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Birth weight: nature or nurture?

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Abstract

Objective: To investigate the relative role of environmental and genetic factors in the determination of birth weight following ovum donation. *Methods*: Data from 62 cases of ovum donation were used to examine the relative influence of donor and recipient on birth weight. *Results*: The only discernible factors that significantly influenced birth weight were gestational age and recipient's weight. Donor weight, her own birth weight, and the birth weight of the donor's own children were not significantly correlated with the birth weight of the child following ovum donation. *Conclusions*: It is concluded that the environment provided by the human mother is more important than her genetic contribution to birth weight.

Keywords: Birth weight; Ovum donation; Genetic; Environment

1. Introduction

Human birth weight is an important factor in perinatal survival, infant mortality [1] and adult pathology [2–4]. Polani [5] estimated from the work of Penrose, Karn and others, that in the human, fetal genotype accounts for only 15% of the variation in birth weight, while the environment provided by the mother accounts for over 30%. Maternal factors include body weight at conception and weight gain during pregnancy; both being more important than maternal height or age [6]. A dramatic

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illustration of the effect of the maternal environment is seen in the cross breeding of Shetland ponies with Shire horses. If the mother is a Shetland, the foal is born small but grows very rapidly thereafter; if the mother is a Shire, the foal is born large and then hardly grows at all as it matures [7]. However, genetic factors in the fetus can also have a demonstrable effect; siblings of children with phenylketonuria are larger than average at birth [8].

The relative contributions of fetal genome and maternal environment in the human are difficult to separate, as the fetus normally shares half the genome of the mother, and hence genetic factors can operate at both fetal and maternal levels simultaneously. While it is known that there are large variations in birth weight according to race (for example, mean birth weight in the Luni tribe of New Guinea is only 2.4 kg [9], while in the Afro-Caribbeans of Anguila it is 3.8 kg [10]), it is not clear whether the variation in birth weight is controlled genetically by the fetus, or is a response to the difference in the adult size of the mother, as in the Shetland/Shire experiment. Obviously, deliberate cross-breeding between human races cannot be conducted to examine this question. However, the recent development of ovum donation as a treatment for infertility has provided an opportunity to examine a situation in which on the one hand, a woman carries a fetus with whom she has no genetic connection while on the other hand, the mother providing half its genome has no input into its growth environment. Therefore, we decided to carry out a retrospective analysis of the relationship between birth weight and both donor and recipient characteristics (age, height, weight) to examine the following hypotheses. Firstly, that the genetic connection between the donor and fetus means that there will be a correlation between the characteristics of the donor and the birth weight of her fetus even though it grows within an unrelated mother. Secondly, for the same reason, there will be a correlation between the previous children of the donor and the birth weight of the donated child. Thirdly, there will also be a correlation between the characteristics of the recipient and birth weight, because the recipient is providing the environment in which the fetus develops.

2. Subjects and methods

One-hundred sixty-one pregnancies occurred following 541 ovum donation IVF cycles at the Lister Fertility Centre between November 1988 and October 1992. However, in only 62 of the singleton pregnancies which delivered at or later than 28 weeks gestation (the lower limit of viability during the study) was donor and baby data available. Missing data were due to the donor being unwilling to have her physical characteristics recorded and/or the baby delivering at a distant location so that the birth weight was not available. There is no reason to suppose that this introduced any systematic bias into the subjects for which full data were available; each case served as its own control. Fifty-seven donors made 61 donations (one donation was to two recipients, and one donor donated on three occasions): each individual donation (n = 62) has been treated as a separate case. One recipient had two singleton babies, separated by 2 years, using the same donor: these two donations have been treated as separate cases. For social reasons, recipients were matched, as far as possible, with the donors according to their physical characteristics and race. This had the effect of reducing the power of the study to examine the hypotheses stated above, but was obviously desirable to the recipients. The height and weight of each donor was recorded on the day of oocyte collection. The height and weight of each recipient was recorded on the day of ovum transfer.

Fifty-two recipients were Caucasian, eight Indian, one Thai, and one African. They were all in good health, did not smoke during the pregnancy and had all been resident in Europe for 5 years. All donations were racially matched except three Caucasian to Indian and one Caucasian to Thai. Fifty-eight donors were parous and four nulliparous. Forty-three recipients (69%) were nulliparous and the remaining 19 (31%) had one or more previous normal pregnancies (range 1–4, median 2). All patients gave informed consent for the study and approval was obtained from the hospital ethics committee.

The date of birth and birth weight of the 62 babies resulting from ovum donation were obtained from hospital records. Gestation at delivery was calculated from the date of oocyte collection plus 14 days. The birth weight of oocyte donors and the first born child of the donors was obtained by postal questionnaire. Excluding multiple deliveries, the birth weights of 29 donors and of the children of 35 donors were obtained. In donor and recipient pregnancies, there were no complications requiring medical treatment or obstetric intervention other than those commonly encountered during labour. The reasons for delivery by Caesarean section did not include intrauterine growth retardation or significant proteinuric hypertension.

Statistics were calculated using Students paired t-test, Pearson's linear correlation test (r), stepwise multiple (linear) regression (T = t-value for partial correlation coefficient) and Chi squared. All P-values are two tailed except for correlations which are one tailed. Calculations were made using SPSS for Windows (version 6) statistics software. Birth centiles were calculated using nomograms [11].

3. Results

The mean birth weight (kg) of the 62 study babies was 2.99 ± 0.65 S.D. In comparison, the mean (± S.D.) birth weights (kg) of the donor's previous children were 3.38 ± 0.42 S.D. for 35 first born children, 3.36 ± 0.45 S.D. for 29 second born children, and 3.48 ± 0.52 S.D. for 19 third born children. There was a significant difference between the birth weights of the study group and the donors' own children (e.g. 35 pairs of study vs. donors' first born babies, mean birth weights 3.01 kg vs. 3.38 kg, $t = 2.82$, $P = 0.008$). This difference was due to earlier delivery in the study babies (mean weeks ± S.D. of study babies vs. 1st, 2nd and 3rd born: 37 ± 2.2 vs. 39.9 ± 1.28, 39.9 ± 1.44, 39.9 ± 2.2) compared to the donors' previous pregnancies (e.g. study babies vs. 1st born: $t = 5.98$, $P < 0.0005$). This difference was reflected in the mode of delivery of the study babies; 46 (74%) babies were delivered by Caesarean section. There were no perinatal deaths.

Mean donor and recipient ages (years) were 30.4 ± 3.6 S.D. and 39.2 ± 6.6 S.D., respectively. This is a highly significant difference (paired $t = 8.73$, $P < 0.0005$). However, neither donor nor recipient age correlated significantly with birth weight

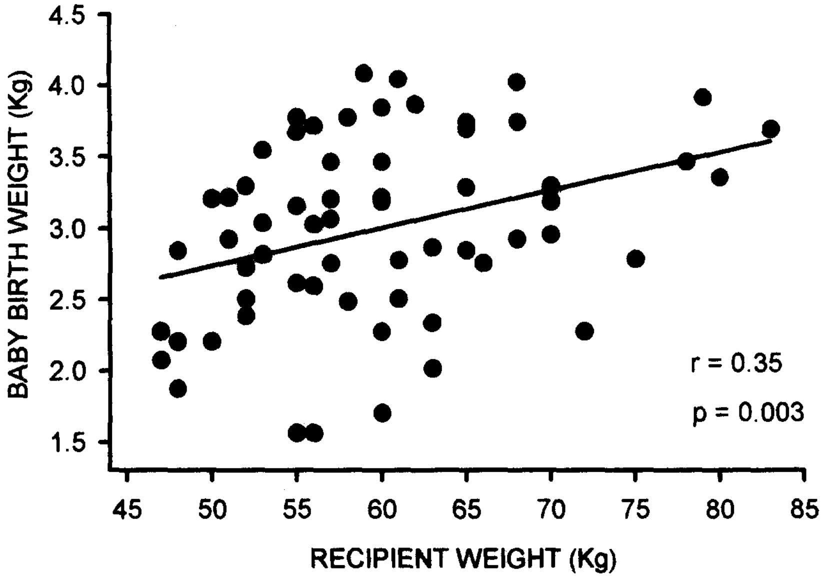

Fig. 1. Relationship between birth weight and recipient weight.

or gestational age at delivery of the study babies. Mean donor and recipient heights (cm) were 161.7 ± 6.5 S.D. and 160.2 ± 8.0 S.D., respectively. This is not significantly different (paired $t = 1.39$, $P = 0.17$). Mean donor and recipient weights (kg) were 63.3 ± 10.6 S.D. and 59.8 ± 8.5 S.D., respectively. This is significantly different ($t = 2.38$, $P = 0.02$). Before ovum donation, an attempt was made to match

Table 1
Variables analysed for their influence on birth weight and birth weight for gestation (birth centile)

Variable	
Recipient	Age
	Race (Caucasian or not)
	Height
	Weight (at the time of ovum donation)
	Parity (primiparous or multiparous)
	Previous abortions (yes or no)
Donor	Age
	Race (Caucasian or not)
	Height
	Weight (at the time of ovum donation)
Fetal	Sex
	Gestation at birth
Method	Fresh transfer or transfer after embryo freezing
	Zift/tubal transfer or intra-uterine embryo transfer

donor and recipient body build. Therefore, as expected, they were significantly correlated (weight, $r = 0.30$, $P = 0.018$; height, $r = 0.31$, $P = 0.014$).

The main determinant of birth weight was gestational age ($r = 0.67$, $P < 0.0005$). Birth weight was also significantly correlated with recipient weights ($r = 0.35$, $P = 0.003$) but not donor weights ($r = 0.15$, $P = 0.12$) (Fig. 1). Birth weight also correlated weakly with recipient height ($r = 0.20$, $P = 0.056$) but not with donor height ($r = 0.02$, $P = 0.44$). A stepwise multiple (linear) regression analysis of all variables (Table 1) showed a multiple r of 0.71; only gestational age and recipient weight contributed significantly to birth weight with $T = 6.7$ and 2.4, $P < 0.0001$ and $= 0.018$, respectively. When birth weight for gestation (birth centiles) was considered as the determinant variable in place of birth weight, recipient weight was the only variable that contributed significantly with $T = 2.047$ and $P = 0.045$.

There was a significant correlation between the donor's own birth weight and the birth weight of the donors' own first born child ($n = 27$, $r = 0.41$, $P = 0.024$). Similarly, there was a significant correlation between the birth weights of the donors' own children (1 vs. 2, $n = 29$, $r = 0.56$, $P = 0.002$; 1 vs. 3, $n = 19$, $r = 0.73$, $P = 0.001$; 2 vs. 3, $n = 19$, $r = 0.70$, $P = 0.001$). However, there was no significant correlation between the birth weights of the donors or the birth weight of her first, second or third born children and the study group's birth weights ($n = 29$, $r = 0.10$, $P = 0.6$; $n = 35$, $r = 0.10$, $P = 0.58$; $n = 29$, $r = 0.08$, $P = 0.64$; $n = 19$, $r = 0.15$, $P = 0.53$).

4. Discussion

Previously, it has been inferred that environmental factors and uterine constraints contribute more to human weight at birth than genetic factors [12–16]. This study has demonstrated the truth of this hypothesis. Although many factors contribute to birth weight [6], the effect of the recipient's weight (an environmental factor) at the time of egg donation was shown to have a greater influence on birth weight than the weight of the matched donor (a genetic factor). The clinical decision to select donors with similar physical characteristics to recipients probably reduced the random chance of finding a significant difference in correlation. This selection was made by doctors without a knowledge of this study and was, therefore, not considered to contribute a bias.

The possibility of separate genes for adult weight and birth weight should also be considered, since this may explain the failure to find a correlation between adult weight and birth weight. There was a correlation between the donor's birth weight and the birth weight of her first born children, suggesting the existence of a genetic factor controlling birth weight. The failure to find a correlation between the birth weight of the donors or the donor's own children and the children resulting from ovum donation suggests that any such factor is weak. However, the numbers ($n = 27$) involved in this part of the study were very small and much larger studies need to be made before drawing firm conclusions.

It has been suggested that subfertility is a risk factor for low birth weight [17]. It may be argued that ovum recipients are a special group of infertile women, as most have ovarian failure (primary or secondary) [18,19]. This may explain why the birth weight for gestation (centile) of the 62 babies studied was not significantly different to that expected for a standard (singleton) population (n = 39 326: North West Thames Region: annual maternity figures for 1991, St. Mary's maternity information system). Further, there is no direct evidence to suggest that babies born following ovum donation are at increased risk of low birth weight. The number of recipients with a previous spontaneous abortion, prior freezing of embryos or fresh transfer, and method of zygote/embryo transfer was not found to influence birth weight. Therefore, it is unlikely that the need to become an ovum recipient or the procedure of ovum donation had any influence on the correlation between donor or recipient weight and birth weight.

Birth weight for gestation (birth weight centile) is an important factor when considering intrauterine growth rates, but is of lesser importance than birth weight as a factor determining the natural gestation of delivery. Stepwise multiple (linear) regression analysis of the selected variables in this study did not indicate that the sex of an infant was a significant factor; this finding is probably due to the small number of cases studied. There was a high rate of Caesarean section in the study group, which may have influenced the birth weight but was unlikely to affect the correlation with donor or recipient weights. The same variables were analysed against weight for gestation which showed that recipient weight was the only significant factor. It explained 12% of the variation in birth weight but only 6.5% of variation in the birth weight for gestation, confirming that gestational length is a significant outcome variable in relation to maternal body weight [20].

Forty-five percent of the variation in birth weight in the study group was explicable by gestational length. Pregnancy was almost 3 weeks shorter in the study group than in the donor's pregnancies. Variation in gestational length in the study group could not be explained by the recipient's age [18,19]; therefore, we hypothesise that the major factor was anxiety on the part of both the prospective parents and the medical attendants, leading to the very high caesarean section rate, much of which was elective.

Race can be an important factor determining birth rate [21]. However, if Asian mothers are well nourished, they can achieve a standard of intrauterine growth comparable to Europeans [22]. In this study, 52 recipients were Caucasian, nine Asian and one African. Race was examined as a factor determining birth weight (Caucasian or not) and not found to be correlated with birth weight. This may be due to the small number of births studied but may also be related to the social circumstances of the Asian recipients, who were all financially secure and had resided in Europe for 5 years.

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