

Factors Influencing the Accuracy of Fetal Weight Estimation with a Focus on Preterm Birth at the Limit of Viability: A Systematic Literature Review

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Key Words

Fetal weight estimation · Limit of viability · Ultrasound · Factors affecting accuracy

Abstract

Background: Fetal weight estimation (FWE) is an important factor for clinical management decisions, especially in imminent preterm birth at the limit of viability between 23^{0/7} and 26^{0/7} weeks of gestation. It is crucial to detect and eliminate factors that have a negative impact on the accuracy of FWE.

Data Sources: In this systematic literature review, we investigated 14 factors that may influence the accuracy of FWE, in particular in preterm neonates born at the limit of viability.

Results: We found that gestational age, maternal body mass index, amniotic fluid index and ruptured membranes, presentation of the fetus, location of the placenta and the presence of multiple fetuses do not seem to have an impact on FWE accuracy. The influence of the examiner's grade of experience and that of fetal gender were discussed controversially. Fetal weight, time interval between estimation and delivery and the use of different formulas seem to have an evident effect on FWE accuracy. No results were obtained on the impact of active labor. **Discussion:** This review reveals that only few studies investigated factors possibly influenc-

ing the accuracy of FWE in preterm neonates at the limit of viability. Further research in this specific age group on potential confounding factors is needed.

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Background/Objectives

Preterm birth, defined as live birth before 37^{0/7} weeks of gestation, is the major reason for neonatal morbidity and mortality in developed countries [1]. Especially neonates with a very low birth weight (VLBW, <1,500 g) or very low gestational age (GA, <32^{0/7} weeks) are at risk for neonatal impairment or death [1]. Survival for neonates with an extremely low birth weight (ELBW, <1,000 g) or extremely low GA (<28^{0/7} weeks) is even more endangered [1]. When a fetus is at risk of being born between 22 and 26 weeks of gestation, physicians and parents are faced with clinically as well as ethically difficult decisions regarding treatment and a further course of action. A prediction as accurate as possible in terms of morbidity and mortality is required in order to make such decisions [1]. The Swiss recommendations of 2011 suggest that care of preterm neonates with a GA between 22^{0/7} and 23^{6/7} weeks should be limited to palliative care, whereas for ne-

Table 1. Factors contributing to the accuracy of FWE independent from ultrasound conditions

Factors independent from ultrasound conditions
Gestational age
Fetal weight
Fetal gender
Time interval between estimation and delivery
Formula accuracy
Examiner's grade of experience (expert vs. less experienced investigator)
Averaging of multiple measurements

Table 2. Factors contributing to the accuracy of FWE by affecting the ultrasound quality

Factors affecting the ultrasound quality
Singleton vs. multiple pregnancy
Presentation of the fetus (breech position vs. cephalic position)
Amniotic fluid index
Ruptured membranes (yes/no)
Active labor (yes/no)
Location of the placenta (anterior wall of the uterus vs. any other location)
Maternal body mass index

onates with a GA $>25^{0/7}$ weeks neonatal intensive care and obstetric interventions such as cesarean section are generally indicated [2]. For neonates in between these age ranges ($24^{0/7}$ – $24^{6/7}$ weeks of gestation), it is more difficult to decide whether therapy or simple comfort care is the better solution, as outcome varies strongly in this group and GA alone is not the only factor influencing it.

In general, GA is a very important tool in predicting neonatal survival and survival without major impairment in neonates born at the limit of viability [2]. However, further factors, such as fetal weight, exposure to antenatal corticosteroids, single or multiple birth and fetal gender, were found to have an impact on neonatal outcome as well [2]. Female neonates with exposure to antenatal corticosteroid therapy, singleton birth and higher birth weight, who received intensive care, were found to have benefits in outcome similar to those born approximately 1 week of GA later [3]. As the sum of positive or negative factors can change the prediction of outcome, each case has to be looked at individually. Based on this knowledge, a web tool has been introduced that allows an individual calculation of risks [3, 4]. While most of these variables are easy to assess, fetal weight is a source of bias as it is an estimation, and the accuracy of these estimations still shows a large variability especially in the VLBW group [5, 6]. Therefore, improvement in the accuracy of fetal weight estimation (FWE) is required.

Data Sources

A systematic literature search in two databases, PubMed and Medscape, was performed. The initial search was broad, focusing on the following search terms: 'fetal weight estimation', 'very low birth weight', 'preterm infants', 'sonographic weight estimation' and 'Hadlock formula'. The Hadlock formula was included as a

search term as it is one of the most accurate and most commonly used formulas for FWE, as will be discussed below. The abstracts of studies found were reviewed, and the studies were further filtered based on preset inclusion and exclusion criteria. Inclusion criteria were information on at least one of the factors listed in tables 1 and 2 as well as FWE by ultrasound. Due to a lack of literature on possible confounding factors of FWE in VLBW neonates, literature on all GAs was included, but a special focus was put on preterm birth at the limit of viability. Studies were excluded if they used newly developed formulas which were only applied to the population they were developed on, if they used FWE on macrosomic fetuses defined as a birth weight (BW) $>90\%$ for GA or if they used neonates born beyond term only and if they were studies based entirely on specific ethnic groups such as the Chinese population, for example. References from included studies were subsequently reviewed and relevant articles were taken up as well – subject to the previously described inclusion and exclusion criteria. Only publications in English and German were included. Both prospective and retrospective case series were included.

We investigated 14 factors that were categorized into two groups: factors independent from ultrasound conditions (table 1) and factors that affect the ultrasound quality and might therefore potentially worsen the accuracy of FWE (table 2).

Results

A total of 29 studies have been included according to our criteria investigating the effect of 14 variables on FWE (table 3). Details on the effects found are summarized in online supplementary table 2a and b (see www.karger.com/doi/10.1159/000358518 for all online supplementary material).

Gestational Age

Only three studies have analyzed the impact of GA on the accuracy of FWE [7–9]. While Heer et al. [7] included neonates with a GA between $22^{0/7}$ and $42^{0/7}$ weeks, Mills

et al. [9] included only neonates with a GA between 22^{0/7} and 28^{6/7} weeks. However, none of these studies reported a significant error in FWE for different age groups.

Fetal Weight

While several studies assume that a lower BW has a negative impact on the accuracy of FWE, seven studies specifically investigated this hypothesis [6, 7, 9–13]. Three studies found that there is an effect [6, 10, 13]. Melamed et al. [6] reported that random error in particular increases with decreasing BW unrelated to the formula used. Meyer et al. [12] on the other hand did not report an effect in their study of 664 neonates. They divided their population into ten different weight groups, including a total of 157 neonates with a BW <1,500 g. Even though they found a significant tendency to underestimate fetal weight in all tested formulas, this finding was unrelated to BW as there was no significant difference in random or systematic error in all BW groups. Heer et al. [7] who did not find an effect either divided their study population into 2 groups: BW >2,000 g versus BW <2,000 g. This rather rough distinction might be the reason for their findings, as they did not pay special attention to the extremes of BW. One study [11] found that depending on the formula used for FWE, different results are obtained. For FWE with the Scott formula, a significant overestimation was found in VLBW neonates, whereas FWE with the Hadlock I formula seems to correlate well with the actual BW [11].

Fetal Gender

There are 4 studies that investigated the effect of fetal gender on the accuracy of FWE [7, 9, 10, 14]. While Heer et al. [7] and Mills et al. [9] found that fetal gender has no effect, Melamed et al. [10] and Siemer et al. [14] reported controversial results. Melamed et al. [10] concluded in their study of 3,672 neonates that ultrasound FWE is less accurate for female fetuses than for male, due to the fact that there is a higher systematic error among female fetuses (–0.2 to 2.1% for male vs. 1.3 to 6% for female fetuses). Siemer et al. [14] compared eleven different weight estimation formulas, and the most exact estimation for neonates with a BW between 2,500 and 3,999 g were made with the gender-specific Schild formula. This is the only formula which includes fetal gender with the commonly used parameters of FWE. Interestingly though, it does not apply to neonates with a BW <2,500 g. Another study in which the Schild gender-specific formula was tested on a population of 989 patients obtained similar results [14]. However, only one

Table 3. Number of studies investigating a specific factor and number of studies that found an effect on FWE of the investigated factor

Investigated factors	Studies investigating the variable, n	Studies that found an effect of the variable on FWE, n
Gestational age	3	0
Fetal weight	7	4
Fetal gender	4	2
Time interval between estimation and delivery	5	2
Formula accuracy	17	14
Examiner's grade of experience	6	2
Averaging	1	1
Multiple pregnancy	3	0
Presentation of the fetus	6	2
Amniotic fluid index	10	1
Ruptured membranes	5	1
Active labor	0	0
Location of the placenta	3	0
Maternal body mass index	6	0

study investigated the effect of fetal gender on FWE in VLBW neonates [9]. In their population of 67 patients with a GA from 22^{0/7} to 28^{6/7} weeks, fetal gender was not a statistically significant impact factor on the accuracy of FWE. Of the 820 neonates in the study by Heer et al. [7], only 21 neonates were in the 22–26 weeks' gestation subgroup. In the study by Melamed et al. [10], the average GA at delivery was 39 weeks and the BW was between 2,653 and 3,751 g.

Time Interval between Estimation and Delivery

Most studies set the limit for the time interval between FWE and delivery at a maximum of 7 days. Five studies further examined this aspect of time [7–11]. Kaaij et al. [11] set the maximum time interval between FWE and delivery at 14 days and did not find an effect. However, the mean time interval was relatively short with 4.1 days. Surprisingly, Scott et al. [8] who set the same maximum time interval of 14 days and had a mean time interval of 3.8 days found that the number of days between FWE and delivery were significantly associated with an error in FWE. While the mean percentage error at 9 days prior to delivery was 9.6%, it increased up to 32% when the FWE was done more than 9 days prior to delivery. Heer et al. [7] compared two groups (0–7 and 8–14 days between FWE and delivery) and found a significantly higher mean percentage error in the 8–14 days group.

Table 4. List of the most frequently investigated formulas [16]

Author	Components	Formula
Hadlock I	BPD, HC, AC, FL	$\log_{10} \text{EFW} = 1.3596 + 0.0064(\text{HC}) + 0.0424(\text{AC}) + 0.174(\text{FL}) + 0.00061(\text{BPD})(\text{AC}) - 0.00386(\text{AC})(\text{FL})$
Hadlock II	AC, FL	$\log_{10} \text{EFW} = 1.304 + 0.05281(\text{AC}) + 0.1938(\text{FL}) - 0.004(\text{FL})$
Hadlock III	BPD, AC, FL	$\log_{10} \text{EFW} = 1.335 - 0.0034(\text{AC})(\text{FL}) + 0.0316(\text{BPD}) + 0.0457(\text{AC}) + 0.1623(\text{FL})$
Hadlock IV	HC, AC, FL	$\log_{10} \text{EFW} = 1.326 - 0.00326(\text{AC})(\text{FL}) + 0.0107(\text{HC}) + 0.0438(\text{AC}) + 0.158(\text{FL})$
Hadlock V	HC, AC, FL	$\log_{10} \text{EFW} = 1.5662 - 0.0108(\text{HC}) + 0.0468(\text{AC}) + 0.171(\text{FL}) + 0.00034(\text{HC})^2 - 0.0003685(\text{AC})(\text{FL})$
Campbell	AC	$\ln \text{EFW} = -4.564 + 0.282(\text{AC}) - 0.00331(\text{AC})^2$
Merz I	BPD, AC	$\text{EFW} = -3,200.40479 + 157.07186(\text{AC}) + 15.90391(\text{BPD})^2$
Shepard	BPD, AC	$\log_{10} \text{EFW} = -1.7492 + 0.166(\text{BPD}) + 0.046(\text{AC}) - 0.002546(\text{AC})(\text{BPD})$
Warsof	BPD, AC	$\log_{10} \text{EFW} = -1.599 + 0.144(\text{BPD}) + 0.032(\text{AC}) - 0.000111(\text{BPD})^2(\text{AC})$

A list of all examined formulas can be found in online supplementary table 1.

Formula Accuracy

Seventeen studies tried to evaluate the best formula for FWE [6, 7, 9, 11–24] (table 4). The most frequently examined formulas are those of Hadlock, which were compared to other formulas in all studies listed above, except in the study by Mills et al. [9] who only compared two formulas (Shepard and Warsof). The formulas of Campbell, Merz, Shepard and Warsof have been examined 7, 8, 12 and 8 times, respectively. Thirteen of the studies found one of the Hadlock formulas to be the most accurate [6, 7, 11, 13–16, 19–24]. All Hadlock formulas seem to be equally accurate, as Meyer et al. [12] who compared five Hadlock formulas found no significant difference in systematic or random error.

3D Formulas

Hasenoehrl et al. [18] compared three 3D formulas to three conventional 2D formulas in a study of 200 fetuses. They found the 3D formula of Schild to be superior to the conventional 2D formulas in all BW ranges as it gave the lowest absolute percentage error. This result disagrees with the findings by Siemer et al. [19] who compared four 3D formulas to four conventional 2D formulas in a study of 3,975 fetuses and found no superiority of any formula in the whole BW range. For a BW <2,500 g, Siemer et al. [19] found the Hadlock I formula to have the smallest systematic error and the lowest absolute percentage error, while Hasenoehrl et al. [18] found the 3D formula of Schild to be more accurate.

Specific Formulas for Very Small Fetuses

The accuracy of FWE decreases at the extremes of BW [5, 6]. In an attempt to solve this problem, several authors developed formulas specifically designed for these BW

categories. Hoopmann et al. [20] compared four formulas specifically designed for small fetuses (Schild, Scott, Weiner I and II) with four commonly used formulas (Hadlock I and III, Hansmann, Warsof). All formulas except for the Hadlock equations had a significant systematic error, while the random error was similar for most of them. Among the four formulas for small fetuses, the Scott formula proved to be the most accurate, but it was not favorable when compared to the Hadlock III formula. These results are in agreement with the results by Kaaij et al. [11] who estimated the fetal weight of 100 fetuses with a BW <1,000 g using the Hadlock I and the Scott formula. They found the Hadlock I formula to be more accurate. Jouannic et al. [23] reported that in addition to the Hadlock IV formula, the Mielke I formula achieved good results with mean errors not significantly different from zero either. This formula has only been examined twice but both studies considered it to be one of the most or the most accurate formula for VLBW fetuses [16, 23]. In summary, the formulas of Hadlock seem to be the most accurate formulas for FWE in all BW ranges. Even though these formulas were developed for term fetuses, they seem to be the most accurate for VLBW fetuses as well.

Examiner's Grade of Experience, Interobserver Differences and Averaging

Six studies investigated the effect of the grade of experience of the investigator on the accuracy of FWE [7, 15, 25–28]. Only two found significant results [15, 28]. Siemer et al. [15] reported that more skilled investigators were able to achieve higher interclass correlation coefficients for all formulas, implying that there is a connection between more skilled investigators and more accu-

rate FWE for all formulas. Ragosch et al. [27] reported a general tendency towards more precise examinations when performed by experts. However, these findings were not significant. Predanic et al. [28] were able to show that the accuracy of FWE can be significantly increased when residents are trained over a period of 24 months.

One study had the weight of 5,612 fetuses estimated by 94 equally skilled examiners [21]. The findings revealed that the accuracy of FWE varied significantly between the examiners even if the level of experience was the same.

There was only one study that investigated the effect of averaging results on FWE [29]. The authors found that especially fetal abdominal circumference (AC) is prone to intra- and interobserver error but can be reduced by averaging results. They also showed that the use of multiple measurements and multiple examiners reduced major discrepancies (>10%) between FWE and actual BW significantly [29].

Multiple Pregnancy

Most studies evaluating the accuracy of FWE as well as most studies designed to introduce new weight estimation formulas excluded multiple pregnancy. Of the 29 studies included, only five did not exclude multiple pregnancy [8, 11, 22–24]. Three examined the possible effect of multiple pregnancy on FWE [8, 22, 30]. A large study conducted by Lynch et al. [30] found similar accuracy in FWE in singleton, twin and triplet pregnancies, even though they found head measurements (biparietal diameter, BPD; head circumference, HC) more difficult to estimate in multiple pregnancy.

Presentation of the Fetus

Six studies investigated the impact of fetal presentation on the accuracy of FWE, yet only two found an effect [7, 9, 17, 22, 27, 31]. These two studies found that random error as well as standardized absolute error was significantly higher for fetuses in breech presentation [17, 31].

Amniotic Fluid Index and Ruptured Membranes

Only one of ten studies reports an effect of low amniotic fluid index (AFI) and ruptured membranes on the accuracy of FWE [7–9, 12, 13, 22, 24, 26, 32, 33]. This study found a tendency of underestimation in patients with oligohydramnios (AFI <5 cm) and ruptured membranes [22]. However, these findings were only significant for the Hadlock formulas and the Shepard equation. Furthermore, the study group with oligohydram-

nios and ruptured membranes consisted of only 20 patients, therefore these findings might be coincidental. Durbin et al. [32] only found a link between AFI and FWE in polyhydramnios. In their study of 90 term neonates, FWE in patients with polyhydramnios was overestimated in 80%, whereas the underestimation in patients with oligohydramnios was the same as in patients with normal AFI.

Active Labor

None of the 29 studies included examined the effect of contractions on FWE.

Location of the Placenta

The three studies that took the location of the placenta into account as a possible confounding factor did not find a significant effect [7, 8, 24]. Although Shamley and Landon [24] reported a lower percentage error for the Hadlock and Shepard equation when the placenta was located at the posterior wall of the uterus, these findings were not significant. The placental location does not seem to affect the accuracy of FWE in general.

Maternal Body Mass Index

The maternal body mass index (BMI) does not seem to have an effect on the accuracy of FWE. All six studies included in this review investigating this factor came to identical conclusions [7, 8, 22, 24, 25, 34]. Two studies reported maternal weight in kilograms and pounds, respectively [22, 24], not taking maternal height into account. Thus, a direct comparison with the BMI is not possible.

Discussion

FWE is an important factor for making management decisions in imminent preterm birth at the limit of viability as it helps in predicting neonatal morbidity and mortality. In the present study, we reviewed the literature for possible factors affecting FWE and a total of 14 factors were analyzed (tables 1–3).

We found that GA, maternal BMI, AFI and ruptured membranes, presentation of the fetus, location of the placenta and the presence of multiple fetuses do not seem to have an impact on the accuracy of FWE in either the VLBW group or in term-born neonates. The influence of the examiner's grade of experience and fetal gender was discussed controversially. Fetal weight, the time interval between estimation and delivery and the use of different

formulas on the other hand seem to have an evident effect on the accuracy of FWE.

A high (maternal) BMI does lead to ultrasound attenuation, as the strength of the returning echoes decreases exponentially with distance and is directly proportional to differences in tissue density [25]. However, the accuracy of FWE is not affected by the decreased ultrasound quality. This might be due to the fact that the parameters most commonly used for FWE – BPD, HC, femur length (FL) – consist mostly of high-density structures (bones) which are strong reflectors. On the other hand, low-density structures such as fat are relatively weak reflectors and are therefore more affected by increased attenuation and decreased wave amplitude of the ultrasound. It is therefore very likely that even if the ultrasound quality is affected by maternal obesity, the fetal landmarks are well visible and the accuracy of FWE is not affected. The same explanation can be assumed for the finding that there was no negative effect on the accuracy of FWE when the placenta is located on the anterior wall of the uterus.

AFI is an important parameter when assessing fetal well-being. It is assumed that the rupture of membranes leads to a decreased amniotic fluid volume which in turn leads to a physical compression of the fetal head and abdomen. This might cause incorrect measurements and reduces the resolution of the ultrasound images, hence resulting in inaccurate FWE [26]. However, this hypothesis is not supported in most studies examined in our review.

In breech presentation, head measurements seem to be a source of error in particular. Dolichocephaly, an anatomical variant in skull shape, might lead to incorrect measurements in breech presentation. The study by Ragošch et al. [27] used a modified BPD derived from measuring BPD, HC and fronto-occipital diameter to take this variant into account. They found a nearly identical accuracy for cephalic and breech presentation, but as their results were measured using a correlate coefficient, they cannot be compared directly to the other two studies that found an effect of fetal presentation on the accuracy of FWE [17, 31]. However, none of the studies cited examined the effect of fetal presentation in a population of VLBW fetuses. Therefore, the impact of fetal presentation on the accuracy of FWE in VLBW and ELBW fetuses is still unclear.

Two of four studies reported a less accurate FWE for female fetuses than for male, due to a higher systematic error in female fetuses [7, 9, 10, 14]. This means that there is a systematic cause that has a negative impact on the ac-

curacy of FWE in female fetuses which cannot be explained by coincidence. Melamed et al. [10] found in their study that AC and FL are the factors that contribute the most to these differences; however, the reason for the persistently higher systematic error for female fetuses remains unclear. The contrary findings by Heer et al. [7] might be due to the fact that they included ultrasound estimations performed up to 14 days prior to delivery. This likely leads to a large systematic error in their study that can mask smaller gender-related differences. In summary, no clear statement on the impact of fetal gender on FWE in VLBW neonates can be made, since the results from appropriate BW groups cannot be extrapolated to the extremes of fetal weight and the impact of this factor has only been investigated in very few studies for this specific group.

Only two of five studies found an effect of time interval between estimation and delivery on the accuracy of FWE [7–11]. These results might be explained by the fact that two of three studies that did not find an effect only included cases with a maximum time interval of 3 days between FWE and delivery [9–11]. Scott et al. [8], who set a maximum time interval of 14 days, reported an increase in the mean percentage error when FWE was done more than 9 days prior to delivery. The study concluded that FWE should therefore be repeated after 10 days. The systematic error increases after 9 days but the confidence interval already increases after 7 days, which in summary indicates that the accuracy already decreases after 7 days. This implies that ultrasound measurements should be repeated if the time interval between FWE and delivery is more than 8 days. This conclusion is in accordance with the findings of other studies [7].

Regarding formula accuracy, the results suggest that the Hadlock formulas, which are also used routinely at our institution, are the most accurate as they seem to have a relatively low systematic error and are not adversely affected by variations in BW. In formulas specifically designed for small fetuses, except for Mielke's formula, only authors who developed a specific formula for very small fetuses and applied it to their own ethnic population reported improved FWE. This shows that parameters other than GA and biometric parameters, such as BPD, AC, HC and FL, might play an important role as well [20]. In general, formulas with more than two biometrical structures are shown to be more accurate if fetal growth is symmetrical [35]. However, in cases of asymmetric growth restriction, the Hadlock VI formula, which excludes FL, seems to be more accurate, as disproportionately short femurs are an early feature of

severe growth restriction and might therefore lead to an underestimation if FL is included [35]. A summary of all investigated formulas can be found in online supplementary table 1.

No clear statement can be made with respect to the advantages of 3D formulas, as the results are controversial. However, 3D ultrasound is more time-consuming and requires more skilled operators, so an advantage of this formula is marginal [18]. Due to the fact that 3D ultrasound is a relatively new technique and that not many formulas are available yet, the improvement of the accuracy of FWE with the 3D technique is subject to further research.

No results were obtained on the impact of active labor on the accuracy of FWE, as no study on this topic could be found and none of the included studies investigated this factor. Several studies suggested that multiple measurements by multiple examiners and averaging the results decrease the random error. This was confirmed by the only study included in our review that applied measurement averaging to reduce errors due to observer differences [29].

None of the included studies examined the accuracy of FWE in emergency situations in the delivery room. Yet,

especially in the particular early GA group at the limit of viability, an overestimation of fetal weight might lead to the decision for early delivery with an overestimation of neonatal outcome at birth, while an underestimation of fetal weight might result in a more conservative treatment and ultimately better outcome at birth.

No time limit for studies has been set, so that older yet still relevant studies could be included as well. We found results on 13 of the 14 investigated factors. One factor (active labor) that might have an impact on FWE was not investigated in any of the included studies. An overview of studies and factors can be found in online supplementary table 2a and b.

To the best of our knowledge, this is the first review that takes into account a total of 14 factors that might influence FWE accuracy. It is an important contribution to the analysis of influencing factors and therefore to the improvement of FWE. It is of utmost importance to detect and eliminate factors that have a negative impact on the accuracy of FWE, as with improvement of the medical care of mother and neonate, the number of preterm born neonates, in particular at the limit of viability between 23^{0/7} and 26^{0/7} weeks' gestation, is rising.

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