Anthropological Review • Vol. 81(2), 111–129 (2018)

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Anthropological Review
Available online at: https://doi.org/10.2478/anre-2018-0009

The impact of maternal age on foetal growth patterns and newborn size

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Abstract: The association patterns between maternal age and foetal growth parameters as well as newborn size were analysed using a dataset of 4737 singleton term births taking place at the Viennese Danube hospital. Foetal growth patterns were reconstructed by the results of three ultrasound examinations carried out at the $11^{th}/12^{th}$, $20^{th}/21^{th}$ and $32^{th}/33^{th}$week of gestation. In detail, crown-rump length, biparietal diameter, fronto-occipital diameter, head circumference, abdominal transverse diameter, abdominal anterior-posterior diameter, abdominal circumference, and femur length were determined. Birth weight, birth length and head circumference were measured immediately after birth. Young teenage mothers (≤15 years), older adolescent mothers (16-19 years), mothers of optimal age range (20-35 years) and mothers of advanced age (>35 years) differed significantly in body height, pre-pregnancy weight status and gestational weight gain. Surprisingly, the foetuses of young adolescent mothers were the largest ones during first trimester. During the second and third trimester however, the foetuses of mothers of optimal age range (20-35 years) and mothers older than 35 years showed larger biometric dimensions than adolescent mothers. According to multiple regression analyses, maternal age was significantly related to Foetal head size (ß =-0.04; 95% CI = -0,08 – 0.01; p=0.034) and abdominal dimensions (ß= 0.03; 95% CI = 0.01-0.05; p=0,011) during the second trimester and to birthweight (ß= -0.03; 95% CI= -4.40 – 0.04; p=0.050). The associations however, are quite weak and the statistical significance is maybe due to the large sample size. At the time of birth, offspring of mothers of optimal age range (20 to 35 years) is significantly larger than that of adolescent mothers and mothers of advanced age. Mothers of advanced age showed the significantly highest (p=<0.0001) prevalence (5.6%) of SGA newborns (<2500g). The small size of newborn among young adolescent mothers may be due to a competition over nutrients between the still growing mothers and the foetuses during the third trimester, while placental ageing may be responsible for smaller size of offspring among mothers of advanced age.

Key words: foetal growth patterns, newborn size, teenage mothers, maternal age, foetal biometry

Introduction

In contrast to human males, female reproductive span is limited to about 35 years starting with menarche, the first spontaneous menstrual bleeding which indicates the onset of female reproductive cycle and ending with menopause, the final step in ovarian ageing (Forman et al. 2013). Fertility however, changes through potential reproductive span. While early adolescence is characteri-

Original Research Article Received December 15, 2017 Revised April 20, 2018 Accepted April 24, 2018
DOI: 10.2478/anre-2018-0009

zed by a high rate of anovulatory cycles, female fertility peaks between the ages of 20 and 30 years but starts to decline slowly at the end twenties (Balsch 2010). Consequently, the probability of successful conception is low at the beginning of reproductive span and decreases with increasing age after a period of optimal fertility. Furthermore, pregnancy outcome varies according to maternal age. Several studies have suggested that adolescents but also women 35 years and older are often vulnerable to adverse perinatal outcome, and increased newborn as well as maternal morbidity and mortality (Gravena et al. 2012). For a long time especially adolescent pregnancies have been interpreted as extremely risky and young maternal age has been associated with an increased risk of anemia, preterm labor, urinary tract infections, preeclampsia, high rate of caesarean sections, preterm birth and low birth weight infants and even maternal and newborn mortality (Fraser 1995, Perry 1996). More recently, however, obstetrical risks of adolescent pregnancies are seen predominantly as results of adverse social and economic factors rather than chronological age (Kirchengast 2009). In addition, advanced maternal age has been associated with a range of adverse pregnancy outcomes, such as low birth weight (Jolly et al. 2009, Joseph et al. 2005, Aliyu et al. 2008), pre-term birth (Jolly et al 2009, Joseph et al. 2005, Debaere et al. 2007), stillbirth, unexplained foetal death (Hoffman et al. 2007, O´Leary et al. 2002, Fleanady et al. 2011), increased rates of caesarean section (Jansens et l 2008), but also hypertensive syndromes, premature rupture of membranes and gestational diabetes (Hsieh et al. 2010). Consequently, the optimal age for childbearing seems to be between 20 to 35 years (Johnson and Tough 2012). At this age, the probability of successful conception is highest and the risk of adverse pregnancy outcome is lowest. Despite of this fact, there is an increasing trend among women to postpone childbirth into their mid-thirties and beyond in high-income countries (Newburn-Cook 2005). On the other hand, the number of young adolescent mothers is declining. Consequently, the mean age at first birth increases drastically in those countries. In Austria for example, the mean age at first birth increased from 23.8 years in 1984 to 29.4 years in 2016. (Statistik Austria 2017).

Beside obstetrical complications young maternal age but also advanced maternal age are associated with impaired foetal growth patterns. Extremely young but also advanced maternal age increase the risk of giving birth to small for gestational age newborn (Lee et al. 1998, Geronimus 1996, Virginia et al. 2001). Among mothers of advanced age, however also an increased incidence of macrosomic newborn is reported (Kenny et al. 2013). Both, small for gestational age newborn and macrosomic newborn increase the risk perinatal complications and peri- and postnatal morbidity. Therefore, the analysis of the impact of maternal age on foetal growth patterns is of special interest to gynaecologists, perinatologists but also public health researchers (Thame et al. 2004). In the majority of studies focusing on the impact of maternal age on foetal growth patterns exclusively newborn size i.e. birth weight was used as an indicator of foetal growth (Briggs et al. 2007, Shrim et al. 2011, Blomberg et al. 2014, Medhi et al. 2016). This is mainly due to the fact that birth weight, birth length and head circumference are direct results of foetal growth. Studies addressing the relationship between maternal age and foetal size measurements are scarce. Bottomley et al. (2009) described a significant influence of maternal age on crown-rump-length in the first trimester. In detail, older mothers had significantly smaller foetuses during early pregnancy (Bottomley et al. 2009). Metcalfe et al. (2013) described a similar trend. According to Johnson et al. (2004) maternal age is significantly associated with biparietal diameter and head circumference. Nevertheless, studies focusing on the association between maternal age and foetal size during intrauterine phase are rare. Therefore, the aim of the present study was to analyse the impact of maternal age on foetal growth patterns based on 14 foetal size dimensions from the first trimester onwards and newborn size. .

Material and methods

Data set

This retrospective study is based on a data set of 4737 singleton births, which took place at the Danube hospital (SMZ Ost) in Vienna, Austria between 2005 and 2013. The Viennese Danube hospital is one of the largest public birth clinics in Vienna. During the period 2005 to 2013 altogether 17430 births have been recorded at the Viennese Danube hospital, however only 4737 births fulfilled the strict inclusion criterions. The marked drop from 17430 births to 4737 births was mainly due to the strict inclusion criterion, that all three prenatal ultrasound examinations had to be performed at the Danube hospital. This was only true of 7590 births. 2853 birth had to be excluded, because they did not meet the following strict inclusion criteria.

1. Healthy primiparae mothers of Austrian or Central European origin
2. Term delivery (39th and 40th week of gestation).
3. Delivery of a single infant without congenital malformations
4. No preeclampsia or other registered maternal diseases such as diabetes mellitus or nephropathy before and during pregnancy, no hypertension (BP< 150/90 mmHg), no protein or glucose in the urine.

Additionally, the following exclusion criterions have been defined: IVF, drug consumption (cannabis, heroin, cocaine, crack, crystal meths and extasy) before and/or during pregnancy, or alcohol abuse and alcohol dependence according to the criteria defined in DSM-5. Finally, 4737 birth corresponded to that inclusion and exclusion criterions.

Maternal parameters

Exclusively primiparae mothers ageing between 14 and 48 years (mean=28.3; SD= 5.5) were enrolled in the present study. This sample was divided into four subsamples according to maternal age. According to Phipps and Sower (2002) mothers who gave birth before their 16th birthday were classified as young adolescent mothers, mother who gave birth between their 16th and 19th birthday were classified as older adolescent mothers. Since the risks for adverse obstetric and perinatal outcomes are especially low among mothers ageing between 20 and 35 years (Briggs et al. 2007, Cleary-Goldman et al. 2005; Delbaere et al. 2007; Salem et al. 2011; Shrim et al. 2011), mothers giving birth between 20 and 35 years were classified as optimal age group. Mothers older than 35 years when giving first birth were classified as advanced age mothers. Beside medical anamnesis, civil status and nicotine consumption of the pregnant women were obtained by interviews at the first prenatal visit (8^{th} week of gestation). Additionally the following maternal somatometric parameters were collected according to the recommendations of Knussmann (1988) at the first prenatal visit (8^{th} week of gestation): Body height and pre-pregnancy weight. Height was measured to the nearest 0.5 cm using a standard anthropometer. Pre-pregnancy weight was obtained by interview using the retrospective method. Additionally body weight was measured to the nearest 0.1kg on a balance beam scale at the 8^{th} week of gestation. Since during the first 13 weeks of gestation an extremely small weight gain of only 1.7% was reported in literature (Gueri et al. 1982), in the present study the mean of retrospective pre-pregnancy weight and weight at the 8^{th} week of gestation were used. Consequently, pre-pregnancy weight was calculated as the mean value of the retrospective estimated weight and the weight at the 8^{th} week of gestation. For further analyses, such as calculation of pre-pregnancy BMI this mean value was used. Maternal pre-pregnancy weight status was determined by the body mass index (BMI) kg/m^2 using height and pre-pregnancy weight. To classify maternal weight status the cut-offs published by the WHO (1995) were used.

Underweight = BMI < 18.50 kg/m^2

Normal weight = BMI 18.50 kg/m^2 to 24.99 kg/m^2

Overweight = BMI 25.00 kg/m^2 to 29.99 kg/m^2

Obesity = BMI > 30.00 kg/m^2

Additionally, maternal weight was measured before delivery when the woman entered the hospital for delivery (=at the end of pregnancy). The weight gain during pregnancy was calculated by subtraction of pre-pregnancy weight, i.e. mean value of the retrospective estimated weight and the weight at the 8^{th} week of gestation from body weight before delivery. A gestational weight gain of less than 7kg was classified as low. A gestational weight gain between 7 and 15 kg was considered as an average weight gain, while a gestational weight gain of more than 15kg was defined as a high gestational weight gain.

Prenatal examinations - foetal biometry

Gestational age was calculated in terms of the number of weeks from the beginning of the last menstrual bleeding to the date of delivery (= duration of amenorrhoea). In the present study the data of three sonographic examinations, one at each trimester, and the birth outcome were analysed. All these sonographic examinations had to be carried out at the Danube hospital. More than forty years ago the so called “Mother-child-Passport”, a highly sophisticated monitoring system of pregnancy, intrauterine and postnatal development was developed in Austria. Since that times seven prenatal check-ups starting at the 8^{th} week of gestation and eight postnatal check-ups of the child between birth and the fourth year of life are strongly recommended. The prenatal examinations are mainly performed in consulting rooms of gynaecologists or at the clinic where birth was scheduled to take place. Paediatricians carry out the postnatal check-ups. All examinations are free of charge. All data collected at the individual check-ups were documented at the hospital and in the so-called mother-child passport, which belongs to the mother. The government rewards a completed mother-child-passport with a financial premium. Foetal growth pattern were reconstructed by the results of three ultrasound examinations. The first examination took place at the 11th or 12th week of gestation (first trimester), the second examination took place at the 20th/21th gestational week (second trimester) and the third examination at the 32th/33th week of gestation (third trimester). Consequently, the foetuses could vary in age up to at least two weeks at each trimester. All transabdominal ultrasound examinations were performed by a limited number of trained specialists (< 15examiniers) using Voluson 730 and Voluson S6 (GE 8) ultrasonography. The following routine sonographic measurements, performed according to Hadlock´s criteria (Hadlock et al.1982a,b,c) were documented. At the first scan (11th or 12th gestational week) crown-rump length was determined. At the second (20th or 21th gestational week) and the third examination (32th or 33th week of gestation) biparietal diameter, fronto-occipital diameter, head circumference, abdominal transverse diameter, abdominal sagittal diameter, abdominal circumference and femur length were measured. Crown-rump length was defined as the distance between the top of the head (crown) to the bottom of the buttocks (rump). Femur length was measured from the greater trochanter to the lateral condyle. Biparietal diameter was defined as the distance from the proximal outer table to the distal outer table of the skull at the level of the thalamus. Fronto-occipital diameter follows a line extending from a point just above the root of the nose to the most prominent portion of the occipital bone. Head circumference is the measurement around the calvarium excluding soft tissues. Transverse and anterior –posterior abdominal diameter were taken at the level of the stomach and at the bifurcation of the main portal vein into its right and left branches. Abdominal circumference was calculated (Hadlock et al. 1982a,b,c, Hadlock et al. 1984, Kurmanavicius et al. 1999a,b, Snijders and Nicolaides 1994, Abdella et al 2014).

Newborn characteristics

Immediately after birth the following parameter were directly taken from the newborn: birth weight in grams using a digital infant scale, birth length in centimetres using a standard measurement board for infants and head circumference in centimetres using a tape. Ponderal index (kg/m^3) of the newborn was calculated (Roje et al. 2004). Small for gestational age was defined as a birth weight less than 2500g, a high birth weight (macrosomia) as a birth weight above 4000g according to the recommendations of the WHO (1980).

Statistical analysis

Statistical analyses were carried out by means of SPSS for Windows (version 24). A Kolmogorov-Smirnov-test was performed in order to test somatometric variables for normal distribution. Although the majority of parameters were normally distributed non parametric Kruskall Wallis tests + Dunn-Bonferroni post hoc tests and Fisher exact tests have been calculated in order to test maternal somatometrics, foetal biometry and newborn size differences between four maternal age group, because of the extremely low number of young teenage mothers (age group 1). Multiple regression analyses were performed to test associations between maternal age and foetal biometry, pre-pregnancy weight status and foetal biometry and newborn size adjusted for maternal height, pre-pregnancy weight status and gestational weight gain. A p-value below 0.05 was considered as statistically significant.

Results

Maternal and newborn characteristics

Table 1 demonstrated absolute and relative values maternal and newborn characteristics, such as maternal age groups, maternal civil status, nicotine consumption pre-pregnancy weight status as well as gestational weight gain, newborn sex and newborn weight status. The vast majority of women were between 20 and 35 years old when giving birth (81.5%). Only 0.2% of the mothers were younger than 16 years, 6.1% of the mothers were ageing between 16 and 19 years and only 12.2% of the mothers were older than 35 years. About 50% of the women enrolled in the present study were married at the time when they gave birth. 15% of the women continued smoking during pregnancy. The majority of women (65.7%) corresponded to the WHO definitions of normal weight. Only 7.2% of the women

Table 1. Maternal and newborn characteristics (descriptive statistics)

Maternal and newborn characteristics	n	%
Civil status		
unmarried	2230	48.5
married	2367	51.5
Nicotine consumption during pregnancy		
no	4026	85.0
yes	711	15.0
Maternal age group		
≤15years	9	0.2
16-19 years	287	6.1
20-35 years	3862	81.5
>35 years	579	12.2
Maternal pre-pregnancy weight status		
underweight BMI < 18.49 kg/m^2	341	7.2
normalweight BMI 18.50-25.99 kg/m^2	3112	65.7
overweight BMI 25.00-29.99 kg/m^2	862	18.2
obese BMI ≥30.00 kg/m^2	422	8.9
Gestational weight gain		
<7kg	251	5.3
7-15kg	2586	54.6
>15kg	1900	40.1
Newborn sex		
male	2392	50.5
female	2345	49.5
Newborn weight status		
small for gestational age < 2500g	81	1.7
normal weight 2500-3999g	4268	90.1
macrosomia ≥ 4000g	388	8.2

met the classification criterions of underweight, on the other hand 27.1% of the mothers were overweight or obese before pregnancy. While 40% of the mothers experienced a gestational weight gain of more than 15kg, only 5.3% gained less than 7kg during pregnancy. The number of male newborns (50.5%) was slightly higher than that of female ones (49.5%). Only less than 2% of the newborn were lighter than 2500g, while 8.2% corresponded to the definition of macrosomia (≥ 4000g).

Maternal age and maternal somatometrics

As presented in table 2, young and older adolescent mothers were significantly shorter ($p<0.0001$) and lighter before pregnancy ($p<0.0001$) and at the end of pregnancy ($p<0.0001$) than mothers ageing between 20 and 35 years and mothers older than 35 years. The pre-pregnancy body mass index however, was significantly highest among young adolescent mothers ($p<0.0001$), although none of the young adolescent mothers were classified as obese. In contrast, the highest prevalence of pre-pregnancy underweight (BMI <18.50kg/m^2 was found among young adolescent mothers (see fig. 1). Concerning gestational weight gain, however, young adolescent mothers experienced the significantly highest weight gain ($p<0.0001$). More than 55% of the young adolescent mothers experienced a weight gain above 15kg (fig. 2)

Maternal age and foetal biometry

As demonstrated in table 3, crown--rump length at the 11th/12th gestational week was highest among young adolescent mothers and lowest among older adolescent mothers ($p=0.017$). From the second trimester onwards however, mothers of optimal age range and mothers of advanced age showed the largest foetal head and abdominal dimensions, while the foetuses of young adolescent mothers showed the longest femur length. During

Table 2. Maternal somatic characteristics according to age group (Kruskall-Wallis test and Dunn-Bonferroni post hoc tests)

Somatic characteristics	≤ 15 years	16-19 years	20-35 years	> 35 years	Sig.
n	9	287	3862	579	*p*-value
	Median (range)	Median (range)	Median (range)	Median (range)	
Maternal body height (cm)	161 (155-167)^{c,d}	165 (150-180)^{c,d}	166 (149-189)^{a,b}	167 (150-187)^{a,b,c}	<0.0001
Maternal pre-pregnancy weight (kg)	56 (42-72)^{c,d}	57 (40-124)^{c,d}	61 (41-148)^{a,b,d}	62 (45-149)^{a,b,c}	<0.0001
Maternal end of pregnancy weight (kg)	72,5 (59-82)^{c,d}	72 (48-142)^{c,d}	77 (48-153)^{a,b}	76 (50-148)^{a,b}	<0.0001
Pregnancy weight gain (kg)	16 (12-18)^{c,d}	15 (2-29)	14,5 (0-52)^{a,d}	13 (-9 -28)^{a,c}	<0.0001
Pre-pregnancy body mass index kg/m^2	22.29 (16.41-25.10) ^{b,c}	21.09 (14.87-41.43) ^{a,c,d}	22.06 (14.83-52.73) ^{a,b}	22.21 (16.98-48.26)^{,b}	<0.0001

Legend: a= significantly different from ≤ 15 years; b = significantly different from 16-19 years; c = significantly different from 20-35 years; d = significantly different from >35 years.

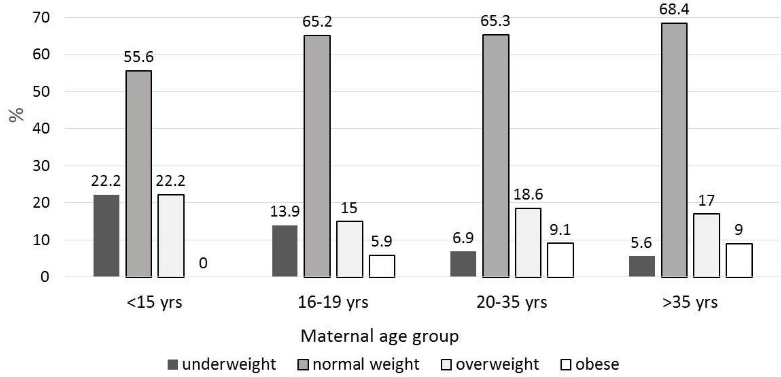

Fig. 1. Prepregnancy weight status according to maternal age group Fisher exact test ($p<0.0001$)

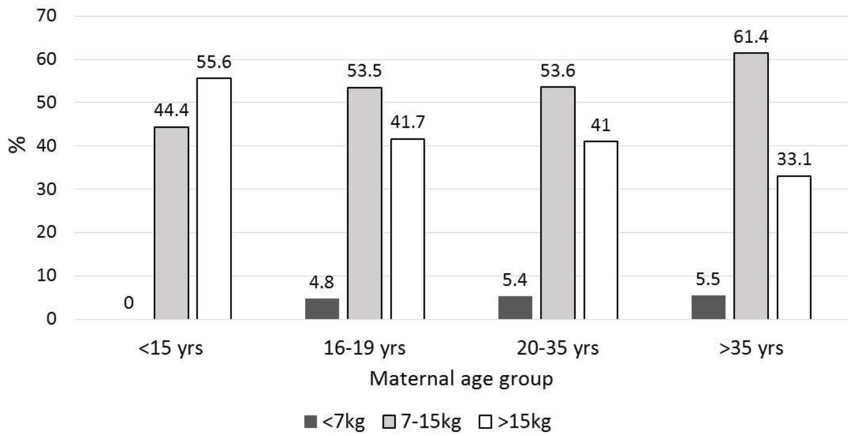

Fig. 2. Gestational weight gain according to maternal age group Fisher exact test ($p<0.0001$)

the second trimester statistically significant differences between maternal age groups were found for abdominal circumference ($p=0.050$) and abdominal sagittal diameter ($p=0.018$) only. During the third trimester however, young adolescent mothers showed the lowest foetal dimensions, while advanced age mother (>35yrs) showed the highest values. Statistically significant differences were found for the biparietal diameter and the head circumference only.

Maternal age and newborn size

According to the Kruskall-Wallis tests and Dunn-Bonferroni post hoc tests, newborns of mothers ageing between 20 and 35 years showed the significantly highest birth weight ($p=0.001$), birth length ($p=0.003$) and head circumference ($p=0.001$). The significantly lowest dimensions exhibited the newborns of young adolescent mothers. The significantly highest ponderal index was found among the newborns of older adolescent

Table 3. Foetal characteristics according to maternal age group (Kruskall-Wallis test and Dunn-Bonferroni post hoc tests)

Foetal biometric characteristics	≤ 15 years	16-19 years	20-35 years	> 35 years	Sig.
n	9	287	3862	579	*p*-value
	Median (range)	Median (range)	Median (range)	Median (range)	
1.Trimester					
Crown-crump length (mm)	65.0 (60-66)[b,c,d]	59.0 (40-82)[a,d]	60.0 (40-95)[a,d]	61.0 (40-84)[a,bc]	0.017
2.Trimester					
Biparietal diameter (mm)	50.2 (47.9-56.5)	52.7 (47.8-72.3)	53.0 (44.5-84.9)	52.8 (42.8-60.5)	0.402
Fronto-occipital diameter (mm)	64.9 (61.9-74.5)	67.1 (59.2-98.8)	67.1 (53.8-99.5)	67.0 (58.8-90.1)	0.733
Head circumference (mm)	180.8 (172.5-205.8)	188.6 (172.3-268.8)	188.7 (153.7-289.7)	188.2 (169.3-220.9)	0.558
Abdominal transverse diameter (mm)	48.0 (46.1-51.0)	48.5 (41.5-65.0)	49.2 (36.2-84.6)	49.5 (40.9-61.3)	0.883
Abdominal sagittal diameter (mm)	48.9 (48.5-52.1))[b,c,d]	50.9 (42.1-70.0)[a,c,d]	51.3 (39.0-81.1)[a,b]	51.8 (38.8-72.6)[a,b]	0.018
Abdominal circumference (mm)	151.7 (149.7-161.9)	156.1 (136.8-211.0)[c,d]	157.9 (118.6-254.0)[b]	159.0 (135.4-210.3)[b]	0.050
Femur length (mm)	36.6 (35.2-38.0)	35.8 (31.3-49.8)	35.8 (29.4-63.9)	35.5 (28.0-45.8)	0.894
3.Trimester					
Biparietal diameter (mm)	82.8 (81.1-91.0)[c,d]	85.9 (77-95.5)[c,d]	87.0 (73.0-100.0)[a,b]	87.2 (73.6-97.06)[a,b]	0.002
Fronto-occipital diameter(mm)	101.6 (99-106.8)	107.9 (90.5-119.0)	107.9 (81.0-126.8)	108.0 (95.0-122.0)	0.067
Head circumference (mm)	291.2 (284.7-295.2)[b,c,d]	304.9 (269.2-351.3)[a,c,d]	306.3 (244.9-344.5)[a,b]	306.8 (273.2-343.1)[a,b]	0.005
Abdominal transverse diameter (mm)	85.0 (76.2-89.0)	85.0 (70.4-99.5)	85.8 (67.6-108.0)	85.9 (69.4-110.0)	0.086
Abdominal sagittal diameter (mm)	79.9 (76.7-88.3) [b,c,d]	88.3 (74.9-106.6)[a]	88.3 (67.9-111.5)[a]	88.3 (72.3-110.0)[a]	0.050
Abdominal circumference (mm)	259.9 (240.4-277.9)	272.1 (230.8-316.7)	273.6 (227.0-330.8)	272.6 (223.5-344.0)	0.064
Femur length (mm)	63.3 (60.6-69.0)	63.0 (55.4-73.0)	63.3 (52.3-73.0)	63.7 (51.9-71.0)	0.389

Legend: a= significantly different from ≤ 15 years; b = significantly different from 16-19 years; c = significantly different from 20-35 years; d = significantly different from >35 years.

mothers (see table 4). Furthermore, newborn weight status differed significantly between the four maternal age groups. While young teenage mother gave birth exclusively to normalweight offspring, more than 8% of the mothers ageing between 20 and 35 years gave birth to a macrosomic newborn. The highest amount of small for gestational age newborns (<2500g) was found among mothers older than 35 years (5.6%) (see fig. 3).

Association patterns between maternal age, foetal growth and newborn size

Association patterns between maternal age, but also maternal height, pre-pregnancy BMI and gestational age at visit, and foetal size were tested by means of multiple regression analyses. During the first trimester (11th/12th week of gestation) maternal age, maternal height and

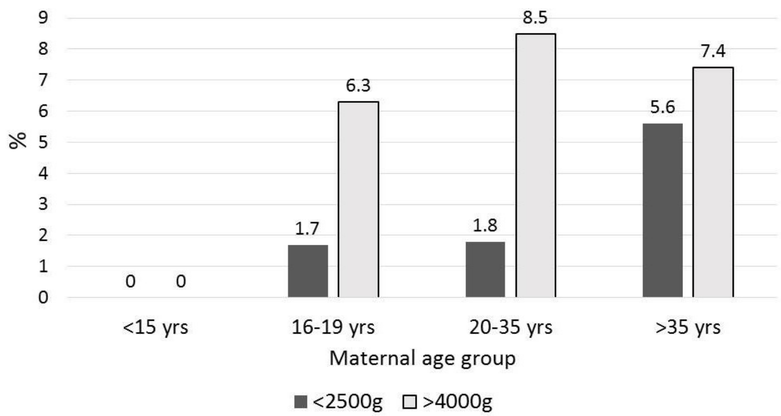

Fig. 3. Newborn weight status according to maternal age group Fisher exact test ($p<0.0001$)

Table 4. Newborn size according to maternal age group (Kruskall-Wallis test and Dunn-Bonferroni post hoc tests)

Newborn characteristics	≤ 15 years	16-19 years	20-35 years	> 35 years	Sig.
n	9	287	3862	579	*p*-value
	Median (range)	Median (range)	Median (range)	Median (range)	
Birth weight (g)	3085.0 (2520.0-3550.0)^{b,c,d}	3275.0 (2450.0-4880.0) ^{a}	3380.08 (1745-5110) ^{a,d}	3310.0 (2190-5020) ^{a,c}	0.001
Birth length (cm)	50.0 (48.0-52.0)^{c}	50.0 (45.0-56.0)^{c}	51.0 (37.0-60.0) ^{a,b,d}	50.0 (44.0-58.0) ^{c}	0.003
Head circumference (cm)	33.5 (32.0-35.0)^{b,c,d}	34.0 (3.0-38.0)^{a,c}	34.0 (29.0-43.0)^{a,b}	34.0 (29.0-39.0)^{a}	0.001
Ponderal index (kg/m^3)	2.56 (2.02-2.65) ^{b,c,d}	2.59 (2.15-2.99)^{a,c,d}	2.58 (1.86-8.74)^{a,b,d}	2.56 (1.98-3.49)^{a,b,c}	0.018

Legend: a= significantly different from ≤ 15 years; b = significantly different from 16-19 years; c = significantly different from 20-35 years; d = significantly different from >35 years.

maternal pre-pregnancy BMI showed no significant associations with crown-rump length. Crown rump length however, was significantly associated with the gestational age at the first visit. As demonstrated in table 5 maternal age was significantly negatively associated with the fronto-occipital diameter and the head circumference but significantly positively associated with abdominal sagittal diameter during the second trimester. Maternal height and maternal pre-pregnancy index were significantly positively associated with the majority of foetal biometric parameters during second as well as third trimester. The gestational age at visit, however, was not significantly related to foetal biometric parameters during second and third trimester. The percent variability (r^2) however, was quite low for the all regression analyses. At the time of birth maternal age was significantly negatively related with birth weight and ponderal index (see table 6). Furthermore, a significantly positive association could be observed between birth length as well as newborn head circumference and maternal height, maternal pre-pregnancy index and gestational weight gain.

Discussion

The present study focused on the association patterns between maternal age and foetal biometric parameters during first, second and third trimester as well as newborn size based on a data set containing 4737 singleton births, which took place in Vienna, Austria. Maternal age ranged from 14 to 48 years. Consequently, adolescent mothers but also mothers of advanced age were included in the analyses. Before we start to discuss the results in detail, we have to state that the present study has certain limitations. The main shortcoming is the small number of young adolescent mothers (<16years). Only nine girls giving birth between 14 and 15 year of age represented the age group young adolescent mothers. This low number is mainly due to the fact that young adolescent mothers (<16 years) are extremely rare in Austria. During the period 2005 to 2013 only 83 girls younger than 16 years gave birth in whole Austria (Statistik Austria 2016). Another shortcoming is that foetal biometry was taken only once per trimester and the measurements were taken at the $11^{th}/12^{th}$, 20th/21th and 32th/33th week of gestation. Consequently, the foetuses could vary in gestational age by up to at least 14 days. Therefore, the association patterns between maternal parameters and foetal biometry were corrected by the gestational age at visit in the multiple regression analyses. The strength of the study is the large data set comprising 15 foetal and three newborn measurements of 4737 children.

It is well documented that foetal growth is associated with maternal somatic parameters (Pölzlberger et al. 2017). Consequently maternal height, pre-pregnancy weight status and gestational weight have been recorded in the present study. As to be expected, adolescent mothers were significantly shorter and lighter than mother of optimal age range and mothers of advanced age. In contrast, adolescent mothers experienced the significantly highest gestational weight gain. Surprisingly, the foetuses of young adolescent mothers surpassed those of their older counterparts in crown rump length significantly during the first trimester. Considering the small number of young adolescent mothers, these differences are not representative. During the second and the third trimester however,

Table 5. Association patterns between maternal age, stature, pre-pregnancy weight status, and gestational weight gain and foetal biometry (11th/12th, 20th/21th and 32th/33th week of gestation) Multiple Regression analyses

	R^2	β	*p*-value	95% CI	R^2	β	*p*-value	95% CI
Dependent Variable: Crown-rump length	11th/12th week of gestation							
Maternal age	0.700	0.01	0.583	-0.01 – 0.03				
Maternal height		0.01	0.598	0.01 – 0.02				
Pre-pregnancy BMI		-0.01	0.539	-0.03 – 0.02				
Gestational age at 1.visit		10.59	<0.001	10.38 – 10.81				
	20th/21th week of gestation				32th/33th week of gestation			
Dependent variable: biparietal diameter								
Maternal age	0.003	-0.01	0.613	-0.02 – 0.01	0.027	-0.01	0.758	-0.02 – 0.02
Maternal height		0.02	0.002	0.01 – 0.03		0.08	<0.001	0.07 – 0.10
Pre-pregnancy BMI		-0.01	0.356	-0.02 – 0.01		0.05	<0.001	0.02 – 0.07
Gestational at visit		-0.08	0.169	-0.19 – 0.03		-0.15	0.076	-0.29 – 0.01
Dependent variable: fronto-occipital diameter								
Maternal age	0.006	-.0.02	0.030	-0.03 – 0.01	0.013	-0.01	0.725	-0.30 – 0.02
Maternal height		0.03	<0.001	0.01 – 0.04		0.08	<0.001	0.06 – 0.10
Pre-pregnancy BMI		0.02	0.040	0.01 – 0.04		0.05	<0.001	0.21 – 0.82
Gestational age at visit		0.05	0.460	-0.08 – 0.18		-0.01	0.989	-0.21 – 0.20
Dependent variable: head circumference								
Maternal age	0.005	-0.04	0.034	-0.07 – 0.01	0.023	-0.01	0.932	-0.06 – 0.06
Maternal height		0.07	<0.001	0.04 – 0.11		0.25	<0.001	0.19 – 0.30
Pre-pregnancy BMI		0.02	0.371	-0.03 – 0.07		0.15	<0.001	0.08 – 0.22
Gestational age at visit		-0.06	0.702	-0.38 – 0.25		-0.17	0.445	-0.67 – 0.29
Dependent variable: Abdominal transverse diameter								
Maternal age	0.005	-0.01	0.797	-0.02 – 0.02	0.018	0.01	0.597	-0.02 – 0.04
Maternal height		0.03	<0.001	0.02 – 0.05		0.01	0.798	-0.02 – 0.03
Pre-pregnancy BMI		0.01	0.620	-0.02 – 0.03		0.15	<0.001	0.12 – 0.18
Gestational age at visit		-0.13	0.083	-0.27 – 0.01		-0.22	0.088	-0.45 – 0.01
Dependent variable: Abdominal sagittal diameter								
Maternal age	0.008	0.03	0.011	0.01 – 0.05	0.015	0.01	0.690	-0.02 – 0.04
Maternal height		0.02	0.025	0.01 – 0.04		0.02	0.118	-0.01 – 0.05
Pre-pregnancy BMI		-0.01	0.267.	-0.04 – 0.01		0.12	0.001	0.09 – 0.16
Gestational age at visit		0.36	0.010	0.18 – 0.53		0.41	0.078	0.32 – 0.71
Dependent variable: Abdominal circumference								
Maternal age	0.006	0.04	0.111	-0.01 – 0.09	0.021	0.02	0.595	-0.05 – 0.09
Maternal height		0.09	<0.001	0.04 – 0.13		0.04	0.227	-0.03 – 0.10
Pre-pregnancy BMI		-0.01	0.694	-0.07 – 0.05		0.43	<0.001	0.34 – 0.52
Gestational age at visit		0.35	0.087	-0.04 – 0.76		0.55	0.087	-0.04 – 1.14
Dependent variable: Femur length								
Maternal age	0.013	-0.01	0.505	-0.01 – 0.01	0.360	0.01	0.277	-0.01 – 0.02
Maternal height		0.07	<0.001	0.01 – 0.03		0.07	<0.001	0.05 – 0.08
Pre-pregnancy BMI		0.09	<0.001	0.03 – 0.05		0.07	<0.001	0.05 – 0.08
Gestational age at visit		0.01	0.579	-0.11 – 0.06		0.11	0.073	0.01 – 0.23

Table 6. Association patterns between maternal age, stature, pre-pregnancy weight status, and gestational weight gain and newborn size Multiple Regression analyses

	R^2	Regression coefficient β	Sign. *p*-value	95% CI
Dependent Variable: birth weight				
Maternal age	0.104	-0.03	0.050	-4.40 – 0.04
Maternal height		0.18	0.001	10.62 – 14.51
Pre-pregnancy BMI		0.18	0.001	14.84 – 20.21
Gestational weight gain		0.21	0.001	14.35 – 18.68
Dependent variable: birth length				
Maternal age	0.078	-0.01	0.480	-0.01 – 0.01
Maternal height		0.18	0.001	0.05 – 0.07
Pre-pregnancy BMI		0.15	0.001	0.05 – 0.08
Gestational weight gain		0.17	0.001	0.05 – 0.07
Dependent variable: head circumference				
Maternal age	0.051	0.006	0.707	-0.01 – 0.01
Maternal height		0.16	0.001	0.03 – 0.04
Pre-pregnancy BMI		0.11	0.011	0.02 – 0.04
Gestational weight gain		0.13	0.001	0.02 – 0.04
Dependent variable: ponderal index				
Maternal age	0.016	-0.03	0.028	-0.01 – 0.00
Maternal height		0.02	0.484	-0.01 – 0.01
Pre-pregnancy BMI		0.07	0.001	0.01 – 0.02
Gestational weight gain		0.10	0.001	0.01 – 0.02

the foetuses of young as well as older adolescent mothers were smaller than the foetuses of mothers of optimal age range and mother of advanced age. Consequently, young adolescent mothers gave birth to the significantly smallest newborns. These results are in accordance with those of Amini et al. (1996), Demirci et al. (2016), and Kirchengast and Hartmann (2003) who reported similar outcomes for very young mothers. Multiple regression analysis revealed that the third trimester head dimensions, as well as birth weight, birth length and newborn head circumference are significantly associated with maternal height, pre-pregnancy body mass index and gestational weight gain. Since very young mothers were significantly shorter than older mothers, the detected differences in foetal head size and newborn parameters may be attributable to the difference in maternal body size between adolescent mothers and their older counterparts. According to Moerman (1982) pre-menarcheal growth spurt does not include the bony pelvis, which follows its own, slow growth pattern. Adult pelvic size is achieved not before 17 or 18 years of age (Moerman 1982). According to Alves et al. (2013) adolescent girls (10 - 19 years) have a significantly smaller pelvis than their older counterparts (over 20 years). Consequently, the reduced foetal growth among young adolescent mothers in the present study, resulting in smaller intrauterine head as well as abdominal size and smaller birth size (birth weight, birth length, head circumference) may be due to the smaller body size of adolescent mothers. Even among adult women, short maternal body height is associated with smaller pelvic size, which may increase the risk of cephalic-pelvic-disproportion and obstructed labor. Consequently, maternal shortness increases the caesarean section due to cephalo-pelvic disproportion is significantly (Kirchengast and Hartmann 2007). Therefore, the reduced foetal growth among young adolescent mothers from the second trimester onwards, observed in the present study, may be interpreted as an adaptation to the small body size .of adolescent mothers. Scholl et al. (1990, 1997) provided another explanation and mentioned that more than 55% of 12 to 15 year old gravidas are still growing in height resulting in a competition for nutrients between the young mother and her foetus. The metabolic needs of the maternal organism are being prioritized over the demands of the foetal organism, by reducing nutrient transmission and blood flow to the unborn child, in particular in the third trimester, the period where the foetus grows the most (Scholl et al.,1997). This may lead to reduced infant weight at birth (Scholl et al., 1997). The smaller birth size of newborns of young adolescent mothers in the present study might correspond to these findings. Moreover, still growing pregnant teenagers gain more weight during gestation, than non-growing counterparts (Scholl et al., 1994). Normally, these energy reserves are mobilized late in pregnancy to meet the maximum demands of the unborn child at this time. Growing adolescent gravidas, however, do not mobilize fat stores but reserve them for their own continuing development, leading to smaller infants despite excess weight gain (Scholl et al., 1994). In the present study, young adolescent mothers gained more weight than their adult counterparts did, adding to the picture of still growing young women.

Mothers of advanced age are significantly taller than, as to be expected, adolescent mothers but also than mothers of optimal age range (20 to 35 years). This may be due to the fact, that women giving first birth at an advanced age have mostly a higher socioeconomic status than women who gave first birth during adolescence or during their twenties (Barclay and Myrskylä 2016). Socioeconomic status on the other hand is strongly associated with stature height (Egolf and Corder 1991). In the present study mothers of advanced age are not only the tallest, they are also the heaviest, but experienced the significantly lowest gestational weight gain. Concerning foetal biometry in the present study, mothers of advanced age have foetuses with a significantly larger crown-rump-length (CRL) than women of optimal age range (20 to 35 years). This result is in contrast to that of Bottomley et al. (2009), who found smaller foetuses among older women than among younger mothers. Bottomley et al. (2009) however, determined crown rump length between gestational weeks 5 and 14, which is a considerably larger timeframe than in the present study, where crown--rump-length was documented between gestational week 11th and 12th. Metcalfe et al. (2013) found, similar to Bottomley et al. (2009), an inverse linear relationship between maternal age and CRL early in pregnancy, in that women over 40 had smaller fetuses than women under the age of 25, at 11 weeks of gestation. In the present study, foetuses of mothers of advanced age did not differ from those of mothers of optimal age range during the second and third trimester.

The newborn of mothers of advanced age (>35 years) were significantly lighter and shorter that the newborn of mothers of optimal age range. These findings are in accordance with those of Blomberg et al. (2014), who found that mean birth weight decreased significantly after the age of 30. Furthermore, Delbert et al. (2007) as well as Yoga et al. (2010) reported, that mean birth weight was significantly lower for mothers aged 35 or older compared to women from 25 to 29 years of age, and significantly lower for women aging 30 or older, compared to women from 20 to 29 years, respectively. Additionally the prevalence of small for gestational age newborn (<2500g) was highest (5.6%) among mother of advanced age, while the prevalence of macrosomic newborn was lower among mothers of advanced age (7.4%) in comparison with mothers of optimal age range (8.5%). Among older adolescent mothers and mothers of optimal age range the prevalence of small for gestational age newborn was 1.7% and 1.8% respectively. The elevated frequency of small for gestational age newborn among mothers of advanced age is in accordance to the results of several other studies (Carola 2013; Chan and Lao 2008; Cleary-Goldman et al. 2005; Delbert et al. 2007; Jerome and Husseini 2008; Salem et al., 2011; Yoga et al. 2010). A biological explanation for the smaller newborn size among mothers of advanced age might be the effect of age on the uterus and placenta. Advanced maternal age is indeed associated with accelerated placental ageing (Lean et al., 2014) and increased oxidative stress (Gamin et al., 2013; Soars et al., 2016). According to Nakeya et al (1983) advanced maternal age is associated with decreased blood flow to the placenta, uteroplacental under perfusion and placental infarcts, which makes it difficult for older women to adapt to the increased demands of pregnancy. Godfrey et al. (1999) reported poorer placental perfusion and transplacental nutrient flux in older women. Significantly smaller uterine spiral vasculature volume in women aged 35 years or older, compared to younger counterparts, leading to decreased uterine blood supply, was found by Zalud and Shaha (2008). Lean et al. (2014) supported these findings by showing changes in placental and myometrial vascular function, affecting blood flow to the placenta and foetus adversely. In humans, rats and mice, increasing maternal age has been shown to be associated with higher total placental weight (Care et al. 2015; Haavaldsen et al., 2011; Torres et al., 2017) and higher placental weight relative to birth weight (Haavaldsen et al., 2011). The enlargement of the placenta may due to a biological compensatory mechanism for placental dysfunction, to balance out the decreased uteroplacental blood flow and prevent foetal hypoxia (Care et al., 2015; Haavaldsen et al., 2011; Torres et al., 2017). Thus, we may conclude, that the significantly smaller newborn size, found among mother of advanced age may be due to age related changes in the placenta and in further consequence decreased blood and nutrient supply to the foetus. Considering the current trend of delaying reproduction, the findings of the present study have implications for obstetrics but also for public health strategies. Especially the high prevalence of small for gestational age newborn (5.6%) among mothers of advance age is alarming in Austria, a country where prenatal care is highly developed. In contrast, the Austrian strategies to prevent extremely early motherhood on the one hand and to provide special support for adolescent mothers from the first trimester of pregnancy onwards seem to work very well.

Conclusion

From the results of the present study we can conclude, that even in a country of highly sophisticated prenatal care, .maternal age is significantly associated with parameters of foetal growth. On the one hand, young adolescent mother experience reduced foetal growth from the second trimester onwards, resulting in smaller and lighter newborn than among mothers of optimal age range and advanced age. On the other hand, mothers of advanced age had the highest risk to give birth to small for gestational age newborn (<2500g). Both observations are a matter of particular interest for obstetricians and public health services.

Authors' contributions

FK designed the study, prepared the data for statistical analyses, provided statistical analyses, prepared the first draft, SK worked out the idea and prepared the first draft and the final version, EH collected the data, IS collected the data, BH worked out the idea and designed the study.

Conflict of interest

There is no conflict of interest regarding publication of this paper.

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