The placenta as modulator of fetal prosperity
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Chapter 2:

Ted (G.J.) Kloosterman: On Intrauterine Growth, The Significance of Prenatal Care. Studies on Birth Weight, Placental Weight and Placental Ratio

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Abstract

Kloosterman studied 80,000 birth weights and 30,000 placental weights in relation to gestational age at birth, fetal sex, maternal parity, and perinatal mortality. He concluded that pregnancies with heavier placentas last longer. He also concluded that from about 30 weeks of gestational weeks onwards, children from primiparous women as compared to those from multiparous women, and twin children as compared to singleton children are relatively growth retarded, most likely related to prior relatively poor placental growth. Obviously, poor fetal growth is not the cause, but the result of poor placental growth. Future early detection of poor placental growth may prospect poor fetal growth, and may even allow for early interventions to improve fetal outcome.
From 1954 until 1970 Ted Kloosterman published several articles on the significance of birth weight, placental weight, and Placental Ratio. From 1970 keynote paper ‘On intrauterine growth’, was based on a group of 80,000 consecutive singleton pregnancies of women, visiting two clinics in Amsterdam (the Training School for Midwives and the University Clinic at the University of Amsterdam) between 1931 and 1967. From these women, 30,000 consecutive placentas were processed and weighed by one single and devoted person, miss Huidekoper, a midwife and scientific co-worker of Kloosterman. According to a standard protocol, directly after birth, all blood clots were removed, the membranes were trimmed off along the edge of the placenta, the umbilical cord was cut within 2 cm and ligated after being allowed to bleed freely. The placenta was placed in a 10% formalin solution and weighed within a week. Insertion of the umbilical cord, and the macroscopic stage of ‘infarction’, observed on placental slices were registered.

In those days a heated discussion took place on the significance of a small placenta with respect to the fetal growth. According to Fox and Gruenwald, a small placenta, being a fetal organ, just as a small fetal liver, was a manifestation rather than a cause of poor fetal growth. They therefore saw ‘no reason why the practice of routinely weighing the placenta should be continued’. Kloosterman on the other hand argued that a baby is small because the placenta is small. In the next paragraphs we will provide the data on which Kloosterman based his arguments.

Birth weight, placental weight and Placental Ratio in relation to gestational age
From cross-sectional birth weight data, fetal growth seems to decelerate after 38 weeks. Kloosterman concluded that, as 4 weeks after birth acceleration of growth of the newborn occurs, the cause of the intrauterine deceleration of growth must be a limitation of the maternal supply line; that is the placenta and the mother.

Data on placental weight suggest a constant rate of growth during pregnancy unto and even beyond term, which he considered unlikely for an organ at the end of its lifespan. At 20 weeks, the mean Placental Ratio (PR), i.e. placental weight divided by birth weight, is found to be about 35%, and subsequently to decrease unto 15% at 38 weeks, as the fetus grows more rapidly than the placenta. Oddly enough, after the 38th week, the Ratio did remain on the same level. Kloosterman thought it very unlikely that the fetus decreases its growth very dramatically after 38 weeks, or that the placenta will accelerate its growth at the end of its lifespan. His elegant explanation for these findings was, that in
Figure 1: Birth Weight, Placental Weight and Placental Ratio. Mean (continuous line) and 10th and 90th centiles of birth weight (BW), placental weight (PW) and Placental Ratio (PR) in singletons, by gestational age, according to Kloosterman's key article 'On Intrauterine Growth'; Figure 1, and Tables 5 and 7.4
the presence of a relatively heavier placenta, pregnancies last longer, which means that the placental ‘growth curve’, based on cross-sectional data, does not reflect real longitudinal growth.2-4

Influences of fetal sex, maternal parity
Boys are by 24 weeks of pregnancy, heavier than girls, the mean difference at 40 weeks being 140 g. Placental weights of boys and girls are the same throughout pregnancy.1-4 Kloosterman concluded that boys, being heavier, demand more from their placentas as compared to girls. As expected, boys show indeed a relatively higher perinatal mortality, as compared to girls, especially after 40 weeks of gestational age.2 Children from multiparous women, from about 32 weeks onwards, are heavier than children from primiparous women, the mean difference at 40 weeks being 200 g.1-4 In multiparous women, the placentas are also heavier than in primiparous women, already from 25 weeks onwards.1-4 Kloosterman concluded that multiparous women offer, through remodelling of the maternal vasculature in former pregnancies, a more favourable environment for both placental development and placental function in next pregnancies.2-4
Taken together, these data suggest that the influence of fetal sex with respect to intrauterine growth is limited to the fetus and not extended to the placenta. This also suggests that, compared to children from multiparous women, children from primiparous women are relatively growth retarded, most likely due to a prior relatively poor placental growth. It is therefore not surprising that children from primiparous women show higher perinatal mortality, as compared to those from multiparous women, especially at and after 40 weeks of gestational age.2-4

Influence of litter size
Kloosterman found that, in comparison to singletons, the mean birth weight of twin children is found to be smaller, from about the 32nd week, the difference at 39 to 40 weeks being about 600 g.3,7,8 Where the mean placental weight of twin children as compared to singleton children is found to be consistently smaller from 22 weeks to term, they concluded that, compared to singleton children, twin children are relatively growth retarded, most likely due to a prior relatively poor placental growth. These observations, though from cross-sectional data, confirm Kloosterman’s concept, that smaller placentas are the cause and not the result of poor fetal development.4 McKeown and Record9 and Gruenwald10 who found higher PRs in twins as compared to singletons, concluded that relatively more placental tissue is available to the twin fetus and therefore, the restriction of fetal growth in twins (after 32 weeks) must be due to influences outside the placenta. In
contrast, Kloosterman’s co-workers found lower PRs in twins, up to 37 to 38 weeks, and therefore the placenta may very well limit fetal growth in twins. After 38 weeks, in twins, the PRs were found to be relatively higher as compared to singletons, which was explained by twin pregnancies, related to relatively heavier placentas, last longer.\textsuperscript{7,8}

The small placenta
Kloosterman’s first publication on intrauterine growth dealt with ‘the significance of the placenta in obstetrical mortality’, and was based on the first 2000 singleton placentas, examined as described above. The lowest perinatal mortality of 1.6\% was found in placental weight groups of 500 to 800 g. In lower placental weight groups a much higher perinatal mortality was met: 43.2\% among the 200-300 g group, and as high as 97\% among the less than 200 g group, the majority being ante partum mortality in that last group.\textsuperscript{1}

In 1983, his co-worker miss Huidekoper published an additional study on ‘the significance of the small placenta’, based on 227 singleton pregnancies with placentas of 100-200 g, born in the University Clinic at the University of Amsterdam, in 1958-1981.\textsuperscript{11} These very small placentas were found to be related to higher incidences of preeclampsia, placental infarction, lower birth weight, and perinatal mortality, especially ante partum mortality.

Comments
The historic significance of the work of Kloosterman is the study of consecutive birth weights, according to carefully assessed gestational ages, related to placental weights, measured according to a rigorous protocol. Even today this set of data is the largest ever reported. A limitation of his studies is that inferences are made on longitudinal fetal and placental growth, based on a cross-sectional design.

Of high interest are Kloosterman’s observations on the relationship between fetal and placental growth. His cross-sectional curves demonstrate that poor placental development, as observed in primiparous women versus multiparous women, and in twins versus singletons, precedes poor fetal growth by many weeks of gestation. These observations seem to confirm his conclusion, that small placentas may be very well the cause, and not the consequence of poor fetal growth.

Kloosterman’s observations point to the importance of the first half of pregnancy with respect to placental development. Most likely even the first trimester of pregnancy, being essential for early placental development, defines the course of pregnancy, and the outcome of pregnancy.
Recent ultrasound studies on the relationship between early (12-26 weeks) placental volume and fetal growth seem to confirm this suggested sequence of events: poor placental growth precedes poor fetal growth, lower second trimester placental volumes and lower placental growth rates are good predictors of lower birth weights, and even lower first trimester placental volume seems to be related to lower birth weight at term.\textsuperscript{12-15} In daily practice, estimation of placental size by ultrasound, and other techniques, is still a technical problem and very time consuming. Improved ultrasound or other visual techniques may enable to estimate placental size in early pregnancy, in normal clinical settings and with enough accuracy. Future early detection of poor placental size, may prospect poor fetal growth, and may even allow for early interventions to improve fetal outcome.
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