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Full length article

Correlation of sonographically measured fetal abdominal wall thickness with birth weight in diabetes

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ABSTRACT

Objective: To determine the association between sonographically measured abdominal wall thickness (AWT) and birth weight of fetuses of pregnant women with diabetes.

Methods: This retrospective study included 185 pregnant women who presented to a level I perinatal centre between January 2021 and December 2022. All mothers had diabetes, and were divided into the following subgroups: diet-controlled gestational diabetes mellitus; insulin-dependent gestational diabetes mellitus; type 1 diabetes mellitus; and type 2 diabetes mellitus. At the time of admission, gestational age varied between 29 + 2 and 41 + 2 weeks (+days) of gestation. Weight estimation was performed routinely using the Hadlock I formula. Fetal AWT was determined retrospectively at the same axial level as used for the measurement of abdominal circumference. Only women with a sonographic fetal weight estimation within 5 days before delivery were included.

Results: For the whole cohort, a moderate positive correlation was found between fetal AWT and estimated fetal weight ($r = 0.411$, $p < 0.001$), a moderate correlation was found between fetal AWT and birth weight ($r = 0.493$, $p < 0.001$), a weak correlation was found between fetal AWT and body length ($r = 0.365$, $p < 0.001$), and a weak correlation was found between fetal AWT and body length percentile ($r = 0.276$, $p < 0.001$). No strong differences in parameters were found between the diabetes subgroups. Receiver operating characteristic (ROC) curve analysis was performed to identify newborns with birth weight > 4000 g (macrosomia) and birth weight > 90th percentile according to Voigt in the group with gestational age > 37 weeks. ROC curve analysis was performed to identify newborns with birth weight > 90th percentile in the whole cohort. AWT and sonographically estimated fetal weight were included in the calculation. The combination of AWT and estimated fetal weight only led to a marginal improvement compared with estimated fetal weight alone for predicting newborns with birth weight > 4000 g in the group with gestational age > 37 weeks [area under the curve (AUC) 0.857 vs 0.871], and for predicting newborns with birth weight > 90th percentile in the group with gestational age > 37 weeks (AUC 0.840 vs 0.846) and in the whole cohort (AUC 0.816 vs 0.826).

Conclusion: A sonographically measured AWT of 7.1 mm in fetuses of diabetic mothers is predictive of birth weight > 90th percentile with sensitivity of 61 %, specificity of 85 %, and AUC of 0.748. ROC curve analysis showed that estimated fetal weight determined by ultrasound (using Hadlock formula I) seems to be slightly superior for the identification of macrosomic fetuses with birth weight > 90th percentile. A threshold value for estimated fetal weight of 3774 g had sensitivity of 70 %, specificity of 86 %, and AUC of 0.816. The combination of AWT and estimated fetal weight in a single formula only yielded a marginal improvement in accuracy compared with the use of estimated fetal weight alone.

Introduction

Increased maternal age and obesity are the main risk factors for several diseases, as well as adverse pregnancy outcomes [1,2]. Increased incidence of cardiovascular diseases and various degrees of insulin resistance and disturbed glucose metabolism play a crucial role. The

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prevalence of gestational diabetes mellitus (GDM) has increased continuously over the last decades; currently, it is approximately 5.4 % in Europe [2] and approximately 6 % in the USA, while the rate of pre-existing diabetes in non-pregnant cohorts is stable at 0.9 % [3].

Diabetes mellitus is one of the main risk factors for fetal macrosomia [4,5]. The pathogenesis can be explained by the so-called 'Pedersen hypothesis' (i.e. maternal serum glucose crosses the placenta and stimulates the fetal beta cells, from the second trimester onwards, to secrete insulin). This results in fetal hyperglycaemia and increased triglyceride synthesis in adipose cells [6–8]. This hypothesis has been proven by examination of adipose cells of newborns; infants of diabetic women have been shown to have larger adipose cells compared with infants of non-diabetic women [9]. The overall result is a higher body fat percentage in full-term infants that exceeds the normal level of 14 % [10]. Interestingly, the rate of macrosomia is approximately 12 % for mothers without diabetes mellitus, rises to 15 % in mothers with GDM, and reaches 22–27 % in mothers with known pre-pregnancy diabetes mellitus [11,12].

Although there is no uniform definition of fetal macrosomia, a threshold value of birth weight > 4000 g is often used [4,13]. Negative maternal and neonatal outcomes increase with the degree of macrosomia, including perineal trauma, peripartal haemorrhage, caesarean section, shoulder dystocia and respiratory problems [4,14,15].

It is expected that optimal control of maternal blood glucose in pregnancy could be a guarantee for a eutrophic newborn, as it is known that there is a significant positive correlation between neonatal skinfold thickness and mean maternal blood glucose and fasting glucose [9]. In contrast, ultrasound measurements in pregnant women with well-controlled insulin-dependent diabetes mellitus showed that adipose tissue deposition in fetuses is increased compared with healthy controls [16]. Additionally, glucose tolerance disorders that do not meet the criteria for GDM also result in a significant increase in fetal subcutaneous fat tissue. In turn, measurements of lean body mass components do not differ compared with fetuses of metabolically healthy women, and appear to be determined genetically [17]. Fetuses of women with GDM have a higher fat mass/lean mass ratio (independent of gestational age), showing a trend towards faster growth at advanced gestational age [18].

In order to give women the best possible advice regarding their preferred mode of delivery, it is necessary to estimate fetal weight as accurately as possible during the last trimester of pregnancy. The mere expectation of fetal macrosomia appears to influence the management of labour, and leads to more caesarean sections in eutrophic neonates [19]. However, unfortunately, the accuracy of sonographic measurements in fetal macrosomia is known to be unreliable. Ultrasound biometry is characterized by low sensitivity and low positive predictive value, but high negative predictive value. The accuracy of sonographic weight estimation decreases as birth weight increases [20]. Macrosomy in fetuses of women with diabetes is even more likely to be underestimated, probably because the abdominal circumference is proportionally larger compared with the head circumference. As a result, the proportion of the head is systematically underestimated in the weight estimation formula, resulting in an estimated fetal weight that is too low [21]. Furthermore, measurement errors in ultrasound examinations occur because the fetus has an irregular three-dimensional body of varying density and tissue composition [11]. Among the available formulae, the Hadlock and Shepard formula seems to predict fetal macrosomia most accurately [13,19,22].

It is known that prenatal sonographic measurements of fetal subcutaneous tissue thickness at the abdomen and femur correspond with postnatal mechanical measurements [23]. Based on this knowledge, studies have been undertaken to improve the predictive power of weight formulae by adding sonographic measurements of fetal subcutaneous tissue, which reflect fetal fat mass. The sonographically determined fetal abdominal wall layer appears to be significantly thicker in macrosomic fetuses, and this applies to pregnancies with [24,25] and without [26,27] diabetes.

The present study investigated the association between sonographically measured abdominal wall thickness (AWT) and birth weight of fetuses of pregnant women with diabetes. The aim was to improve the prediction of fetal macrosomia (i.e. fetal growth > 90th percentile) by implementing this parameter and setting a threshold value.

Materials and methods

This retrospective study included 185 pregnant women who presented to a tertiary maternity university clinic between January 2021 and December 2022. All mothers were diagnosed with diabetes, and were divided into the following subgroups: diet-controlled gestational diabetes mellitus (DGDM); insulin-dependent gestational diabetes mellitus (IDGDM); type 1 diabetes mellitus (T1DM); and type 2 diabetes mellitus (T2DM). At the time of admission, gestational age varied between 29 + 2 and 41 + 2 weeks (+days) of gestation. All parameters and measured values were drawn from the digital archives of the clinic, and had been collected during inpatient treatment of the participants. Fetal AWT was determined retrospectively by an experienced ultrasound sonographer at the same axial level as is used for the measurement of abdominal circumference. The distance from the outermost to the innermost area of the lateral abdominal wall closest to the ultrasound transducer was measured (Fig. 1).

The study was approved by the Ethics Committee of the University of Regensburg (Ref. No. 24–3725-104). Sonographic examinations were carried out using a high-resolution convex transducer (3.5 mHz). Voluson S8, P8 and E8 ultrasound machines were used (GE Healthcare, Solingen, Germany). The examinations were carried out in accordance with everyday clinical practice by experienced sonographers. The fetal parameters were documented using ViewPoint Version 5.6 (GE Healthcare).

The parameters collected in the four subgroups included: maternal age (years); body mass index (kg/m^2); gestational age at birth (days); fetal body length at birth (in g and in percentiles according to Voigt); birth weight (in g and in percentiles according to Voigt [28]); estimated fetal weight (g); time between performance of fetal scan and date of birth (days); difference between estimated fetal weight and birth weight (percentage); and fetal AWT (mm).

The percentiles according to Voigt were determined via 'https://www.pedz.de'. The percentage difference between the estimated and final weights was calculated using the formula 'estimated fetal weight – birth weight/birth weight x 100′. Weight estimation is performed routinely using Hadlock's estimation formula, which is based on measurements of biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur length (FL). The formula, referred to as 'Hadlock formula I', is: log10 G=1.3596—0.00386 x AC x FL+0.0064 x HC+0.00061 BPD x AC+0.0424 x AC+0.174 x FL [29]. Only women with a sonographic fetal weight estimation within 5 days before delivery were included. Statistical analysis was performed using R Version 4.4.0. The Kruskal–Wallis test and post-hoc Mann–Whitney *U* test with Holm's method for *p*-value adjustments were used to compare more than two groups. A receiver operating characteristic (ROC) curve analysis was performed to assess the performance of a predictor, with evaluation of area under the curve (AUC), sensitivity and specificity. The two predictors, AWT and estimated fetal weight, were combined with a multiple logistic regression.

Results

In total, 185 pregnant women with diabetes were included in the study. Table 1 shows all analysed parameters for the whole study group and for the subgroups of women with DGDM ($n = 71$), IDGDM ($n = 95$), T1DM ($n = 15$) and T2DM ($n = 4$).

In the whole study group, the median age of women was 33 [interquartile range (IQR) 30–36] years, and median body mass index was 27 (IQR 22–31) kg/m^2. Median gestational age at birth was 276 (IQR

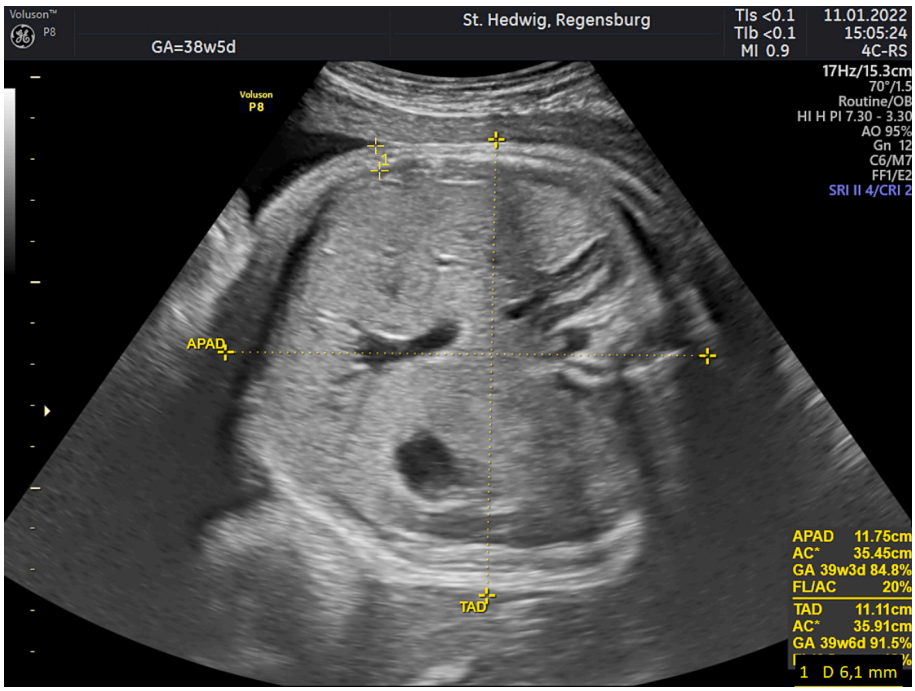

Fig.1. Measurement of abdominal wall thickness (AWT) at the axial level used for measurement of abdominal circumference.

Table 1
Analysed parameters.

		Total (n = 185)	DGDM (n = 71)	IDGDM (n = 95)	T1DM (n = 15)	T2DM (n = 4)	p-value[a]
Maternal age (years)	Median (IQR)	33.0 (30.0–36.0)	32.0 (28.5–36.0)	34.0 (31.0–36.5)	33.0 (30.0–35.5)	34.5 (32.5–37.3)	0.3
Maternal BMI (kg/m^2)[a]	Median (IQR)	27.0 (22.3–30.6)	24.2 (21.7–29.6)	27.9 (22.4–32.0)	27.9 (23.5–29.2)	24.6 (23.5–27.5)	0.093
Gestational age at birth (days)	Median (IQR)	276 (269–281)	278 (271–283)	275 (271–281)	268 (262–281)	274 (260–282)	0.14
Period between ultrasound and birth (days)	Median (IQR)	1.00 (1.00–3.00)	1.00 (1.00–3.00)	1.00 (1.00–3.00)	1.00 (1.00–3.00)	2.50 (2.00–3.25)	0.3
Body length (cm)	Median (IQR)	52 (50–53)	51 (50–53)	52 (51–53.5)	52 (51–53)	51 (47.25–53.75)	0.3
Body length percentile	Median (IQR)	53 (33–74)	44 (24–69)	58 (42–73)	59 (49–90)	29 (10–59)	0.029
Estimated weight (g)	Median (IQR)	3457 (3211–3686)	3461 (2942–3676)	3436 (3251–3727)	3460 (3263–3720)	3560 (2860–3973)	0.7
Birth weight (g)	Median (IQR)	3470 (3157–3810)	3430 (3100–3710)	3520 (3246–3820)	3530 (3310–3840)	3470 (2721–4245)	0.3
Birth weight percentile	Median (IQR)	54 (29–77)	46 (24–72)	61 (37–81)	75 (37–96)	41 (11–90)	0.059
Difference between estimated weigh and birth weight (%)	Median (IQR)	5.5 (2.6–9.4)	5.3 (2.6–9.1)	5.8 (2.8–10.9)	3.5 (1.7–8.6)	4.3 (2.4–9.6)	0.5
Abdominal wall thickness (mm)	Median (IQR)	5.70 (4.90–6.80)	5.60 (4.90–6.60)	5.70 (4.90–6.85)	6.50 (5.45–7.10)	6.20 (4.68–7.45)	0.5
pH[b]	Median (IQR)	7.26 (7.19–7.30)	7.27 (7.20–7.31)	7.27 (7.19–7.30)	7.20 (7.18–7.28)	7.19 (7.19–7.22)	0.4
Base excess (mmol/l)[b]	Median (IQR)	−4.30 (−6.50 to −2.90)	−4.40 (−6.80 to −2.60)	−4.40 (−6.30 to −3.00)	−4.00 (−6.83 to −2.10)	−3.75 (−4.15 to −3.25)	0.9

BMI, body mass index; IQR, interquartile range; DGDM, diet-controlled gestational diabetes mellitus; IDGDM, insulin-dependent gestational diabetes mellitus; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.
[c]Kruskal–Wallis test.
[a] Total n = 184; DGDM n = 70.
[b] At birth from the umbilical cord artery, total n = 183; DGDM n = 69.

269–281) days. Median fetal birth weight was 3470 (IQR 3157–3810) g, which corresponds to the 54th (IQR 29th–77th) percentile according to Voigt. Median fetal body length was 52 (IQR 50–53) cm, which corresponds to the 53rd (IQR 33rd–74th) percentile. Median fetal AWT was 5.7 (IQR 4.9–6.8) mm. Concerning prenatal measurement parameters, median estimated fetal weight was 3457 (IQR 3211–3686) g. There was a median difference between estimated fetal weight and birth weight of 5.5 % (IQR 2.6–9.4 %) at a median period between ultrasound and birth of 1 (IQR 1–3) day. Median base excess and pH from the umbilical cord at birth were −4.3 (IQR −6.5 to −2.9) mmol/l and 7.26 (IQR 7.19–7.30), respectively. In the whole group, 78 % (145/185) of fetal weight estimations were within 10 % of the actual birth weight, with a deviation range of 0 % to 21.8 %. Overall, 15.7 % of all newborns (29/185) had a birth weight ≥ 4000 g (4000–5190 g), and 84.3 % (156/185) had a birth weight < 4000 g (1320–3990 g).

For the whole cohort, there was a moderate positive correlation

between fetal AWT and estimated fetal weight ($r = 0.411$, $p < 0.001$), a moderate correlation between fetal AWT and birth weight ($r = 0.493$, $p < 0.001$), a weak correlation between fetal AWT and body length ($r = 0.365$, $p < 0.001$), and a weak correlation between fetal AWT and body length percentile ($r = 0.276$, $p < 0.001$).

A significant difference was observed between the subgroups for body length percentile ($\chi 2(3) = 9.027$, $p = 0.029$). However, no pairwise comparisons were found to be significant (Table 2).

ROC curve analysis was performed to identify newborns with birth weight > 4000 g and birth weight > 90th percentile according to Voigt in the cohort of gestational age > 37 weeks. Furthermore, ROC curve analysis was performed to identify newborns with birth weight > 90th percentile in the whole cohort. AWT and sonographically estimated fetal weight were included in the calculation. The results are presented in Tables 3 and 4.

Estimated fetal weight determined by ultrasound (using Hadlock formula I) appears to be better at identifying macrosomic fetuses with birth weight > 90th percentile compared with fetal AWT.

Only marginal improvement was seen for the combination of AWT and estimated fetal weight, compared with estimated fetal weight alone, for the prediction of babies with birth weight > 4000 g in the group of gestational age > 37 weeks (AUC 0.857 vs 0.871), and for babies with birth weight > 90th percentile in the group of gestational age > 37 weeks (AUC 0.840 vs 0.846) and in the whole cohort (AUC 0.816 vs 0.826) (Tables 3 and 4).

Discussion

This study showed that a sonographically determined AWT of 6.1 mm in fetuses of diabetic mothers at gestational age > 37 weeks predicts birth weight ≥ 4000 g with sensitivity of 81 % and specificity of 65 %, and an AWT of 7.1 mm predicts birth weight > 90th percentile with sensitivity of 61 % and specificity of 83 %.

A strength of these results is the inclusion criterion of fetal weight estimation within 5 days of delivery. Furthermore, Hadlock formula I was used to estimate fetal weight. As shown in a study on 8721 singleton pregnancies, optimal results were gained when Hadlock formula I or II was used, with superiority over the formula of Merz, Shepard and Warsof [30]. It was also shown that the most accurate values are obtained for scan-to-delivery interval < 7 days [30,31]. This is in line with the results of a retrospective study on the prediction of macrosomia that included 7977 women, of whom 13.7 % delivered a macrosomic newborn with birth weight > 4000 g. The authors compared 20 different estimating formulae, and showed that formulae including BPD, AC and FL (such as the Hadlock formulae) are better predictors of macrosomia. In case of doubt, they recommended the inclusion of tissue measurements, such as subcutaneous fat, in order to achieve more valuable results [13]. In summary, the design of the present study fits with currently available best knowledge for the estimation of fetal weight.

In addition to using the optimal formula, it is also necessary to measure as accurately as possible. In the present study, the mean deviation between estimated fetal weight and birth weight was 6.5 %. For the whole study group, 78 % (145/185) of fetal weight estimations were within 10 % of actual birth weight. This is more accurate compared with results given in the literature; a review including 54 articles with a total of 14,384 patients showed that only 62 % of predictions were within 10 % of actual birth weight [31]. This reflects the accuracy of the measurements in the present study, and can be indirectly transferred to the measurement of AWT. In addition, AWT is easy to measure and has high reproducibility.

The present measurements with Hadlock formula I tended to slightly underestimate actual birth weight. This is in line with the results of a study of 5612 pregnant women, which showed that Hadlock formulae I and II have a tendency to underestimate the weight of fetuses in all weight classes (500–5000 g) [32].

The present findings regarding the measurement accuracy of macrosomic fetuses in diabetic pregnancies contradict those of a previous retrospective study. The authors found that birth weight was underestimated by ≥ 15 % using Hadlock formula in 26.3 % (5/19) of cases [21]. In the present study, 29 newborns had birth weight ≥ 4000 g, of whom only 2 (6.9 %) had been estimated to weigh ≥ 15 % less. The difference may be due to the fact that more precise measurements are possible nowadays due to high-resolution sonographic images.

The present results regarding the influence of the type of diabetes on fetal AWT differ from recently published results to some extent [11]. Stanirowski et al. analysed sonographically determined fetal soft tissue and its application in fetal weight estimation. Overall, 22.2 % of participants (32/144) delivered a newborn with birth weight > 4000 g. Their results showed a significantly higher AWT in fetuses of mothers with IDGDM or pre-existing type 1 diabetes compared with DGDM or healthy controls, while the present study found no significant difference between the subgroups [$\chi^2(3) = 2.152$, $p = 0.5$]. In the present study, there were fewer samples in the T1DM group (15 vs 24), and only four samples in the T2DM group. Nevertheless, a strong positive correlation was observed between fetal AWT and birth weight [11].

Finally, the threshold value for fetal AWT of 6.1 mm to predict fetal macrosomia > 37th gestational week found in the present study is lower than that reported in previous publications, and corresponds to the values of current studies. In 1997, Petrikovsky et al. took sonographic measurements of the abdominal subcutaneous tissue thickness of 133 term fetuses within 72 h before delivery to predict fetal macrosomia. The mean thickness was 8.4 mm. This differed significantly between normal and macrosomic fetuses (mean 7.0 vs 12.4 mm). A significant positive correlation was found between abdominal subcutaneous tissue thickness and birth weight [26].

In a prospective cohort study on 125 women, Higgins et al. aimed to investigate whether fetal anterior AWT in diabetic pregnancies in the third trimester is predictive of macrosomia, and can therefore reflect glycaemic control. The authors defined 5.5 mm anterior AWT as the most appropriate threshold for the prediction of macrosomia at 36 gestational weeks in diabetic pregnancies [24].

In 2013, Garabedian et al. conducted a study to determine whether serial antenatal ultrasound measurements of fetal soft tissues can predict macrosomia in women with pregestational diabetes ($n = 29$). Comparison of sonographic measurements between large-for-gestational-age versus appropriate-for-gestational-age fetuses at 34 gestational weeks showed significant differences: anterior AWT was 7.1 mm vs 5.6 mm ($p = 0.006$). The authors defined a threshold value for AWT of 6.35 mm for the prediction of macrosomia at 34 gestational weeks [25].

Larcriprete et al. aimed to determine reference values of fetal subcutaneous tissue thickness throughout gestation. Serial ultrasound examinations were performed approximately every 3 weeks until delivery at term, starting at approximately 20 gestational weeks. They included 303 women (85 with GDM and 218 controls). Fetal fat mass values were found to be greater in women with GDM compared with healthy women, especially in late gestation. There was a significant difference in the abdominal fat mass (AWT) at 39–40 gestational weeks between fetuses of healthy women and those with diabetes (6.18 ± 1.32 mm vs 6.80 ±

Table 2
p-values of pairwise comparisons of body length percentile for all subgroups, tested with the Mann–Whitney *U* test, and *p*-values adjusted using Holm's method.

p-values body length percentile	DGDM	IDGDM	T1DM
IDGDM	0.051	–	–
T1DM	0.251	1.000	–
T2DM	1.000	1.000	1.000

DGDM, diet-controlled gestational diabetes mellitus; IDGDM, insulin-dependent gestational diabetes mellitus; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

Table 3
Complete cohort: results of receiver operating characteristic curve analysis to identify newborns with certain birth weight thresholds.

BW threshold	AWT (mm)	AUC	Sens (%)	Spec (%)	EFW (g)	AUC	Sens (%)	Spec (%)	AUC
>90th percentile	7.1	0.748	61	85	3774	0.816	70	86	0.826

AWT, anterior wall thickness; AUC, area under the curve; sens, sensitivity; spec, specificity; EFW, estimated fetal weight.
Grey boxes indicate results related to AWT, blue boxes indicate results related to EFW, and yellow boxes indicate results from both AWT and EFW in combination.

Table 4
Gestational age > 37 weeks: results of receiver operating characteristic curve analysis to identify newborns with certain birth weight thresholds.

BW threshold	AWT (mm)	AUC	Sens (%)	Spec (%)	EFW (g)	AUC	Sens (%)	Spec (%)	AUC
>4000 g	6.1	0.754	81	65	3502	0.857	96	60	0.871
>90th percentile	7.1	0.729	61	83	3817	0.840	72	86	0.846

AWT, anterior wall thickness; AUC, area under the curve; sens, sensitivity; spec, specificity; EFW, estimated fetal weight.
Grey boxes indicate results related to AWT, blue boxes indicate results related to EFW, and yellow boxes indicate results from both AWT and EFW in combination.

0.89 mm, $p = 0.03$) [33].

Elessawy et al. performed a prospective observational study to explore the predictive power of the abdominal fetal fat layer (FFL) in 80 women with GDM to improve the detection of fetal macrosomia. At 37 gestational weeks, the mean FFL was 0.49 cm, and the FFL of macrosomic fetuses at 37 gestational weeks was 0.60 cm. The cut-off > 0.59 cm at 37 gestational weeks showed sensitivity of 60 % and specificity of 90.6 % to predict birth weight > 4000 g [27].

Limitations of this study include its retrospective design and the fact it was carried out at a single institution. The risks of the retrospective design include possible miscoding and lack of precision in the reported diagnoses of medical conditions. Furthermore, detailed information on the level of glycaemic control in the patients is not available. A control group of non-diabetic pregnancies was not included as this study aimed to focus on women with pre-existing diabetes mellitus or GDM.

Conclusion

A sonographically measured AWT of 7.1 mm in fetuses of diabetic mothers is predictive of birth weight > 90th percentile with sensitivity of 61 %, specificity of 85 %, and AUC of 0.748. ROC curve analysis showed that estimated fetal weight determined by ultrasound (using Hadlock formula I) appears to be slightly superior for the identification of macrosomic fetuses with birth weight > 90th percentile. A threshold value for estimated fetal weight of 3774 g had sensitivity of 70 %, specificity of 86 %, and AUC of 0.816.

The combination of AWT and estimated fetal weight in a single formula only yielded a marginal improvement in accuracy compared with the use of estimated fetal weight alone.

CRediT authorship contribution statement

M. Rauh: Writing – original draft. **M. Voigt:** Data curation. **M. Kappelmeyer:** Formal analysis. **B. Schmidt:** Formal analysis. **A. Köninger:** Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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