

## Reference Weights for Placentas Delivered before the 28th Week of Gestation

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Accepted 11 April 2007

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### Abstract

**Context:** Very few studies have measured the weight of large numbers of placentas delivered before the 28th post-menstrual week.

**Methods:** We measured the weight of 930 singleton placentas delivered before the 28th post-menstrual week, and examined the distributions of weights in selected groups (week of gestation, reason for preterm birth, birth weight Z-score categories, placenta histology). We excluded 90 singleton placentas based on growth restriction as indicated by birth weight Z-score, resulting in a normative sample of 840 placentas. Weights for unfused twin placentas are also presented.

**Results:** Standard weights derived from our data set differ from those previously published, partly due to a larger sample size. Placenta weight varied with birth weight. Placentas from pregnancies ending due to preeclampsia, fetal indications or those showing evidence of poor perfusion on histology were among the smallest and their weights correlated with the smallest birth weights for gestational age.

**Conclusions:** Placenta weights appear to be influenced by multiple maternal and fetal processes. We present a standard weight table for singleton placentas among live infants born between 23 and 27 completed weeks.

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**Keywords:** Placenta; Early gestation; Prematurity; Chorioamnionitis; Weight

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### 1. Introduction

Placental weight is easily and reliably measured and often mirrors problems of fetal growth and development. Increased weight is associated with hydrops fetalis, amniotic fluid infection, maternal diabetes, and maternal anemia; while low

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weights are associated with disorders attributed to utero-placental hypoperfusion (i.e. preeclampsia or karyotype abnormality) [1,2].

The reference values for placental weights of singleton pregnancies [1–3], and twin pregnancies [4,5] do not include early gestations or are based on very small samples. The largest published data set for live born infants between 21 and 28 weeks gestation includes only 67 cases [5]. To develop a more robust standard, we examined the weight distribution among 930 singleton and 197 unfused twin placentas from infants born between 23 and 27 completed weeks.

## 2. Materials and methods

### 2.1. Population

The placentas were collected as part of the ELGAN study, which was designed to identify factors that increase the risk for neurologic problems in ELGANs (the acronym for *Extremely Low Gestational Age Newborns*). During the years 2002–2004, all women delivering before 28 weeks gestation at 14 participating institutions were asked to enroll in the study. One thousand two hundred and fifty mothers of 1507 infants consented. It is estimated that 260 women were either missed or did not consent to participate; no data were collected on these women. The population is diverse with a mean maternal age of 28 years and a range of 13–47 years; 55% of mothers are white. The enrollment and consent processes were approved by the individual institutional review boards.

### 2.2. Placentas

Placentas were examined grossly within 12–24 h of delivery, and the weight of the disc was recorded after trimming of the membranes and cord (within 2 cm of insertion). Placentas were kept at 4 °C while awaiting examination; no attempt was made to adjust the weight based on the storage time. Although the cord was clamped at the time of delivery, no effort was made to control for blood drainage from the placenta before the exam. Study pathologists examined the slides for histologic characteristics listed on the data form. Following the guidelines of the CAP Conference [6] representative sections were taken from all abnormal areas as well as routine sections of the umbilical cord and a membrane roll, and full thickness sections from the center and a paracentral zone of the placental disc. Among the parameters coded were the presence or absence of infarcts and chorioamnionitis with neutrophilic inflammation infiltrating at least into the chorionic plate. Chorionic villi were scored for syncytial knots (none, occasional, increased).

### 2.3. Clinical information

The gestational age estimate was based on the following hierarchy: dates of embryo retrieval or intrauterine insemination or fetal ultrasound before the 14th week (62%), a fetal ultrasound at 14 or more weeks and a compatible LMP (13%), fetal ultrasound only at 14 or more weeks (16%), LMP without fetal ultrasound (7%), and gestational age recorded in the log of the neonatal intensive care unit (1%). The birth weight Z-score is the number of standard deviations the infants' birth weight is above or below the mean weight of infants at the same gestational age in a standard data set [7].

Labor was defined as the onset of contractions that led to delivery. Preterm labor (PTL) was considered the initiator of delivery if labor began while membranes were intact. The initiator was considered preterm premature rupture of membranes (pPROM) if the mother, vaginal fluid testing or medical personnel confirmed this prior to the onset of regular uterine contractions with accompanying cervical change. Preeclampsia (PE) was considered the initiator of preterm delivery if the patient presented with consecutive blood pressures >140/90 mmHg and proteinuria as demonstrated by either consecutive >2+ dip stick or >300 mg/24 h. Placental abruption was diagnosed in those patients

presenting with significant vaginal bleeding and alteration in their post-admission hematocrit. Painful uterine contractions or ultrasonic evidence of partial placental separation were not required. Cervical insufficiency (CI) was diagnosed in those patients with advanced cervical exams (>3 cm) and intact fetal membranes, but without regular uterine activity. Deliveries occurred for fetal indications (FI) in patients without the former set of diagnoses who were admitted with either one or several of the following: oligohydramnios, intrauterine growth restriction, or non-reassuring fetal testing.

### 2.4. Data analysis

Data were collected into a central database and analyzed using Stata Version 9.2 (2006, StataCorp LP, College Station, TX) statistical software. We excluded placentas from infants whose birth weights were more than 2 SD below or above the mean birth weight at the same gestational age in an external standard [7]. To implement this criterion, we ranked the placental weight data by birth weight Z-score; the Z-score is the number of standard deviations above or below the mean birth weight. We characterized the excluded group based on their clinical mode of presentation for delivery and placental histology.

## 3. Results

We examined 930 singleton placentas delivered before the 28th post-menstrual week. Mean placental weights and percentiles for each gestational week were established. The population studied is heterogeneous with respect to the indication for delivery, but can be divided into two overlapping groups; one where normal fetal growth was interrupted by a trigger for delivery, and a second in which growth was increasingly restricted leading to delivery. Previous weight standards [5] were based on analyses that attempted to exclude growth-restricted gestations, and we present a comparable analysis.

Gestations with extremely low or high birth weight, suggesting abnormal growth, were excluded before calculating percentiles that might be used as a standard. Cases were excluded if birth weight was more than 2 SD below or above the mean birth weight at the same gestational age. We excluded 90 placentas of infants with birth weight Z-scores below –2 and above 2 and calculated 10th, 25th, 50th, 75th and 90th percentiles and mean and standard deviation for each week of gestation (Table 1a). The excluded placentas are those outside the vertical lines that mark Z-scores of –2 and 2 in Fig. 1. The ratio of placental weight to birth weight is also presented (Table 1b).

Placentas excluded based on birth weight Z-score extremes are more likely than placentas included in our normative sample to have been delivered for preeclampsia or fetal indications (Table 2). The excluded group also has a high prevalence of

Table 1a  
Placental weight for gestations with birth weight Z-score between –2 and 2 presented as percentiles, mean and standard deviation by gestational age

GA	Percentile					Mean	SD	N included	% excluded
	10	25	50	75	90				
23	120	152	181	220	260	187	57	82	1
24	129	153	197	228	280	198	60	166	6
25	142	169	200	242	270	206	54	171	22
26	160	184	212	260	300	223	56	192	39
27	154	186	225	280	330	234	67	229	22

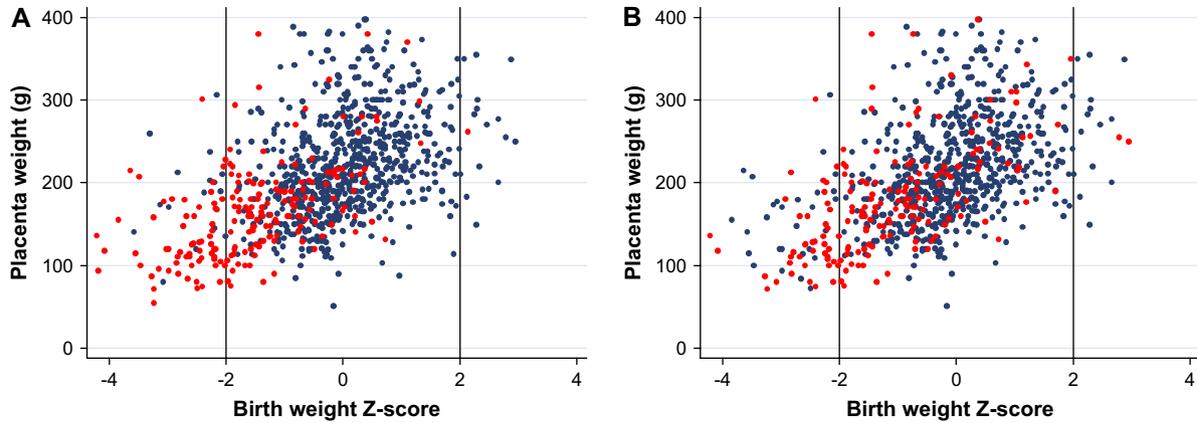


Fig. 1. Placenta weight vs. birth weight Z-score. Vertical lines enclose Z-scores between  $-2$  and  $+2$ . In panel A, red dots represent placentas of infants delivered for preeclampsia or fetal indications. In panel B, red dots represent placentas with histology characteristic of poor perfusion.

histologic evidence of poor utero-placental perfusion including infarcts and increased syncytial knots. While only 3% of placentas with histologic inflammation were part of the group excluded based on birth weight Z-score, 22% of placentas with evidence of poor perfusion were part of the excluded group. Placentas with inflammation were used in the comparison since chorioamnionitis is not associated with the same degree of growth restriction. The overlap between the placentas excluded based on birth weight Z-score and both clinical and histologic parameters is graphically demonstrated in Fig. 1.

At each gestational age, mean weights differed between placentas delivered vaginally and those delivered by c-section. As gestational age increased, the c-section placentas were smaller, likely reflecting the higher rate of preeclampsia. The tables represent the combined sample.

Placental weights of unfused twin placentas are smaller than those of singletons at all gestational ages (Table 3).

#### 4. Discussion

Our study has established reference values of placentas delivered before the 28th post-menstrual week of gestation. The high rate of fetal growth restriction associated with prematurity is seen in our population. In a normal distribution, approximately 2.5% infants are expected to have a birth weight more than 2 SD below the mean. In our sample, 8% of infants had birth weight Z-scores below  $-2$  and the proportion of

growth-restricted infants increased with increasing gestational age. To correct for fetal growth restriction, we excluded cases based on extremes of birth weight. The resulting subset of placentas was taken to represent babies with normal growth.

The data analysis is based on a dichotomized model of premature delivery. In this model, normal fetal growth is interrupted by a trigger for delivery such as chorioamnionitis or it is interrupted by delivery due to increasingly restricted growth related to utero-placental insufficiency. Although such classification is obviously artificial, the division is supported by our characterization of placentas from the excluded group. The excluded placentas were more likely to have been delivered for preeclampsia and/or to have histologic features characteristic of poor perfusion, both of which are highly associated with growth restriction [8].

Low weight of the placenta has been associated with histologic abnormalities of the placenta [8], maternal illnesses and with neonatal morbidity and mortality [2,9,10]. Previous standard tables by Moltini [3] and Pinar [5] were based on 30 and 67 cases, respectively (Table 8, Pinar [5]). Pinar used sequentially acquired placentas from “uncomplicated” deliveries and specifically excluded cases with intrauterine growth restriction, prolonged rupture of membranes, amniotic fluid infection or histologic findings of chorioamnionitis, pregnancy-induced hypertension or histologic findings of infarcts, perivillous fibrin or thrombi. Except for infection, these exclusions seem appropriate in ELGANs based on our finding of association

Table 1b  
Placenta to birth weight ratio for gestations with birth weight Z-score between  $-2$  and  $2$  presented as percentiles, mean and standard deviation by gestational age

GA	Percentile					Mean	SD	N included
	10	25	50	75	90			
23	0.209	0.225	0.309	0.368	0.426	0.316	0.090	82
24	0.196	0.237	0.280	0.344	0.431	0.300	0.090	166
25	0.197	0.223	0.260	0.304	0.361	0.268	0.070	171
26	0.185	0.215	0.248	0.291	0.322	0.254	0.058	192
27	0.167	0.199	0.230	0.268	0.336	0.240	0.064	229

Table 2  
Percent of placentas excluded based on Z-score by initiator of delivery

Presumed initiator of delivery	Total N	% excluded based on Z-score
Preterm labor	369	4
pPROM	207	2
Preeclampsia	169	28
Abruption	109	6
Cervical insufficiency	44	0
Fetal indication	31	45
Total	930	10

Table 3  
Percentiles of placental weights for twin gestations with unfused placentas

GA	Percentile					Mean	SD	N included	% excluded
	10	25	50	75	90				
23	79	99	137	160	220	143	58	14	13
24	115	131	147	190	280	171	66	33	11
25	117	140	182	203	250	179	56	32	18
26	133	160	195	242	260	197	50	30	25
27	160	181	206	245	282	222	61	48	11

Data includes infants with birth weight Z-scores between  $-2$  and  $2$ .

of low placental weight, birth weight, and histologic evidence of poor utero-placental perfusion. In contrast, placentas with evidence of chorioamnionitis did not show placental weights different from those presenting in preterm labor. Although quantitatively similar to Pinar, our standard weights are slightly higher at younger age and lower at later age and show a broader separation between the percentiles. Their fitted curve used to derive their standards shows a flattening of the weight curve at low gestational age that may reflect the very limited numbers of placentas at that end.

Molteni et al. [11] reported placental weights for three groups of singleton placentas based on fetal weight for gestational age (appropriate, large, and small). Table 8 of their paper lists the ‘appropriate group’. Those weights are much lower than either Pinar’s or ours. Our data are closer to their ‘large for gestational age’ group. One difference is in the sample preparation since Molteni specifically drained the fetal circulation of blood, a factor that has been reported to effect weight by up to 10% [12]. Pinar suggests that the differences may reflect “a generational or nutritional change over the 30 years” between studies. Another difference may be in the younger age of their study population; the average maternal age for Molteni’s sample was 21.2 years vs. a mean maternal age of 28 years and a range of 13–47 years in our sample. Both Molteni’s and our study population were predominantly Caucasian.

Specific literature reference to the effects of abnormal cord insertion [13], maternal smoking [14] could not be addressed due to small number of cases involving these variables in our dataset. Also, we did not stratify by race in light of the literature documenting that whites and blacks do not differ appreciably in the distribution of their placental weights, at least among third trimester births [15,16].

Mean weights of unfused twin placentas (each disc) were smaller than singletons at each gestational age and is consistent with the literature [2,5].

## 5. Conclusion

Our large sample of placentas from pregnancies that ended before the 28th week of gestation allowed us to create tables of the normal range of placental weights at each of these early weeks of gestation. We have expanded the literature

experience for placental weights in the low gestational age group and made specific reference to multiple gestations.

## Acknowledgments

The study is funded by a cooperative agreement with the National Institute of Neurological Disorders and Stroke (1 U01 NS 40069-01A2). The authors are from the Department of Pathology at their respective institutions unless otherwise noted. We wish to thank several ELGAN study investigators for their contribution to the data collection for this study: John Christie, MD, PhD (Eastern Carolina Medical Center, Greenville NC), Bo Xu, MD (formerly at U. Mass. Memorial Medical center, Worcester, MA).

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