwil used the A-mode transvaginal transducers to identify the fetal heart rate during week 7 of gestation [4,5]. The use of an improved Diasonograph in 1973 enabled H. Robinson to obtain a detailed fetal crown-rump length (CRL) growth chart from weeks 7 to 16 of gestation; this chart is still in use [4,5,7]. Moreover, using A and B mode ultrasound equipment, H. Robinson developed the chart of the fetal heart rate at week 7 of gestation and was the

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INVESTIGATION OF ABDOMINAL MASSES BY PULSED ULTRASOUND

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VIBRATIONS whose frequency exceeds 20,000 per second are beyond the range of hearing and therefore termed “ultrasonic”. One of the properties of ultrasound is that it can be propagated as a beam. When such a beam crosses an interface between two substances of differing specific acoustic impedance (which is defined as the product of the density of the material and the velocity of the sound wave in it), five things happen:

(1) Some of the energy is reflected at the interface, the amplitude of the reflected waves being proportional to the difference of the two acoustic impedances divided by their sum (Rayleigh's law). Therefore the greater the difference in specific acoustic impedance between two adjacent materials the higher will be the percentage of energy reflected. This fact makes a liquid-gas interface almost impenetrable to ultrasound and is important in relation to gas-filled intestine within the abdominal cavity.

(2) Much of the energy which is not reflected is transmitted into the second medium but is somewhat attenuated.

(3) Some refraction may occur, particularly when the ultrasonic beam is not at right-angles to the plane of the interface.

(4) Some of the energy may be absorbed and produce heat. The ability to absorb ultrasound varies with different tissues –e.g., that of bone is considerable.

(5) Cavitation may be produced if considerable energies are present at the lower ultrasonic frequencies. This phenomenon, whose mechanism is not yet fully understood, can develop when the negative sound pressure exceeds the ambient hydrostatic pressure, giving rise to small temporary voids in the material. Cavitation becomes increasingly difficult to produce as the frequency of the ultrasound is raised, and usually develops only when the ultrasonic energy is applied continuously or in

Fig. 1 – Page 1 of the article “Investigation of abdominal masses by pulsed ultrasound” by Donald et al.

first to describe the relationship between decreased fetal heart rate at week 8 of gestation and the later death of the fetus. This work underpinned further research on spontaneous abortion risk indicators.

The first reports about congenital fetal anomalies identified during ultrasound scans were published in 1964 and in 1970. In one case fetal anencephaly was described and in another – fetal polycystic kidney syndrome [4,5]. However, it is 1972 that is considered as the official beginning of ultrasound prenatal diagnosis when S. Campbell together with colleagues F. D. Johnstone, E. M. Holt and P. May detected anencephaly in the fetus of a woman at 17-week gestation, which led to the termination of the pregnancy [11].

The first ultrasound screening program in obstetrics was developed and applied in practice in Malmö, Sweden, in 1974 [4]. Its main purpose was to diagnose a multiple pregnancy. After two years' experience, the specialists of the same clinics offered a two-stage program of ultrasound examinations at gestation weeks 19 and 32 in order to detect any major fetal malformations [4]. Soon afterwards ultrasound screening spread in different European countries. For example, 1980 Germany included a two-stage and France – a three-stage ultrasound screening in their health care programs [4,12]. In 1985 the British doctor S. Thacker generalized the results of all investigations carried out until that time and published his conclusion that there were no reliable results to recommend ultrasound as a routine screening method, but that the use of ultrasound examination effectively reduced induced labor rates [4]. Three years later this finding was supported by Swedish scientists who demonstrated that even a single ultrasound examination at week 15 of gestation allowed to reduce induced labor rates in the case of a pregnant woman potentially going over her due date [13].

The ultrasound screening of pregnant women in the USA, however, was less popular. The conference that took place in Washington in 1984 presented findings stating that there were no reliable results proving that the routine ultrasound screening of pregnant women improved perinatal outcomes, reduced perinatal morbidity or mortality. Thus, ultrasound examination was recommended only for high-risk pregnant women [4].

These and further disagreements triggered prospective randomized trials to assess the effectiveness of routine ultrasound fetal examinations during pregnancy, extended the possibilities of the ultrasound technique and improved the design of fetal biometry charts for different populations. Because of this, ultrasound fetal biometry has become the key and most widely spread method of ultrasound diagnostics in obstetrics.

2. Fetal biometry

Fetal biometry means the measurement of the anatomic segments of the fetus by ultrasound. The following measurements are the most common: CRL, BPD, head circumference (HC), AC, and femur length (FL) [14]. In order to refine the measurement data of standard parameters and obtain more detailed information, sometimes other anatomic structures, e.g., transverse cerebellar diameter, binocular distance, fetal foot length and other measurements are taken.

Fetal biometry is particularly complicated in the case of a multiple pregnancy. This area is the subject of ongoing research, e.g., for the determination of fetal weight, it is recommended to use only FL and AC measurements because in the case of a multiple pregnancy HC and BPD distort the relevant results most of all. Moreover, different ultrasound measurements are included to evaluate gestational age, fetal growth and estimated fetal weight. A brief overview of the key biometry parameters – CRL, BPD, HC, AC, and FL – is provided in the next chapter [14].

3. Different biometric parameters

3.1. Crown-rump length

CRL is most often measured in the first trimester of gestation in order to determine gestational age (Fig. 2). The optimum measurement time is between weeks 8 and 12 when CRL is above 10 mm, because the slope of the embryonic growth curve is small before this time and it can be difficult to clearly identify a very early fetus [15,16]. The measurement used for dating should be the mean of three discrete CRL measurements when possible and needs to be obtained in a true midsagittal plane, with the genital tubercle and fetal spine longitudinally in view and the maximum length from cranium to caudal rump measured as a straight line [17,18]. The relationship between CRL and gestation age has been identified in the measurements of CRL for women when their gestation age was known precisely. The accuracy of this measurement for determining gestation age is within 3–5 days, although it can be found, that CRL is somewhat less accurate (e.g. ± 7.73 days) [16,18]. The study for assessing intra- and inter-observer agreement of routinely performed measurements to evaluate the likelihood of miscarriage in the first trimester of pregnancy showed that CRL has lower inter-observer variability than mean gestational sac diameter [15,19]. There is no doubt that CRL correlates best with gestation age [20,21].



Fig. 2 – Crown-rump length (CRL) dimension.

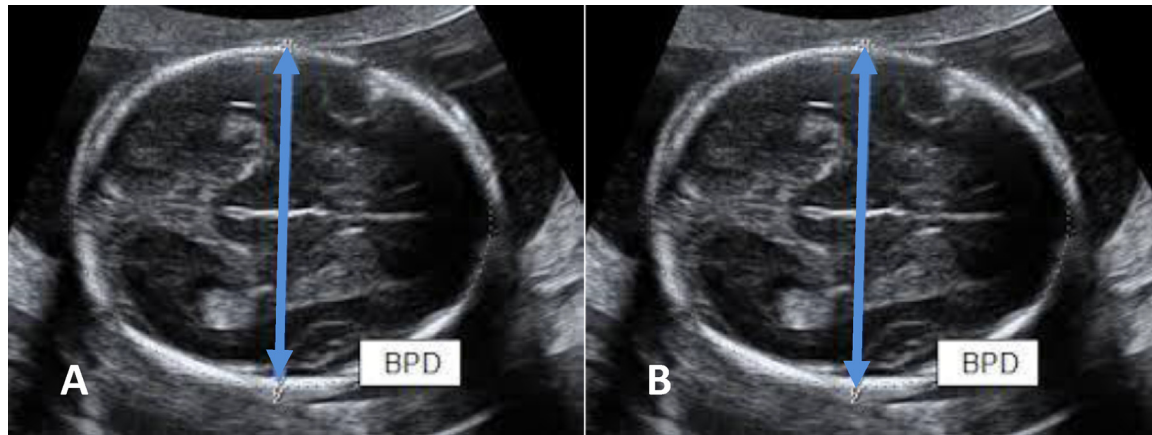


Fig. 3 – Biparietal diameter (BPD) dimension: outer to inner (A) and outer to outer (B).

3.2. Head measurements

BPD was the first ultrasound parameter used to determine gestational age and assess fetal growth (Fig. 3A and B). BPD is the widest axial dimension of the skull measured from the outer edge of the proximal parietal bone to the outer edge of the distal parietal bone. The anatomic reference points are the thalami and the cavum septi pellucidi [22]. It is important to note that different countries use different BPD measurement standards, e.g., in the Scandinavian countries, BPD is measured at the widest part of the fetal skull from the outer edge of the proximal parietal bone to the inner edge of the distal parietal bone (outer to inner) (Fig. 3A). Meanwhile, in Germany and Switzerland, BPD is measured according to E. Merz principle, i.e. at the widest part of the fetal skull from the outer edge of the proximal parietal bone to the outer edge of the distal parietal bone (outer to outer; skin-inclusive) (Fig. 3B) [23]. The calculation of gestational age based on BPD at gestation weeks 14–24 is sufficiently accurate. Variability is ± 1 –1.5 weeks while it subsequently increased to ± 3 –4 weeks. The optimum time for measuring this dimension is between gestation weeks 12 and 24 [21]. The results of other studies showed that the BPD measurement before gestation week 20 predict gestation age with an accuracy of ± 7 –11 days [24–26]. The precision tolerance of BPD dimension decreases during the third trimester of pregnancy [27].

HC is the outer perimeter of the skull. HC may be measured using the ellipse facility of ultrasound equipment at the same level as BPD or calculated according to the geometrical formula (ellipse-traced, ellipse-calculated, and circle-calculated) [28,29]. For clinical use the ellipse-traced method is recommended by Schmidt and colleagues [29].

When determining gestation age according to BPD, however, much depends on the head form. For example, during the ultrasound imaging the fetal head shape should be ovoid, not round (brachycephalic), because this can increase gestational age, just as a flattened or compressed head (dolichocephalic) can decrease BPD [30–32]. So, it is important to remember that brachycephaly (the skull's disproportion characterized by flattened anteroposterior axis of the skull) and dolichocephaly (the skull's disproportion characterized by the boat-shaped or

elongated anteroposterior axis of the skull) can not only be the result of an inaccurate ultrasound imaging plane, reflect congenital disorders (brachycephaly due to the premature closing of the cranial sutures (e.g., trisomy 21) or dolichocephaly due to the premature closing of the sagittal suture (e.g., Marfan syndrome) [33]), but also can be related with the fetal position in the uterus.

Lubusky et al. published the study about a comparison of fetal ultrasonographic biometric parameters of the head (HC and BPD) in breech presented fetuses [34]. According to their results, fetuses in the breech position had an elongated head shape which determined significantly lower BPD in comparison with HC or FL (the difference between BPD and HC was 16.2 days, 95% CI 14.3–18.1; $P = 0.001$), then HC and FL parameters correlated with gestational age [34]. These results confirmed previous studies, in which fetuses in the breech position have a significantly smaller BPD compared to fetuses in the head-down position in the third trimester by dolichocephaly with a prominent occiput with a suboccipital shelf, the so-called “breech head”, which occurred in at least one-third of fetuses in the breech position [35–37]. This deformation can be the result of fundal pressure on the growing fetal cranium as the fetus is constrained in the breech position, often with the head retroflexed and the posterior placental side [34,37–39]. Also, gestational age, primiparity and oligohydramnion can play a part in determining the skull shape [34,37–39].

According to these facts, HC is less affected than BPD by head shape variations and the presentation of the fetus, so HC is preferred as a more valuable measurement in assessing gestational age [21,30–32,34,37–39].

3.3. Femur length

FL measurements include the ossified portion of the diaphysis and metaphysis (Fig. 4). While not included in the FL measurement, the proximal epiphyseal cartilage and the distal epiphyseal cartilage should be visualized to ensure that the entire osseous femur can be measured without foreshortening or elongation [40]. It has been identified that the accuracy of FL in the predictions of gestational age is ± 2.8 weeks (2 SD) [41]. With increasing gestational age, the accuracy

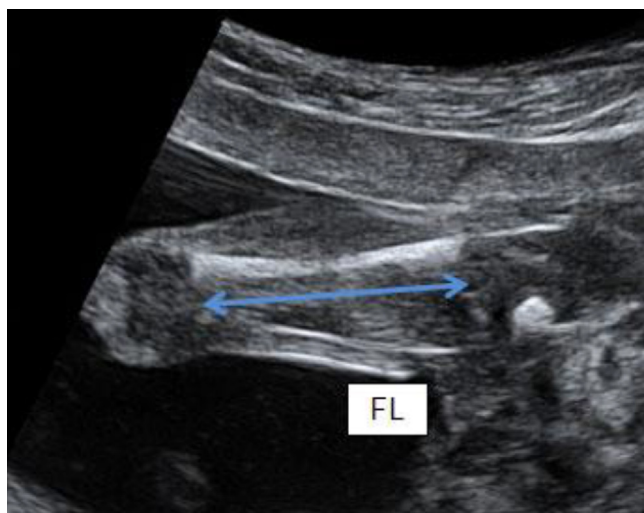


Fig. 4 – Femur length (FL) dimension.

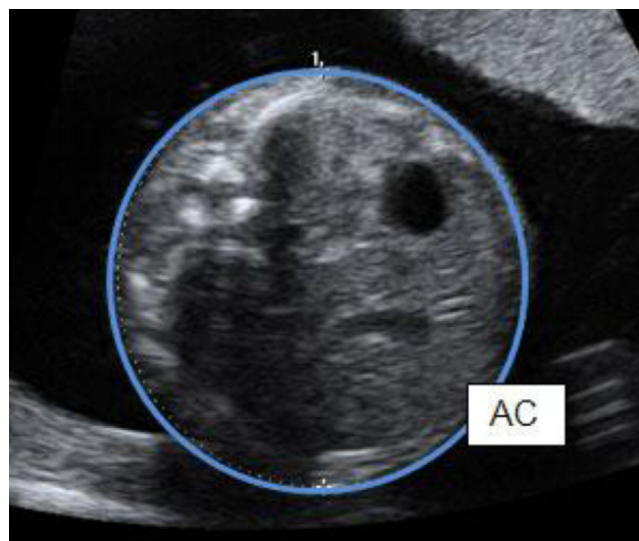


Fig. 5 – Abdominal circumference (AC) dimension.

of FL decreases [42,43]. The study of fetal age assessment based on FL at 10–25 weeks of gestation, and reference ranges for FL to HC ratios showed that fetal age assessment based on FL is equally as reliable as HC and FL/HC is a more robust ratio to characterize fetal proportions than FL/BPD [44]. The reliability of measurements of other long bones is lower compared to FL.

3.4. Abdominal circumference

AC is measured by the ellipse facility of ultrasound equipment with the stomach bubble and a short segment of the umbilical vein at the level of the portal sinus visible (Fig. 5). AC should not be used at all to determine gestational age; however, it is one of the key dimensions to assess intrauterine growth restriction (IUGR) and fetal macrosomia [45,46].

4. Intrauterine growth restriction

IUGR is predetermined by many genetic factors and by determinants related to the placenta and the mother. It is believed that each fetus has a particular growth potential when, under normal conditions, it grows to the appropriate gestational weight.

The “normal” neonate is one whose birth weight is between the 10th and 90th percentile as per the gestational age, gender and race with no feature of malnutrition and growth retardation [47]. IUGR is a pathology involving reduced fetal growth potential of a specific infant as per the race and gender of the fetus [47]. Although there is no universally accepted definition of IUGR, it is most commonly defined as a birth weight below the 10th percentile considering gender and gestational age; a birth weight lower than 2500 grams in a pregnancy of 37 weeks or more; the birth weight is more than 2 SD below the average mean [48]. There are basically two different types of IUGR [47]:

- Symmetric (primary) IUGR is characterized by all internal organs being reduced in size and indicates that the fetus has

developed slowly throughout the duration of the pregnancy and was thus affected from a very early stage. Symmetric IUGR accounts for 20–30% of all cases of IUGR. Common causes include early intrauterine infections, such as cytomegalovirus, rubella or toxoplasmosis, chromosomal abnormalities, anemia and maternal substance abuse;

- Asymmetric (secondary) IUGR is characterized by the head and brain being normal in size, but the abdomen is smaller. Asymmetric IUGR accounts for 70–80% of all cases of IUGR. Typically, this is not evident until the third trimester. The most common causes are placental insufficiency and pre-eclampsia.

IUGR is associated with high risk short-term and long-term complications for neonates, for example, perinatal asphyxia, meconium aspiration, hypoglycemia, abnormal physical growth, neurodevelopmental outcome, etc. [47].

Usually, IUGR and small for gestational age (SGA) are used interchangeably in literature, even though there are differences between them. SGA definition has been used for those neonates whose birth weight is less than the 10th percentile for that particular gestational age or two standard deviations below the population norms on the growth charts [47]. This definition considers only the birth weight without any consideration of the impaired development. Approximately 70% of the newborns with a birth weight below the 10th percentile are small in their constitutional factors including maternal height, weight, ethnicity, and parity, although they are proportionate, healthy, well developed and well nourished (e.g. born to parents who are small and/or into an ethnic population that is smaller than the reference population) [49]. These infants are not at increased risk for perinatal mortality or morbidity [50].

Intrauterine fetal weight is usually determined according to the relevant formulas (most often M. J. Shepard's and F. P. Hadlock's) which include BPD, HC, FL and AC measurements. The parameter classically affected is AC, so the highest diagnostic accuracy of IUGR is achieved when this dimension

is used. The sensitivity of the latter examination is as high as 95% if the AC value during the measurement is below the 2.5th percentile [51,52]. For the purposes of diagnosing IUGR, efforts have been made to use other methods as well, for example, Ponderal index, HC/AC ratio, etc. However, they are seldom used due to their low sensitivity and specificity [53-55].

Thus, ultrasound fetal biometry remains the “golden standard” for assessing IUGR in case of singleton and multiple pregnancies [56]. Supplementary ultrasound examination methods, e.g., Doppler test and measurements of the quantity of amniotic fluid, are helpful in providing additional information about fetal growth and development during the prenatal period.

5. Differences between fetal biometry charts in the world

An appropriate evaluation of fetal biometry represents a cornerstone in the assessment of fetal growth given that abnormal growth may be associated with an adverse perinatal outcome and may require specific obstetrical care [57]. Nowadays, researchers distinguish many variables, which affect fetal growth; these include physiological and pathological changes, such as maternal height and weight, drug or tobacco exposure, fetal sex, ethnicity, genetic syndromes, congenital anomalies and placental failure [58].

For example, in the cross-sectional study which was designed in Belgium significant differences for ultrasound-measured fetal head circumference, AC, FL, and estimated fetal weight between different ethnical groups were found [59]. Other investigators have also argued for ethnic-specific standards. The results of these studies have shown that Chinese, Japanese, and (especially) South Asian infants are smaller for their gestational age, whereas North American Indian and North African infants are larger than Caucasian infants, in the same geographic setting, even after controlling for socio-demographic differences among the different ethnic groups [60,61]. Moreover, ethnical differences in mid gestation have been found for femur measurements in a study which was designed to determine whether current methods for detecting Down syndrome based on fetal femur length calculations are influenced by ethnicity. There was a statistically significant difference in femur length in the Asian group compared with all other groups, as well as in the white group compared with the black and Asian groups ($P < 0.05$) [62]. Therefore, each particular population or ethnic group should have their own reference charts for the different fetal anthropometrical variables in order to provide the most accurate fetal assessment [58,63].

Moreover, in recent decades, increasing attention has been paid to the impact of fetal sex on intrauterine fetal size. Some researchers claim that the assessment of fetal biometry data depending on gender can be misleading, e.g., a large-scale trial carried out in North America has not identified any correlation between fetal intrauterine size and sex [64,65]. On the other hand, the study of 4000 pregnant women carried out by Schwärzler et al. suggested that fetal sex had an impact on biometric parameters and fetal weight [66]. The major difference between male and female fetuses was observed in the measurements of

fetal weight and the lowest – in femur measurements. The biometry curves of different fetal sexes showed that the key difference during the second trimester was in head dimensions while during the third trimester – in AC. Another study revealed that male fetuses were larger [67]. The study by Shild et al. also concluded that fetal BPD, HC, AC, and FL correlated with fetal sex [68]. However, sex-related assessment of intrauterine fetal growth does not have major clinical significance.

Regardless of factors, which could affect fetal growth, fetal nomograms need to be revised regularly as fetuses have become bigger in recent decades and need to be constructed in accordance with the recommended method of analysis [69]. For example, Royston and Wright published the methodology on how to draw up nomograms for fetal biometry. According to them, standard curves should vary consistently depending on gestational age [70]. Furthermore, it is often not possible to identify what methods of statistical analysis were used in the articles on fetal biometry assessment, the percentiles varied inconsistently with the increasing gestational age, changes in the measurement variability were assessed inadequately, there were no data scattering diagrams, and 'super normal' groups of pregnant women were analyzed.

6. Fetal biometry charts in Lithuania

Foreign fetometry curves have been used in Lithuania, because the last national reference charts based on ultrasound fetal biometry were designed in the 1980s, when Assoc. Prof. J. Alisauskas published his dissertation “Prenatal diagnosis of fetal hypotrophy” [71]. Unfortunately, 36 years have passed since Assoc. Prof. J. Alisauskas' work and the possibilities to evaluate fetal growth together with the appropriate methodologies have changed significantly (e.g., he did not include measurements of fetal femur length, was not able to use the “ellipse” function for fetal head or abdominal measurement). This is why in every day practice doctors use fetal biometry standards which are integrated in the ultrasound technique. The most common ultrasound machines in Lithuania are from Japan and the USA, but these standards are not appropriate for our population. Therefore, new reference charts based on ultrasound fetometry for BPD, HC, femur length (FL) and AC for the Lithuanian population must be established.

7. Concluding remarks

With the rapid development of technologies in different areas during recent decades, ultrasound diagnostics has also advanced. In conclusion, it is further sought to make fetal biometry more accurate, improve the measurement and use of biometric parameters, in particular, in the first trimester of pregnancy, because this is important not only for a more accurate determination of gestational age, but also for early diagnosis of fetal anomalies and pregnancy follow-up. It is particularly important not to disregard differences in fetal biometry standards for different populations. Appropriate pregnancy and fetal monitoring and treatment is possible only if the norm variations characteristic of each population are known, thus, a Lithuanian fetal biometry standard is necessary.

Conflict of interest

The authors state no conflict of interest.

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