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Weight Variation by Sex and Nature of Risk Factors in High-Risk Infants: An Evolutionary Perspective

In memory of Professor Paul T. Baker, who was a pioneer in the field of human adaptability research, human population biology and biocultural anthropology. He viewed much of human diversity, biologically and culturally, as a response to stressful environmental conditions.

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A B S T R A C T

A retrospective cohort study was conducted to explore growth variation during the intrauterine and early postnatal period by sex and nature of high-risk factors (i.e. physiological and pathological) in 831 Korean infants at a University hospital. The results showed that infants with a physiological risk showed a more congruent intrauterine growth pattern compared to those with a pathological risk. Particularly with a physiological risk, female infants experienced more compatible intrauterine and postnatal growth than males, although male infants were heavier than female infants at a given gestational age. In conclusion bigger may not necessarily be better for prenatal growth in humans. A more confluent intrauterine growth in infants with physiological risk can be beneficial for early postnatal catch-up growth. From an evolutionary perspective, female infants with a physiological risk may keep their advantageous edge over male infants during the early postnatal period although such an advantage may not be present with a pathological condition.

Key words: *evolution, gestational age, birth weight, growth variation*

Introduction

While a dramatic decrease in mortality in high-risk infants, including early preterm infants, has occurred due to advances in medical sciences, an increase in prevalence and morbidity of high-risk infants with chronic or permanent sequels have become a challenge since the 1990s[1,2]. A recent US population-based, retrospective cohort study reported 8.3% to 9.4% of preterm birth (PTB) rates of 16.2% among whites to 18.5% among blacks between 1989 and 2000[3]. A recent Korean cohort study reported 7.2% of low-birth-weight (LBW) infants (than 2,500 grams), 1.4% of very LBW infants (less than 1,500 grams), 8.4% of PTB rates (less than 35 weeks gestation), and 0.7% of early PTB rate (less than 32 weeks gestation)[4]. A prospective study of high-risk infants with a gestational age (GA) of 22 to 27 weeks reported survival rates of 0% for less than 23 weeks, 16% at 23 weeks, 44% at 24 weeks, 66% at 25 weeks, 72% at 26 weeks, and 82% at 27 weeks, respectively[5]. The studies above support the current reduction in infant mortality although a greater possibility exists of an increase in morbidity among the surviving high-risk infants.

The first few weeks after birth are critical for the survival and later growth of infants in terms of extrauterine adaptation. Any existing or predisposing risk factors such as LBW, PTB, or pathological conditions from the intrauterine environment or at birth can negatively affect postnatal adaptation, particularly during critical periods of early development. The nature of high-risk factors may be classified primarily as physiological risk or pathological risk. Preterm birth is one of the examples of phy-

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siological risk imposing limited development time within the intrauterine environment. Though most preterm infants have LBW due to shortened intrauterine nutritional supports, their prenatal growth pattern may be normal and fall into an appropriate-for-gestational age category at birth. In this case, the nature of the risk is generally considered physiological or developmental rather then pathological.

Pathological risk factors are those that affect survival and infant growth. The nature of pathological risks in infants presumes the existence of disease or abnormal conditions, such as hemolytic disease, asphyxia, or metabolic disorders, arising from the intrauterine, perinatal or the extrauterine environment. Despite overlapping clinical manifestations between the two types of risk, the primary therapeutic and intervention strategies differ for physiological and pathological risk. The question raised in this study is whether the difference in the nature of the risks affects variation in growth during the intrauterine and early postnatal period.

There is a high degree of variation in human growth during the intrauterine period and early infancy. One of the crucial aspects of growth variation during this period is a change in body weight. While fetal skeletal development appears to be blunted with a decreased velocity near term and after birth[6,7], body weight continues to increase in a fairly linear pattern postnatally. Therefore, early postnatal weight changes may reflect the quality of early extrauterine growth.

Of particular interest in human growth variation is the role of sex. Though male fetuses grow faster[8] and are heavier in full-term births[9], there is a greater mortality risk in males during the prenatal period and in early infancy[10]. This may lead to the assumption that female infants who on average weigh less than males have a favorable survival with less morbidity compared to male infants, when no other factors appear to be involved. If so, this would seem to give females a distinct advantage in terms of evolution and adaptation[11]. If evolution does tend to favor newborn females over newborn males, growth variation by sex during the prenatal and postnatal period needs to be understood within an evolutionary perspective. Likewise, when there is a risk that threatens either growth or health status of the infant, the role of sex on growth variation needs to be investigated relative to the nature of the risk. The present study was conducted, therefore, to explore intrauterine and extrauterine growth variations by sex and nature of the high-risk factors in infants. The quality of intrauterine growth was examined by the relationship between birth weight (BW) and GA as a chronological function of the intrauterine environment. The relationship between postnatal weight changes in percent (WtC) and postnatal age (PA) provides a means of examining extrauterine growth variation during the acute postnatal period.

Materials and Methods

A retrospective cohort study was conducted using secondary data from infants previously enrolled for studies at the neonatal intensive care unit of a Korean University affiliated hospital. As high-risk infants were admitted to the unit, they were categorized into two groups according to the nature of the risk factors (physiological or pathological) using their primary medical diagnosis at the time of admission. Group A represents infants diagnosed with a physiological risk such as PTB or LBW. Group B represents infants with a pathological risk, such as a clinically minor chromosomal anomaly, a metabolic disorder, transient tachypnea of newborn, infection, asphyxia etc. at admission. Infants from multiple gestations, with a major structural anomaly which needed surgical correction (i.e.: tracheoesophageal fistula), with fatal chromosomal anomalies (i.e.: Edward syndrome), or out of the appropriate-for-gestational age category were excluded from this study due to the possible effects that these conditions may have on growth. No additional informed consent was necessary for the utilization of the secondary data from the original studies approved by the participating hospital's institutional review board. Data on sex, GA, BW, PA and WtC were retrieved, and descriptive statistics and univariate analysis including independent t-test and Pearson *r* correlations were applied to explore the relationship between variables of interest with a = .05 in a two-tailed test using SPSS.

Results

In Table 1, among 831 infants (female : male infant ratio = 47.2% : 52.8%), 61% of infants are classified in Group A (physiological risk) while 39% of infants are classified in Group B (pathological risk). The mean GA was 35 weeks and one day at birth with the mean BW of 2,412 grams. The WtC was calculated at a mean of 10.3 days of PA.

Table 2 shows the difference in BW by sex and nature of high-risk factors of the infants. Since Group B included infants beyond 37 weeks of GA, the mean BW of Group B was greater than Group A in both female and male infants. Interestingly, males showed significantly

TABLE 1
DESCRIPTIVE DEMOGRAPHICS OF INFANTS (N = 831)

Variable	Frequency (%)	Mean (SD)
Sex		
Female	392 (47.2)	–
Male	439 (52.8)	
Nature of high-risks		–
Physiological (A)	507 (61.2)	
Pathological (B)	322 (38.8)	
Gestational age (weeks)	–	35^{+1} (4^{+1})
Birth weight (grams)	–	2,412 (890.07)
Postnatal age (days)	–	10.32 (12.96)

TABLE 2
DIFFERENCE IN BIRTH WEIGHT (GRAMS) BY SEX AND RISK FACTORS (N = 831)

Sex	Risk factors		t (p)
	Physiological (Group A)	Pathological (Group B)	
Sex			
Female	1,813 (692.80)	3,200 (672.28)	–18.126 (.000)*
Male	2,012 (638.40)	3,290 (483.24)	–22.632 (.000)*
t(p)	–3.356 (.001)*	–3.286 (.001)*	

* Significant at p <.01

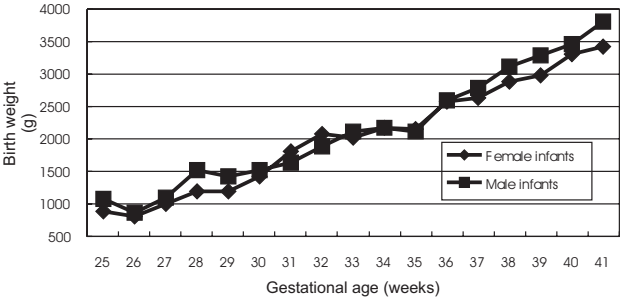

Fig. 1. Variation in birth weight at various gestational ages between females and males.

higher BW than females, regardless of the nature of the risk (t = –3.356, p =.000 for A, t = –3.286, p =.001 for B). Figure 1 illustrates the weight variation by sex of the infants, showing that males are generally heavier than females at a given GA with few exceptions.

The relationship between GA and BW was examined by sex and nature of the risk to explore intrauterine growth variations in high-risk infants. As presented in Table 3, Group A infants (physiological risk) showed a higher correlation between GA and BW than Group B (pathological risk) (r = 0.775 and 0.378, respectively). In Group A, the intrauterine growth pattern revealed a higher correlation coefficient in female than in male infants (r = 0.835 for females and 0.740 for males). Contrarily, the correlation was reversed in Group B infants, showing a higher correlation in male than in female infants (r = 0.444 and 0.279, respectively).

Table 3 presents the relationship between PA and WtC for extrauterine growth variation in both Group A and B. Female infants in Group A demonstrated a highly significant correlation between PA and WtC (r = 0.596, p = 0.000), while females in Group B showed no significant relationship (r = 0.168, p = 0.115). In addition, male infants in both Group A and B showed a relatively comparable correlation between PA and WtC (r = 0.350 for A; r = 0.466 for B). Interestingly, male infants in Group A revealed a substantial decrease in the correlation coefficient for extrauterine growth variation compared to the intrauterine period (r = 0.740 and 0.350, respectively), while male infants from Group B maintained a fairly consistent relationship for both extrauterine and intrauterine growth variation (r = 0.446 and 0.465, respectively).

Discussion and Conclusions

Currently, high-risk infants accounts for approximately 10% of all infants, a rate prone to increase with advances in medical care and increasingly with advances in the health sciences[3,4]. There is a need for health professionals to address the nature and factors influencing variation in both intrauterine and extrauterine growth. Physiological and pathological risk factors and sex differences can affect human growth from prenatal life through later growth and development. Evolution operates to favor populations with an increased survival rate, increased growth and increased reproductive capacity throughout the life span of a species. In humans, it is known that females have an advantageous evolutionary edge for survival and growth[5,9,10] while males have a larger body size associated with greater physical strength[6,8,12]. However, it is not fully understood how sex differences and neo-

TABLE 3
CORRELATION IN INFANTS BETWEEN GESTATION AGE (GA), BIRTH WEIGHT (BW), AND POSTNATAL AGE (PA) AND WEIGHT CHANGES (WTC) BY SEX AND NATURE OF RISK

Risk factors	Sex	Correlation [r(p)]	
		GA and BW	PA and WtC
Physiological risk (Group A infants)	Female	0.835 (0.000)*	0.596 (0.000)*
	Male	0.740 (0.000)*	0.350 (0.000)*
	Total	0.775 (0.000)*	0.532 (0.000)*
Pathological risk (Group B infants)	Female	0.279 (0.001)*	0.168 (0.115)
	Male	0.445 (0.000)*	0.466 (0.000)*
	Total	0.327 (0.000)*	0.355 (0.000)*
Total		0.856 (.000)*	0.498 (0.000)*

* Significant at p <.01

natal risk factors play a role in growth variation during the prenatal and acute postnatal period in humans.

The present study reaffirms that male infants are heavier at birth than female infants at a given GA. Several studies implicate a heavier body weight as one of the possible factors for a male fetus' susceptibility to preterm birth[10,13,14]. One research group reported a higher level of serum type I collagen C-terminal propeptide, a marker for fetal bone formation, as a cause of heavier body weight in male than in female premature and term infants[8]. Though probabilistic sampling was not carried out, our finding in the present study using fairly large sample sizes supports the view of a male's vulnerability to be born prematurely if it is prenatally heavier.

BW reflects the intrauterine developmental status along with GA. The continuity of the positive secular trends in BW and body size has slowed in recent decades in affluent industrialized societies[15]. One of the possible explanations is that environmental factors that positively affect prenatal growth are no longer improving and thus individuals have grown as much as they can[12]. Today, BW in humans may have achieved its evolutionary maximum by showing fairly similar BWs across populations living in an affluent setting[6,9]. Thus acceleration of prenatal growth as evidenced by a heavier BW at a given GA may not be as beneficial as it once was, because it may contribute to a male infants' vulnerability to preterm birth. That is, while large body size is generally accepted as a sign of good growth, bigger may not necessarily be better for prenatal growth in affluent societies.

A second finding in this study is the finding of a more congruent intrauterine growth pattern in infants with a physiological risk compared to those with a pathological risk. The former have a positive correlation coefficient between GA and BW, twice that of infants with a pathological risk. Even though prematurity or LBW involve a certain degree of risk, such risk does not necessarily mean a pathological course. Rather, premature or LBW infants are the babies who abruptly move to a new environment for which they are not yet ready. The relatively stable, regular and favorable intrauterine environment experienced by infants with a physiological risk can serve as a reservoir for future postnatal catch-up growth.

A third finding in this study is that of growth variation by nature of risk. Infants with pathological problems seem to experience a less compatible intrauterine and extrauterine growth by reaching only 42% – 67% of the positive correlation coefficients compared to those infants with a physiological risk. While pathological risk was diagnosed at the time of admission to the unit, some pathological risk may have an intrauterine origin, possibly initiated during the prenatal period.

Meanwhile, the less congruent prenatal and postnatal growth patterns of female infants with pathological risk compared to female infants with a physiological risk in our study call for more attention to the role of sex and the nature of the risk in early human growth and development. By comparing the correlation coefficients between GA and BW, and PA and WtC, the present study showed that female infants compare more favorably to male infants if they have a physiological risk. In contrast, male infants compare more favorably to female infants if they have a pathological risk. That is, female infants appear to keep their advantageous edge during the prenatal and early postnatal period only if their risks are physiological in nature. A female's biological reproductive function through time could play a role in this phenomenon in an evolutionary sense. However, a female's sex-linked advantage likely cannot be sustained with a pathological risk during prenatal and postnatal growth. Some pathological conditions may have a prenatal association and be severe enough such that female infants would not have an evolutionary advantage through the early postnatal period. Rather, when there is pathological disease, a heavier body weight in male infants may be beneficial during the acute postnatal growth phase.

This preliminary study illustrates early human growth variation by sex and nature of their risk factors in high-risk infants. Besides supporting previous findings on heavier BW in male infants, our study suggests that congruency in growth patterns at a very early period of development tends to vary by sex and the nature of the risk factors that infants had, rather than simply by BW itself. Such a finding opens a new area of investigation on the evolutionary function of sex and its influence on early human growth, especially with regard to prenatal risk factors. A longitudinal study is recommended to investigate the carryover effects of prenatal conditions into the later postnatal period as well as into early childhood as a consequence of sex differences and the nature of the risk factors in high-risk infants.

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REFERENCES

1. STEVENS TP, BLENNOW M, SOLL RF, Cochrane Database Syst. Rev., 3 (2004) CD003063. — 2. JORDAN IM, A. ROBERT A, FRANCART J, SANN L, PUTET G, Biol Neonate, 88 (2005) 57. — 3. ANANTH CV, JOSEPH KS, OYELESE Y, DEMISSIE K, VINTZILEOS AM, Obstet Gynecol, 105 (2005) 1084. — 4. SHIN SM, CHANG YP, LEE ES, LEE YA, SON DW, KIM MH, CHOI YR, J Korean Med Sci, 20 (2005) 182. — 5. MARKESTAD T, KAARESEN PI, A. RONNESTAD A, H. REIGSTAD H, K. LOSSIUS K, MEDBO S, ZANUSSI G, ENGELUND IE, SKJAERVEN R, IRGENS LM, Pediatrics, 115 (2005) 1289. — 6. BLAIR EM, Y. LIU Y, DE KLERK NH, LAWRENCE DM, BMC Pediatrics, 5 (2005) 13. — 7. JOHNSEN SL, WILSGAARD T, RASMUSSEN S, SOLLIEN R, KISERUD T, Eur J Obstet Gynecol Reprod Biol, 127 (2006) 172. — 8. ALY H, MOUSTAFA M, AMER H, HASSANEIN S, KEEVES C, PATEL K, Pediatr Res, 57 (2005) 708. — 9. ZHANG J, BOWES W, Obstet Gynecol, 86 (1995) 200. — 10. ZEITLIN J, SAUREL-CUBIZOLLES M, de MOUZON J, RIVERA L, ANCEL P, BLONDEL B, KAMINSKI M, Human

Reproduction, 17 (2002) 2762 — 11. WALDRON I, Soc Sci Med, 17 (1983) 321. — 12. INGEMARSSON I, BJOG, 110 (2003) 34. — 13. ZEITLIN J, ANCEL P, LARROQUE B, KAMINSKI B and the EPIPAGE group, Am J Obstet Gynecol, 190 (2004) 1322. — 14. HALL MH, CARR-HILL R, Br Med J Clin Res Ed, 285 (1982) 401. — 15. STINSON S, Growth variation: Biological and cultural factors. In: STINSON S, BOGIN B, HUSS-ASHMORE R, O'ROURKE D (Eds): Human Biology: an evolutionary and biocultural perspective (Wiley-LISS, New York, 2000).

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EVOLUCIJSKA PERSPEKTIVA NA RASOPODIJELU TEŽINE PREMA SPOLU I PRIRODI RIZIČNIH FAKTORA KOD VISOKORIZIČNE DOJENČADI

S A Ž E T A K

Provedeno je retrospektivno istraživanje u cilju rasvjetljavanja varijacije u rastu za vrijeme intrauterinog i postnatalnog perioda, a u odnosu na spol i prirodu visokorizičnih faktora (fizioloških i patoloških) kod 831 korejske dojenčadi u sveučilišnoj bolnici. Rezultati su pokazali kako dojenčad s fiziološkim rizikom pokazuje kongruentniji obrazac intrauterinog rasta u odnosu na dojenčad s patološkim rizikom. Kod određene gestacijske dobi ženska dojenčad pokazala je kompatibilniji intrauterini i postnatalni rast nego muška i to pogotovo kod fiziološkog rizika. Zaključno, veće neznači nužno i bolje za prenatalni rast kod ljudi. Konfluentniji intrauterini rast u dojenčadi s fiziološkim rizikom može biti koristan za rani postnatalni nadoknadni rast. Gledano s evolucijske perspektive, ženska dojenčad s fiziološkim rizikom mogu održati prednost pred muškom dojenčadi za vrijeme ranog postnatalnog perioda iako takva prednost nemora biti prisutna i kod patološkog stanja.