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**Optimal birth weight and term
mortality risk differ among different
ethnic groups in the U.S.**

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Optimal birth weight and term mortality risk differ among different ethnic groups in the U.S.

Directed by Professor Min Soo Park

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Doctor of Philosophy

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ABSTRACT

Optimal birth weight and term mortality risk differ among different ethnic groups in the U.S.

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Background: Among different U.S. ethnic groups, mortality at term may differ according to optimal birth weight at the least mortality and birth weight-specific mortality within the term birth weight distribution. We explored these two questions, examining births among five ethnic groups in the U.S.

Methods: Our study population was derived from U.S. birth data from 1995 to 2006, consisting of singleton live births at between 37 and 42 weeks from five parental groups: 1) non-Hispanic White (WW), 2) non-Hispanic Black (BB), 3) Hispanic (HH), 4) Korean, Japanese, and Chinese (KJC), and 5) Filipino, Vietnamese, and Asian Indian (FVA).

Results: The WW ethnic group had the highest mean birth weight (3,475 g), while FVA had lowest (3,228 g). KJC had the longest mean gestational age (39.2 wks), while FVA had the shortest mean gestational age (39.0 wks). Optimal birth weight was higher in WW (3,890 g) than in HH (3,745 g), KJC (3,666 g), or BB (3,650 g), and was the lowest in FVA (3,491 g). Compared to the WW group, neonatal mortality at term was lower in KJC (Odds Ratio(OR), 0.47; Confidence Interval(CI) 0.39, 0.55) and HH (OR, 0.96; CI 0.92, 0.99), higher in BB (OR, 1.27; CI 1.22, 1.32), and the same in FVA. Adjusting for parental sociodemographic characteristics other than parental

race/ethnicity had little effect on these differences in mean birth weight, optimal birth weight, and birth weight-specific mortality in term birth weight distribution.

Conclusions: In the U.S., mean birth weight, optimal birth weight at minimum mortality, and birth weight-specific mortality rates within the term birth weight range differ among different ethnic/racial groups. The optimal birth weight or term birth weight distribution of one ethnic group cannot be applied to other ethnic groups and should not be aimed for or insisted upon.

In conclusion, different guidelines for perinatal care and outcomes should likely be applied for different racial groups.

Key words : *birth weight, neonatal mortality, ethnicity, ethnic disparities*

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I. INTRODUCTION

In general, higher birth weight at term has been attributed to a favorable intrauterine environment and is believed be associated with better survival compared with lower birth weights. In fact, there are many reports that being small for gestational age (SGA) is associated with a high incidence of neonatal mortality and neurological developmental delay.¹ However, one exception is that large birth weight with respect to gestational age (LGA) associated with conditions such as maternal diabetes mellitus (DM) is associated with high mortality risk.² Perinatal obesity and maternal DM affect the fetus's tendency toward hyperglycemia. This activates increased fetal insulin levels, which then activates growth factors.³⁻⁵ Such a mechanism has a large birth weight, but the survival rate is rather poor Some reports have indicated that a birth weight of ≥ 4000 g increases the risks of obstetric and neonatal outcomes, while a birth weight of ≥ 4500 g significantly increases neonatal mortality, Apgar scores below 3 at 5 min, respiratory disease, and neurological disorders. Most journals consistently report a higher incidence of neonatal risk at birth weights greater than 5000 g.⁶⁻¹⁰

Mortality risk at term is a continuous function with an inverted J-pattern risk curve, with higher risk in lower birth weight, the minimal risk at the optimal birth weight, and then increasing risk with further increases in birth weight.¹¹⁻¹³

Neonatal mortality is effected by both birth weight and gestational age.^{14,15} Gestational age is a good predictor of birth weight and neonatal mortality. After gestational age is controlled for, birth weight is the single strongest predictor of infant survival.¹⁴ Susser's report¹⁶ similary showed that when gestational age and weight are analyzed simultaneously, birth weight accounts for 90% of the variance in perinatal mortality, whereas gestational age accounts for barely 5%.

Neonatal mortality is an important indicator of a nation's health and well-being and is often seen as a marker for social progress and human development.^{17,18} The strong correlation between birth weight and neonatal mortality is well documented that birth weight is often used as a proxy for neonatal mortality, and current U.S. policy to reduce neonatal mortality focuses on improving birth weight outcomes.¹⁹⁻²⁶ Some policies designed to reduce neonatal mortality work to reduce preterm delivery, blood stream infections, severe pregnancy complications associated with high blood pressure and hemorrhage, racial/ethnic and geographic disparities, and cesarean births among low-risk pregnant women, while others work to improve identification of and care for infants according to guideline set by the Centers for Disease Control and Prevention(CDC).

Birth weight may be affected by multiple factors, including maternal, age, birth weight, height, weight, weight gain, parity, education, smoking, nutrition, socioeconomic status, health conditions, race or ethnicity, and access to health care.^{27,28} Many research working in various scientific disciplines, including biology, epidemiology,²⁹⁻³⁴ clinical sciences,^{6-8,35-42} animal sciences,⁴³ and sociology,⁴⁴ have devoted substantial effort to providing explanations concerning birth weight and mortality. In 1951, Karn⁴⁵ demonstrated the relationship between birth weight and mortality in one family. Familial birth weight has been studied between siblings, mothers and children, and first cousins.⁴⁶⁻⁶¹ Sibling or maternal birth weight influences the relationship between neonatal birth weight and mortality.

Infant mortality increases when infants' birth weights are lower than those of their siblings or parents.⁵²⁻⁶² This finding demonstrates the correlation between birth

weight and family factors. Catov's results showed that birth weight decreased each year since 1997 and that infants born to African-American women were more strongly affected than were infants born to white women. This was likely due to an increasing accumulation of risk factors, such as hypertension and being overweight or obese during pregnancy, that are known to disproportionately affect African-American women. In other words, the difference in birth weight varies by maternal ethnicity, and maternal race has the strongest influence on birth weight.^{63- 65}

In summary, the first point is that birth weight is affected by ethnicity, which this study hopes to prove. The second point concerns the relationship between birth weight and neonatal mortality. Birth weight is the single strongest predictor for infant mortality and differs by ethnicity, and so we can hypothesize that neonatal mortality will also differ between racial groups. If the above hypothesis is supported, the question arises of whether different racial groups might have different optimal birth weights (term birth weight with minimal mortality) and whether the risk of neonatal mortality is similar at this optimal birth weight, as well as below and above this optimal birth weight. So we tried to analyze the following topics.

In this investigation, we wanted to reduce the impact of varying levels of health care, socioeconomic status, and environmental conditions on neonatal mortality among different ethnic groups in different geographical areas. Thus, we chose one large geographic population, U.S. births, assuming that the level of neonatal care and policies of public health would have been rather uniform among different ethnic groups within the U.S.

In this study, we tried to thoroughly examine the following three hypotheses :

1) the birth weight differs by ethnicity, 2) the risk of neonatal mortality over the term birth weight range also differs by ethnicity, and 3) the different ethnic groups have different optimal birth weights.

II. MATERIALS AND METHODS

1. Study Population

Data about our study population comes from the U.S. National Center for Health Statistics' (NCHS's) Birth Cohort Linked Birth/Infant Death Data (Fig.1) from 1995 to 2006 and includes only singleton live births with gestational ages between 37 and 42 weeks (n=28,876,197). We grouped the enrolled infants by parental ethnicity. We wanted to analyze Korean infants with respect to other ethnicities, but the number of Korean infants was very small compared with the number of non-Hispanic white/black and Hispanic infants. To account for this, we grouped North-Asian infants, including Korean, Japanese, Chinese infants, and South-Asian infants, including Filipino, Vietnamese, Asian Indian infants.

Infants were therefore born to one of five five parental groups with parents of the same ethnicity:

- A. Non-Hispanic White (WW) (n=19,018,822)
 - : newborn from non-Hispanic white mother and father
- B. Non-Hispanic Black (BB) (n=3,086,435)
 - : newborn from non-Hispanic black mother and father
- C. Hispanic (HH) (n=5,905,096)
 - : newborn from Hispanic mother and father
- D. Korean, Japanese, and Chinese (KJC) (n=357,926)
 - : newborn from Korean mother and father
 - : newborn from Japanese mother and father
 - : newborn from Chinese mother and father
- E. Filipino, Vietnamese, and Asian Indian (FVA) (n=507,918).
 - : newborn from Filipino mother and father
 - : newborn from Vietnamese mother and father
 - : newborn from Asian Indian mother and father

the NATIONAL BUREAU of ECONOMIC RESEARCH

Wednesday, March 8, 2017

Search the NBER site

Linked Birth/Infant Death Cohort Data

This page contains the **NBER** collection of Birth Cohort Linked Birth and Infant Death Data of the National Vital Statistics System of the National Center for Health Statistics. The microdata for each year of Birth/Infant Death Data Set consist of three separate data files. The denominator files (such as Den85.dat.Z) contain all births occurring in a given calendar year. The numerator files (such as Num85.dat.Z) to all infants born in that same calendar year for which the death certificate can be linked to a birth certificate in the denominator file. The unlinked files (such as Unl85.dat.Z) include death certificate information for infant deaths that cannot be linked to a birth in the corresponding birth file. The numerator/denominator set can be used to compute infant mortality rates.

Demographic data include variables such as date of birth, age and educational attainment of parents, marital status, live-birth order, race, sex, and geographic area. Health data include items such as birth gestation, prenatal care, attendant at birth, and Apgar score. Geographic data includes state, county, and city of mother's residence and state and county of the place of birth. City and county data are available for areas with a population of 250,000 or more. Check the documentation below for more detail.

Other birth data available are **Nativity Data, 1968-2006, Period Linked Birth/Infant Death Data, 1995-2002, as part of the Perinatal Mortality Data, and Matched Multiple Births Data, 1995-1998. *** NCHS produce Linked Birth/Infant Death from 1992-1994. After 1999, the Linked Birth/Infant Death data is included as part of the Perinatal Mortality Data set.**

SEER provides helpful U.S. Population data for 1969 on.

By using this data you signify your agreement with NCHS data use rules. Works referring to the datasets or codebooks should contain a citation to NCHS. Published material derived from this data should include the following text at the bottom of the table: "Source: National Center for Health Statistics (span of years used)"

The ".zip" files can be uncompressed with **winzip**. To check your ability to uncompress these files, download the small file **compress.zip**. These files give an example of how to read in .Z and .zip ASCII files without decompressing the files. To download files in Internet Explorer, right click on them and select "Save Target As...".

Updates and changes.

Data

	All U.S. ASCII Data Files	PDF Doc	Linked Deaths					Births					Unlinked Deaths					All U.S. Terr ASCII Data Files	Linked Deaths					Births					Unlinked Deaths										
			ASCII	SAS	Stata	CSV	Desc	ASCII	SAS	Stata	CSV	Desc	ASCII	SAS	Stata	CSV	Desc		ASCII	SAS	Stata	CSV	Desc	ASCII	SAS	Stata	CSV	Desc	ASCII	SAS	Stata	CSV	Desc						
2010	US.zip	pdf	num	num	num	num	den	den	den	den	den	unl	unl	unl	unl	PS.zip	num	num	num	num	den	den	den	den	den	den	den	den	den	den	den	den	unl	unl	unl	unl	unl		
2009	US.zip	pdf	num	num	num	num	den	den	den	den	den	unl	unl	unl	unl	PS.zip	num	num	num	num	den	den	den	den	den	den	den	den	den	den	den	den	den	den	den	unl	unl	unl	unl

Fig.1 Website of the U.S. National Center for Health Statistics (NCHS).

Once on the website, one can simply search for the Birth Cohort-Linked Birth and Infant Death Date. This data is publicly available and can be downloaded without registration.

2. Methods

A. Definition of neonatal mortality

: the number of deaths under 28 days of age per 1,000 live births.

$$\text{Neonatal mortality} = \frac{\text{The number of deaths}}{1,000 \text{ live births}} *$$

* Newborns under 28 days of age

B. Optimal birth weight

: the term birth weight associated with the least neonatal mortality.

C. Variables across the five groups

: We analyzed the following variables across the five groups

(A) Birth weight (g)

(B) Gestational age (wk)

(C) Sex

(D) Neonatal mortality

(E) Maternal age(yr)

(F) Education: Whether or not the duration of parental education exceeded
12 years.

(G) Marital status

(H) Smoking (tobacco use during pregnancy)

(I) Alcohol use

(J) Paternal age(yr)

(K) Adequacy of prenatal care

(L) Maternal medical risk factors (Table 1.)

Table 1. The Maternal Medical Risk Factors from U.S. National Center for Health Statistics*

Maternal medical risk factors	Yes or No
Anemia	
Cardiac disease	
Acute or chronic lung disease	
Diabetes	
Genital herpes	
Hydramnios/oligohydramnios	
Hemoglobinopathy	
Chronic hypertension	
Preeclampsia	
Eclampsia	
Incompetent cervix	
Having had a previous infant with a birthweight exceeding 4,000 g	
Previous preterm birth	
Renal disease	
Rh sensitization	
Uterine bleeding	
Other medical risk factors	

* The statistical data refers only to the incidence of maternal medical risk factors from U.S. National Center for Health Statistics

(M) Neonatal medical risk factors at birth (Table 2.)

Table 2. The Neonatal Medical Risk Factors from U.S. National Center for Health Statistics*

Neonatal medical risk factors	Yes or No
Febrile	
Meconium	
Premature rupture of membrane	
Abruptio placenta	
Placenta previa	
Other excessive bleeding	
Seizure during labor	
Precipitous labor	
Prolonged labor	
Dysfunctional labor	
Breech	
Cephalopelvic disproportion	
Cord prolapsed	
Anesthetic complications	
Fetal distress	
Other complications	

* The statistical data refers only to the incidence of neonatal medical risk factors from U.S. National Center for Health Statistics

(N) Neonatal chromosomal and congenital anomalies (Table 3.)

Table 3. The Neonatal Chromosomal and Congenital Anomalies from U.S. National Center for Health Statistics*

Neonatal chromosomal and congenital anomalies	Yes or No
Anecephalus	
Spina bifida/menigocele	
Hydrocephalus	
Microcephaly	
Other central nervous system anomalies	
Heart malformations	
Other circulatory/respiratory anomalies	
Rectal atresia/stenosis	
Trachea-esophageal fistula	
Omphalocele/gastroschisis	
Other gastrointestinal anomalies	
Malformed genitalia	
Renal agenesis	
Other urogenital anomalies	
Cleft lip/palate	
Polydactyly/syndactyly/adactyly	
Club foot	
Diaphragmatic hernia	
Other musculoskeletal anomalies	
Down syndrome	
Other chromosomal anomalies	
Other congenital anomalies	

* The statistical data refers only to the incidence of neonatal chromosomal and congenital anomalies from U.S. National Center for Health Statistics.

D. Primary outcomes

- (A) Birth weight differs by ethnicity
- (B) Neonatal mortality range also differs by ethnicity
- (C) Optimal birth weight
 - : with and without adjustment for the following variables
 - ① Maternal age
 - ② Marital status
 - ③ Education: Whether or not the duration of parental education exceeded 12 years
 - ④ Medical risks
 - ⑤ Prenatal care
 - ⑥ Alcohol use
 - ⑦ Smoking
 - ⑧ Paternal age

3. Statistical Methods

We used Stata (v.13)(Stata Corp LP, College station, TX, U.S.A.) for all statistical analysis.

We established five different racial/ethnic groups. The number of births in each group was very large, so we analyzed the difference in variables between races using a chi-squared test. In order to assess the relative risk of neonatal mortality by race, we calculated the odds ratio with 95% confidence intervals by univariable logistic regression, using non-Hispanic White as the reference group.

In addition, we analyzed the odds ratio before and after adjusting to the variables by multivariable logistic regression, using non-Hispanic White as the reference group. The adjusted variables were maternal age, education, parity, marital status, prenatal care, smoking, alcohol use, paternal age, maternal medical and obstetric risk factors, neonatal medical risk factors, and neonatal congenital anomalies.

To draw a graph of the relationship between birth weight and neonatal mortality based on actual values, we needed an equation for the estimated model by quadratic fit model generated using CurveExpert 1.4.

The raw data was divided by birth weight in 250 g intervals. Neonatal mortality for each interval was obtained and used as the basic data to estimate the equation best fit quadratic equation was derived from this data. The equation came out with standard error(SE) and correlation coefficient. We choose the final equation from among several drawing fits(Fig.2).

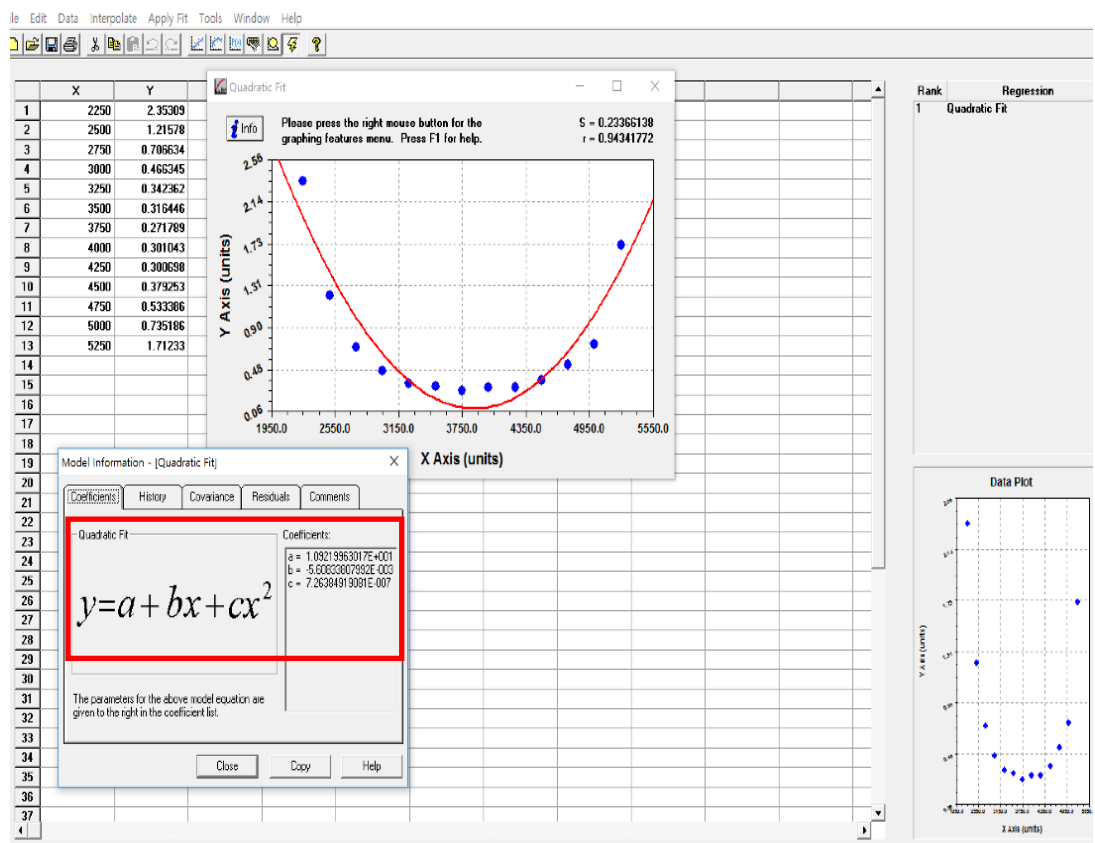


Fig. 2 CurveExpert 1.4. The best fit quadratic equation(red box)was derived from the data on neonatal mortality (y) and birth weight (x) using CurveExpert 1.4. After drawing the best quadratic fit curve, the equation came out with standard error(SE) and correlation coefficient. We choose the final equation from among several drawing fits.

Estimated neonatal mortality was able to be derived from the above equation. We drew the birth weight-specific mortality curve of the five racial groups under study and estimated their individual optimal birth weight with respect to minimal mortality by determining the x and y values of vertex by Excel (Fig.3).

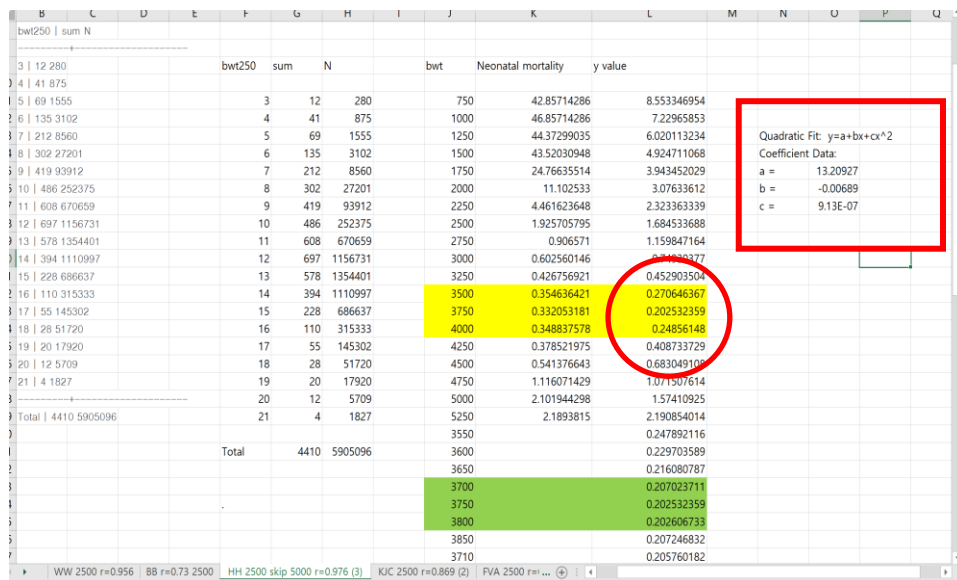


Fig.3 The Excel spreadsheet used to estimate mortality and optimal birth weight. The estimated minimal mortality (red circle) was derived by entering birth weight into the equation obtained above by CurveExpert 1.4. From this, we were able to determine the optimal birth weight.

The optimal birth weight for each group was obtained using the above methods (Fig.3). The optimal birth weight range was calculated from the SE from the equation. Based on the vertex(the estimated minimal mortality), the SE value was taken as the estimated minimal mortality ranges.

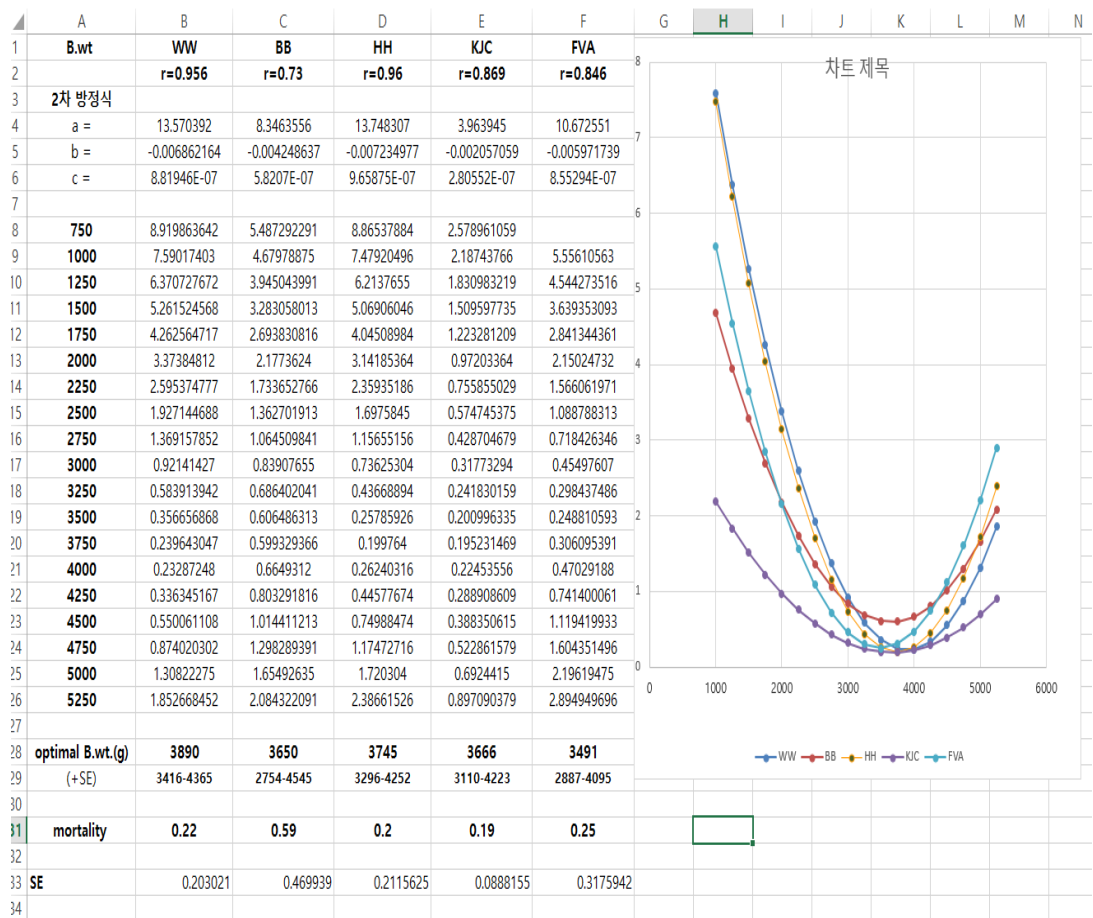


Fig. 4 The method for drawing the mortality graph. This shows that the mortality and optimal birth weight graph was derived from this process.

The estimated neonatal mortality could be taken by the quadratic fit equation from CurveExpert 1.4 (Fig.2). Entering the birth weight into the equation yielded the estimated neonatal mortality values for each racial/ethnic group. With this estimated neonatal mortality, we used this to draw the graph of the relationship between birth weight and neonatal mortality by Excel (Fig.4).

III. RESULTS

1. Term Singleton Live Births and Their Maternal Characteristics

Table 4 shows the study population, singleton term births, and maternal characteristics for each of the five ethnic groups. The WW ethnic group had the highest mean birth weight ($3,475 \pm 470$ g), while FVA group had the lowest ($3,228 \pm 431$ g). However, compared to WW group, FVA group were more likely to exhibit favorable maternal status markers traditionally associated with larger birth weight, including education, marital status, smoking, alcohol use, and maternal medical complications. FVA group also had the shortest mean gestational age (39.0 ± 1.1 wks), while KJC group had the longest mean gestational age (39.2 ± 1.1 wks). However, most maternal characteristics were similar between the FVA and KJC groups (Table 4). The education and married status were the highest in KJC group. The smoking and alcohol use also were the lowest in KJC group. But the maternal age was the oldest in KJC group. The longer the mother's education period is, the older the mother and the father are. So, the order of the education period and parent age was same in 5 groups.

It is interesting to note that the HH group had significant higher mean birth weight than the KJC and FVA groups, despite the HH group's significantly lower level of maternal education (< 12 years of 19% vs. 71% in KJC group and 70% in FVA group), lower marriage rate (64%, vs. 95% in KJC group and 93% in FVA group), higher rate of maternal smoking and alcohol use, and less adequate prenatal care. These observations suggest that when comparing term births among different racial or ethnic groups, maternal ethnicity or race is more influential on term birth weight than many other maternal sociodemographic and health factors.

The crude neonatal mortality rate of the term live births was the least in the KJC group, at 0.36 per 1,000 live births, and the worst in the BB group, at 0.98 per 1,000 live births (Table 4).

Table 4. Term Singleton Live Births and Their Maternal Characteristics in the U.S., 1995-2006

	WW	BB	HH	KJC	FVA
Number	19,018,822	3,086,435	5,905,096	357,926	507,918
BW (g)	3475±470	3280±472	3397±459	3318±418	3228±431
G.A. (wk)	39.1±1.2	39.0±1.2	39.1±1.2	39.2±1.1	39.0±1.1
Male (%)	51.2	50.9	50.8	51.8	51.4
Mortality(per 1000)	0.78	0.98	0.75	0.36	0.72
Maternal age (yr)	27.7±6.7	25.4±7.0	24.9±6.9	30.5±5.7	28.6±6.2
Education>12yr(%)	62	45	19	71	70
Married(%)	86	48	64	95	93
Smoking (%)	10.7	5.6	4.4	3.7	4.1
Alcohol use (%)	0.8	0.6	0.2	0.1	0.1
Paternal age (yr)	30.9±6.7	28.9±8.4	28.3±7.4	34.3±5.6	33.3±6.2
Prenatal care (%)	67.6	56.3	50.2	59.6	56.2
Maternal RF(%)	25.6	28.1	18.5	17.7	19.5
Neonatal RF(%)	5.5	4.8	3.9	3.7	3.7
Neonatal CA(%)	1.2	1.2	0.8	0.8	0.8

Abbreviations: **WW**, Non-Hispanic white mother and father; **BB**, Non-Hispanic black mother and father; **HH**, Hispanic mother and father; **KJC**, Korean mother and father, Japanese mother and father, or Chinese mother and father; **FVA**, Filipino mother and father, Vietnamese mother and father, or Asian Indian mother and father; **BW**, birth weight; **GA**, gestational age; **Prenatal care**, adequate prenatal care; **RF**, risk factors ; **CA**, congenital and chromosomal anomalies. P values from the one-way ANOVA and Chi-squared test for the differences among ethnic groups were all statistically significant (p <0.01).

This crude rate was also higher in the WW group (0.78 per 1,000) than in the KJC and FVA groups. HH group's mortality rate was lower (0.75 per 1,000) than WW group considering the lower level of maternal education (< 12 years of 19% vs. 62% in WW group), lower marriage rate (64%, vs. 86% in WW group), and less adequate prenatal care. Even though the lower level maternal education (< 12 years of 19% vs. 45% in BB group) and less adequate prenatal care (50.2%, vs. 56.3% in BB group) were lower than BB group, BB group's mortality rate was higher than HH group.

The WW group had a higher mean birth weight than the KJC and FVA groups and a higher average gestational age than the FVA group, showing that in term births, birth weight and/or gestational age themselves do not explain the differences in mortality across the different racial or ethnic groups. This again suggests that maternal race or ethnicity is a more powerful determining factor for neonatal survival than many other maternal sociodemographic and health factors.

2. The Risk of Neonatal Mortality Compared with the Non-Hispanic White Group

Table 5. The Risk of Neonatal Mortality Compared with the Non-Hispanic White Group, Singleton Live Births, 1995-2006

Races	Unadjusted OR	95% CI	Adjusted OR	95% CI
BB	1.27	1.22-1.32	1.17	1.12-1.22
HH	0.96	0.92-0.99	0.84	0.81-0.87
KJC	0.47	0.39-0.55	0.49	0.41-0.59
FVA	0.92	0.83-1.02	0.97	0.87-1.08

Abbreviations: **WW**, Non-Hispanic white mother and father; **BB**, Non-Hispanic black mother and father; **HH**, Hispanic mother and father; **KJC**, Korean mother and father, Japanese mother and father, or Chinese mother and father; **FVA**, Filipino mother and father, Vietnamese mother and father, or Asian Indian mother and father; **OR**, Odds ratio; **CI**, Confidence interval; **RF**, Risk factors. **Adjusted variables**: maternal age, education, parity, marital status, prenatal care, smoking, alcohol, paternal age, maternal medical and obstetric risk factors, neonatal medical risk factors, neonatal congenital anomalies

Compared to the WW group, the risk of neonatal mortality was lowest in the KJC group (unadjusted OR 0.47; CI 0.39-0.55) and also lower in the HH group (unadjusted OR 0.96; CI 0.92-0.99). However, neonatal mortality was the same in the FVA group compared with the WW group (unadjusted OR 0.92; CI 0.83-1.02), but higher in the BB group (unadjusted OR 1.27; CI 1.22-1.32) (Table 2). After adjusting for markers of maternal sociodemographic and health status, these mortality risks changed little across all study groups (Table 5), indicating that, among all maternal factors, maternal ethnicity or race was the predominant factor determining the rate of the survival of infants at term.

3. The Optimal Birth Weight with Minimum Neonatal Mortality

We then estimated the optimal birth weight at term associated with minimum neonatal mortality (Table 6).

Table 6. Optimal Birth Weight with Minimum Neonatal Mortality and the Minimum Neonatal Mortality Rate in Five Racial/Ethnic Groups, the U.S., 1995-2006

Racial/Ethnic Group	WW	BB	HH	KJC	FVA
Optimal BW(g)	3890	3650	3745	3666	3491
Estimated Minimum Mortality	0.22	0.59	0.20	0.19	0.25

Abbreviations: **WW**, Non-Hispanic white mother and father; **BB**, Non-Hispanic black mother and father; **HH**, Hispanic mother and father; **KJC**, Korean mother and father, Japanese mother and father, or Chinese mother and father; **FVA**, Filipino mother and father, Vietnamese mother and father, or Asian Indian mother and father

From the derived equation, we then obtained the optimal birth weight for each racial group and the mortality risk at this optimal birth weight (Table 6). This analysis yielded three notable observations. First, the optimal birth weight differed across ethnic groups. Second, in all individual ethnic groups, the optimal birth weight was greater than the mean birth weight. Finally, in all racial groups, lower mean birth weights were associated with lower optimal birth weights (Table 6).

We also calculated the optimal birth weight range from the standard error (SE). The minimal neonatal mortality value was derived from equation with SE. The confidence interval for neonatal mortality was obtained from SE (95% confidence interval = $\pm 1.95 \times \text{SE}$), but the optimal birthweight range could not be obtained below the minimum neonatal mortality value. This phenomenon is natural; even if the confidence interval of mortality was obtained, the optimal birthweight was distributed on both sides of the vertex. In addition, the optimal birth weight range using the 95% confidence interval was so broad that its value as optimal birth weight was not worthy. Optimal birth weight is a goal and an indicator, so it should have a narrow range. We therefore calculated the range using only SE. The optimal birth weight range was 3,416-4,365 g in WW group, 2,754-4,545 g in BB group, 3,296-4,223 g in HH group, 3,110-4,223 g in KJC group, and 2,887-4,095 g in FVA group.

In all groups, the pattern of mortality by birth weight followed a U-shaped curve fitting best to a quadratic equation (Fig. 5).

It is also interesting to note that the pattern of mortality risk below and above the optimal birth weight the (parabola of the u-shaped curve of mortality risk by birth weight) was not uniform across racial groups.

The KJC group had the fattest parabola, lesser increment of the mortality risk with decreasing or increasing birth weight from the optimal birth weight, compared with all other four groups. On the other hand, the WW group had a higher mortality risk than all other groups when birth weight was 3,000 g or less. On the other the WW racial group's mortality risk was lower at a birth weight of 3,750 g or more

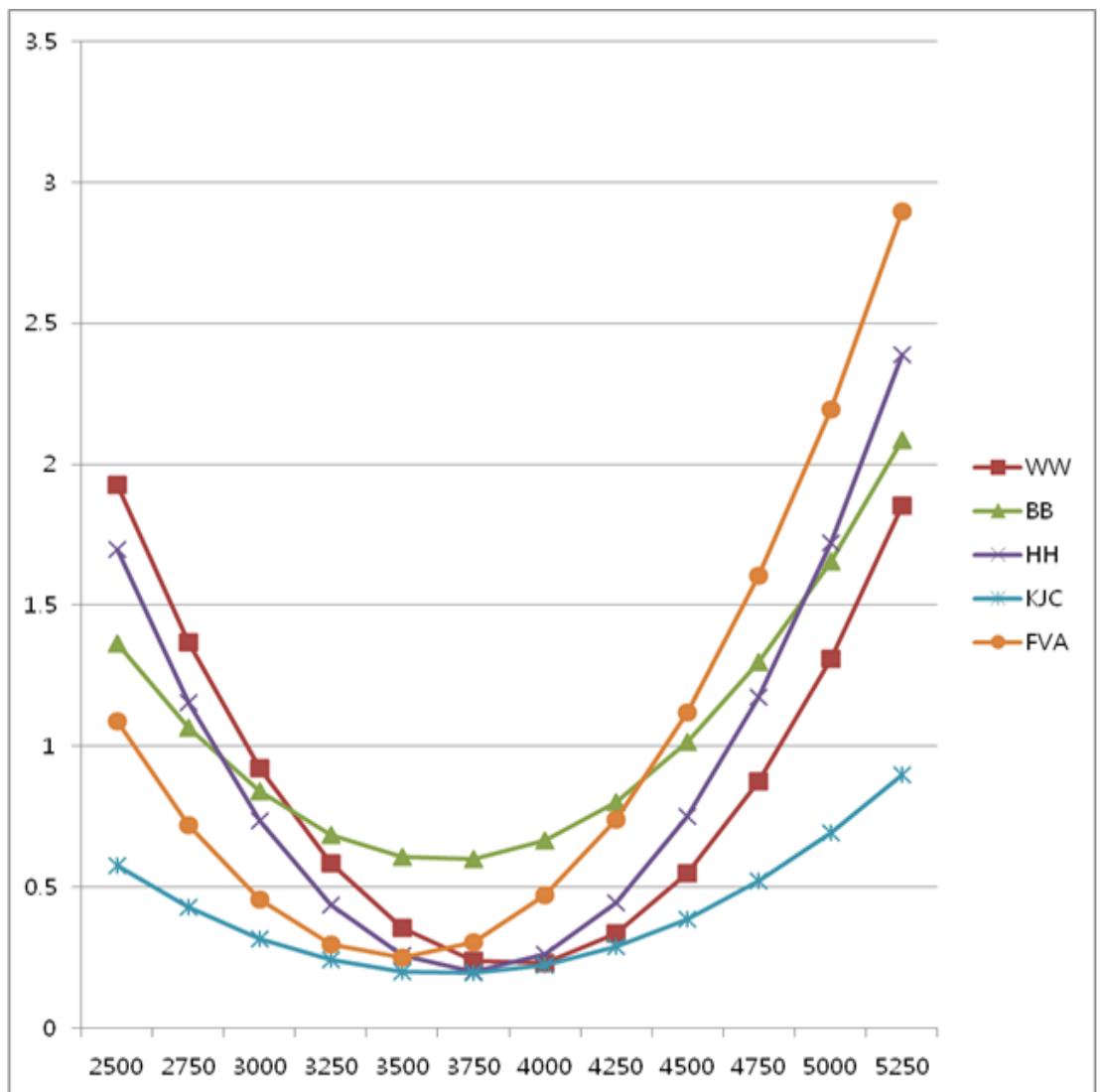


Fig. 5 Neonatal mortality rates (per 1,000 live births) at term in singleton live births among five racial groups in the U.S, 1995-2006.

Abbreviations: **WW**, Non-Hispanic white mother and father; **BB**, Non-Hispanic black mother and father; **HH**, Hispanic mother and father; **KJC**, Korean mother and father, Japanese mother and father, or Chinese mother and father; **FVA**, Filipino mother and father, Vietnamese mother and father, or Asian Indian mother and father.

compared with the BB, HH, and FVA groups. This observation indicates that mortality risk at term around the optimal birth weight differs among different racial and ethnic groups and does not show a uniform pattern.

IV. DISCUSSION

Neonatal mortality follows a reversed J curve with respect to birth weight. Mortality risk is very high in smaller birth weight groups, decreases exponentially with an increase in birth weight, reaches a minimum at a certain birth weight at term (optimal birth weight), and then rises again with further increases in birth weight.^{14,66} This pattern of neonatal mortality is universal among all racial or ethnic groups. Neonatal mortality is determined by two components: birth weight distribution, particularly with respect to smaller birth weight groups, and the birth weight-specific mortality rates of individual birth weight groups.^{67,68} Blacks in the U.S. has lower mortality rates in smaller birth weight groups than Whites until birth weight reaches around 2,500 g, after which mortality among Blacks is higher than among Whites. This higher overall mortality is primarily due to unfavorable birth weight distribution, that is, to the higher proportion of small birth weight infants among Blacks. Once the mortality curves are realigned to take into account the difference between Black and White birth weight distributions, the intersection of the mortality curves between them virtually disappears, but the far left-sided residual of the birth weight distribution in Blacks persists.²⁶ However, there is little information on subtle differences in term birth weight distribution and mortality risk among different racial/ethnic groups, so we worked to test our hypotheses using singleton newborns.

National vital statistics reports from the 2006 period showed that the neonatal mortality rate was 3.64 for non-Hispanic white, 8.95 for non-Hispanic blacks, and 3.18 for Asians/Pacific. Total neonatal mortality including all groups was 4.46 deaths per 1,000 live births, in 2006.⁶⁹ In our study, the neonatal mortality of non-

Hispanic Black (BB group) was highest (0.98 per 1,000 live births), while that of the KJC group was lowest (0.36 per 1,000 live births) among five groups (Table 4). The neonatal mortality of non-Hispanic white (WW group) was 0.78 per 1,000 live births. Neonatal mortality of our study is very low comparing with national vital statistics reports. This is because we eliminated the impact of small birth weight or preterm groups on racial difference in crude neonatal mortality by limiting our study population to term singleton births, exploring racial/ethnic differences in mean birth weight, mean gestational age, optimal birth weight with minimum mortality risk, and birth weight-specific mortality rates within the term birth weight range.

The racial proportion of U.S. birth data^{69,70} showed 77% of whites and 15% of blacks. But non-Hispanic white (WW group) is 65.9%, non-Hispanic black (BB group) is 10.7%, while Hispanic (HH group) make 20.4% of our study population. This difference of racial/ethnic proportions may be due to the fact that U.S. birth data is derived from maternal race, while our data focused on parents of the same race.

Mean gestational age at term among five groups was similar 39 wks. Meanwhile, mean birth weight was significantly different among the racial/ethnic groups. Before analysis, it was expected that infants in WW and BB group would be larger in size than infants in other groups (HH group, KJC group, and FVA group). However, the WW group had the highest mean birth weight, followed by HH group, Far Eastern Asian (KJC group), and BB group. Southeastern Asian (FVA group) group had the lowest mean birth weight. Mean birthweight of BB group was lower than expected, primarily due to higher proportion of low birth weight infants in this group.²⁶ Within individual groups, maternal sociodemographic and health status affected birth weight outcomes. However, as shown in the present and other previous studies, maternal factors did not suffice to explain racial differences in birth weight outcome.⁷¹⁻⁷⁵ The proportion of male was higher than female in all groups.

Neonatal mortality rate was the lowest in KJC group, in which maternal education level and the proportion of married couples were the highest. This study showed that maternal education level and marital status were associated with lower rate of neonatal mortality. Our study also demonstrated that higher maternal education level was associated with older parental age and longer gestational age at birth. Prenatal care was received in 59.6% of mother in KJC group, and the rate was higher than in BB, HH, and FVA groups. The rate of smoking (3.7%) and alcohol use (0.1%) which have adverse effect on fetus was the lowest in KJC group.

The WW group had surprisingly the highest rate of smoking (10.7%) and alcohol use (0.8%). The WW group surprisingly had the highest incidence of smoking (10.7%) and alcohol use (0.8%). We had expected the highest rate of prenatal care in WW group, whose maternal education level (education period longer than 12 years in 62% of mothers vs. 45% in BB group mothers) and socioeconomic status was generally high. Even with the highest rate of prenatal care (67.6%), neonatal mortality rate was higher (0.78 per 1,000 live birth) in WW group than in other groups except BB group (0.98 per 1,000 live birth). In both WW and BB groups, factors associated with neonatal mortality including the rate of smoking and alcohol use, the number of maternal risk factors and neonatal risk factors, and the rate of neonatal congenital anomalies were high. Thus neonatal mortality overall was high in these groups.

Maternal medical risk factors include anemia, cardiac disease, diabetes, preeclampsia, eclampsia, previous preterm birth, RH sensitization and so on. Neonatal chromosomal and congenital anomalies include anencephalus and other central nervous system anomalies, heart malformations and other circulatory/respiration anomalies, rectal atresia/stenosis, trachea-esophageal fistula, omphalocele/gastroschisis, renal agenesis, diaphragmatic hernia and other musculoskeletal anomalies, down syndrome and other chromosomal anomalies and so on. The rate of having maternal risk factors (28.1%) and neonatal congenital anomalies (1.2%) were the highest in BB group, followed by WW group.

The rate of having any neonatal medical risk factors such as fever, meconium aspiration syndrome, premature rupture of membrane, abruptio placenta and other excessive bleeding, seizure during labor, precipitous labor, prolonged labor, dysfunctional labor, breech, cephalopelvic disproportion, cord prolapse, anesthetic complications, fetal distress, and other complications were the highest in WW group(5.5%) and then BB group(4.8%). Table 4 demonstrates a trend toward higher neonatal mortality rate with higher rate of having maternal/neonatal risk factors, higher neonatal congenital anomalies, and higher rate of smoking and alcohol use. In KJC group, neonatal mortality rate was the lowest, with the lowest rate of having maternal medical risk factors (17.7%), neonatal medical risk factors (3.7%), and neonatal congenital anomalies (0.8%) among all groups.

National vital statistics reports showed that there were five leading causes of neonatal death.^{69,70} The first was congenital malformations, deformations, and chromosomal disorders, accounting for about 20% of total causes. The second was disorders related to short gestation and low birthweight, accounting for about 17% of total cases. Sudden death syndrome, newborns affected by maternal complications of pregnancy (about 6%), and respiratory distress of newborn (about 4%) are the next most common causes of neonatal mortality.^{69,70} Most racial groups other than the BB group are similar with respect to the most common causes of death. However, in the BB group, the most common cause of death was disorders related to short gestation and low birthweight. This is consistent with Wilcox,²⁶ who found that higher neonatal mortality among Blacks is due to an unfavorable birth weight distribution with a higher proportion of infants with low birth weight.

With respect to the mortality in the WW group, the odds ratio of neonatal mortality in the BB group was the highest of all five ethnic groups (unadjusted OR 1.27, 95% CI 1.22-1.32), event after adjusting (adjusted OR 1.17, 95% CI 1.12-1.22) for maternal age, education, parity, marital status, prenatal care, smoking, alcohol, paternal age, and maternal medical and obstetric risk factors (Table 5). This result is in alignment with Singh's report⁷⁶ that the risk of neonatal mortality in

Black neonates was 109% higher than White neonates in 2017. According to his report, the racial disparity in the neonatal mortality increased between 1916 and 2017, as white infants experienced faster declines (2.9% per year) in neonatal mortality than black infants (2.2% per year).⁷⁶ The rapid decline in mortality from neonatal anomalies, prematurity, low birth weight, and infections might have contributed to improved perinatal and neonatal medical care during 1960-2016.^{17,77} However, birth weight-specific infant mortality analyses show a continuing gap in access to high-quality neonatal healthcare across various social groups.⁷⁷ This provides further evidence that neonatal mortality is related to birth specific distribution in each racial/ethnic group, as in Wilcox.²⁶

In our study, optimal birth weight (where mortality risk is at a minimum) varied among the racial/ethnic groups (Table 6). Among the studied racial/ethnic groups, the rank order of optimal birth weight precisely followed that of mean birth weight. Optimal birth weight was the heaviest in the WW group and the lowest in the FVA group. Optimal birth weight in each group was about 8% to 18% higher than that group's mean term birthweight. These results confirm similar observations made by Graafmans and associates²⁸ in their study on birth outcomes in seven Western European countries: Finland, Sweden, Norway, Denmark, Scotland, the Netherlands, and Belgium. Optimal birth weight varied among these countries. It was higher than mean birth weight in all countries, and among these countries the rank order of optimal birth weight followed that of mean birth weight. Compared to the U.S., Western European countries may have a less heterogeneous racial composition, but among themselves it is possible that they differ in their socioeconomic environments and health care systems. We chose one large geographic population, tracking overall U.S. singleton births. Thus, we could easily conduct an analysis of multiple racial/ethnic groups, and we assumed that perinatal health care was more or less similar across different racial groups in the U.S.

In our study using U.S. births, we attempted to accentuate the racial effect but to reduce differences in health care systems. However, both studies shared similar

observations. The magnitude of difference in mean or modal birthweight was larger among the racial groups in the U.S., perhaps reflecting their diverse racial/ethnic composition, while mortality at the optimal birth weight varied more in the Western European countries than among different racial/ethnic groups in the U.S., possibly reflecting differences in respective countries' health care systems and socioeconomic environments in Western Europe.

Examining racial disparities in neonatal mortality in the U.S., Platt and associates⁷⁸ showed that optimal birth weight was higher and mortality risk at term was lower among Whites than among Blacks. When mortality risk was expressed by relative birth weight (a z-score relative to mean birthweight), they were able to observe consistently higher mortality risks in Blacks than in Whites at both below and above the zero z-score. These observations suggest that racial disparities in mortality at term could not be solely explained by racial disparities in either mean or optimal birth weight. It is determined by the racial disparity in two factors, 1) differences in mortality risks at optimal birth weight and, in addition, at below and above the optimal birth weight, and 2) term birth weight distribution around the optimal birth weight.

This concept of mortality at term is explored by our present study on five racial/ethnic groups in the U.S. Table 6 shows the optimal birth weight associated with estimated minimum mortality. However, it is difficult for pregnant women to reach the optimal birth weight accurately. The optimal birth weight range is needed to guide clinicians. Kato et al. reported that more than 80 percent of mortality could be reduced by attaining optimal GA and birth weight through appropriate perinatal care.⁷⁹ Thus, knowing the optimal birth weight for each race/ethnicity could contribute to reduction of neonatal mortality.

We therefore calculated the optimal birth weight range considering the SE value that could be clinically approached. We chose the range of estimated neonatal mortality by only adjusting SE value, because the 95% confidence interval ($1.96 \times SE$) was so broad and not worthy as the optimal birth weight range. As the SE

value was large, the optimal birth weight range widened. In particular, the BB group (2,754 g - 4,545 g) and FVA (2,887 g–4,095 g) had relatively large standard error and a wide range of optimal birth weights. The KJC group, having the smallest SE, showed a narrow optimal birth weight range (3,110 g–4,223 g). The optimal birth weight range of WW group (3,416 g–4,365 g) and HH group (3,296 g–4,252 g) as well as the 95% CI value and SE value were so broad that the numbers could not be suggested as optimal birth weight guidelines.

We also have tried using the R package (version 3.5.2) statistical program to analyze the optimal birth weight ranges. The 95% CI value was obtained by bootstrapping method. However, the values calculated were not practical. For example, the calculated optimal birthweight for KJP group was 4,510 g with a range of 4,201 g–4,726 g. In practice, a birthweight over 4,500 g is associated with increase in neonatal mortality rate in Korea.

Mortality risk at term by birth weight fits best to a quadratic curve (Fig.5). In this curve, mortality reaches the bottom (μ , the optimal birth weight) and increases more or less symmetrically to either side of the optimal birth weight (σ_p , variance of birth weight-specific mortality).¹⁰ The present study demonstrated that mortality risk both at optimal birth weight and at below and above the optimal birth weight differed among the five racial/ethnic groups under study. The lower the overall crude mortality rate, the lower was the mortality risk at optimal birth weight and the fatter was the parabola of the mortality risk curve. Among five racial groups, the KJC group had the lowest overall crude mortality rate with the lowest mortality risk at optimal birth weight and the fattest parabola of the mortality curve. This was followed by the HH group, the WW group, and the FVA group. The BB group had the highest overall crude mortality rate, with the highest mortality risk at optimal birth weight and the leanest parabola of the mortality curve.

Since this graph (Fig. 5) had a different birth weight distribution and birth weight-specific mortality rates for each race, as mentioned above,^{26,67,68} there was a slope difference to the parabolic curve. The BB group, with the highest neonatal

mortality, had high maternal smoking and alcohol use compared with other groups. In addition, maternal risk factors, neonatal risk factors, and congenital anomalies were the highest in the BB group among the five racial groups. On the other hand, the KJC group had the lowest neonatal mortality and the lowest maternal smoking rates, alcohol use rates, maternal risk factors, neonatal risk factors, and neonatal congenital anomalies. As a result, the risk factors specific to each race affected birth weight-specific mortality, which was shown by the slope of our parabolic mortality curve.

Even after we adjusted the variables for neonatal mortality, the racial disparity among the five ethnic groups had persisted. According to Singh's report⁷⁷, social inequality in neonatal mortality persists despite the decline in mortality over time. Ethnic, socioeconomic, and geographical disadvantages might account for such persistent disparities. Villar⁸⁰ also reported that differences reported in the scientific literature in fetal growth and newborn size were more likely due to environmental and socioeconomic differences than genetic variation, as it had been shown for infants and children.

In our study, we could not clearly explain whether neonatal mortality was affected by genetic or environmental factors alone. However, it was certain that there had been a dramatic decline in neonatal mortality in all ethnic groups over the past century.⁷⁷ Such dramatic decline was the result of public policies and government campaigns. The policies are not only aimed at improving access to and use of early and comprehensive prenatal care, reducing smoking and alcohol use during pregnancy and other medical risks such as anemia, cardiac disease, pregnancy obesity, gestational diabetes, and hypertension, but also at mitigating the effects of inequalities in socioeconomic conditions, the underlying determinants of health inequities in neonatal mortality.^{77,81}

Though we provided possible explanations whether neonatal mortality is more affected by genetic differences or environmental and socioeconomic differences, we could not clearly determine weighted effect of each factor, due to a few limitations

in our study. First of all, we considered multiple variables of socioeconomic status (SES) including education period, smoking, alcohol use, prenatal care, and marital status. However, we did not specify some details in variables that might have affected our results, such as duration, type, and frequency of smoking and alcohol use which were known to affect the birth weight and neonatal mortality. Moreover, time of first prenatal visit, total duration and frequency of prenatal care, and nutritional condition during pregnancy were not specified in our study.

Another limitation was that we could not suggest a clinically acceptable optimal birth weight range. The range of SE value was so broad, because the statistical quadratic equation did not reflect the actual birth weight-specific neonatal mortality. Such discordance might originate from two factors: widely scattered actual birth weight and small number of infants in KJC and FVA groups in comparison to WW, BB, or HH group. The number of infants in WW group was 53.1 times higher than that of KJC group.

The results of this study also have clinical implications relating to the measurement of intrauterine growth retardation and the definition of low birth weight, as birth weights below 2,500 g had a 4.28 times (95% CI : 1.23-14.92) greater risk than birth weights greater than 2,500 g with respect to neurologic morbidity.⁸² Differences in optimal birth weight among racial groups suggest that prenatal growth curves used for the detection of growth retardation and the definition of low birth weight need to be differentiated among populations.

Narrowing the gap in neonatal mortality in ethnic groups might require policies. The policies are not only aimed at improving access to and use of early and comprehensive prenatal care, reducing smoking and alcohol use during pregnancy and other medical risks such as anemia, cardiac disease, pregnancy obesity, gestational diabetes, and hypertension, but also at mitigating the effects of inequalities in socioeconomic conditions, the underlying determinants of health inequalities in neonatal mortality.^{77, 81}

Our results above present the different optimal birth weight, their range, and the

risk factors for each race that could affect neonatal mortality. Based on these results, we can conclude that policies to reduce neonatal mortality at term in the U.S. should be differentiated for various racial/ethnic groups.

V. CONCLUSION

Among different U.S. ethnic groups, mortality at term may differ according to birth weight. We tried to explore the relation of mortality and birth weight among five ethnic groups in the U.S. Our study population was derived from U.S. birth data from 1995 to 2006, consisting of singleton live births at between 37 and 42 weeks from five parental groups.

The present study shows that different racial/ethnic groups in the U.S. have varying mean birth weights and neonatal mortality rates at term gestation. Racial/ethnic differences in mean gestational age at term were minor, at less than a day. In addition, this study suggests that there is a different optimal birth weight for each racial/ethnic group. In all groups, optimal birth weight was about 8% to 18% higher than mean term birth weight. The magnitude of mortality risks both at optimal birth weight and at below and above the optimal birth weight were also different among racial/ethnic groups. Maternal sociodemographic and health factors failed to entirely explain the racial/ethnic differences in the following measures: mean birth weight, optimal birth weight, and mortality risks at optimal birth weight and at below and above the optimal birth weight.

Differences in optimal birth weight among racial groups suggest that prenatal growth curves used for the detection of growth retardation and the definition of low birth weight need to be differentiated among populations.

In the U.S., mean birth weight, optimal birth weight at minimum mortality, and birth weight-specific mortality rates within the term birth weight range differ between ethnic/racial groups. The optimal birth weight or term birth weight distribution of one ethnic group cannot be applied to another ethnic group and

should neither be aimed for nor insisted upon.

Our results above present the different optimal birth weight, their range, and the risk factors for each race that could affect neonatal mortality. Based on these results, we can conclude that policies to reduce neonatal mortality at term in the U.S. should be differentiated for various racial/ethnic groups.

In conclusion, different guidelines for perinatal care and outcomes should likely be applied for different racial groups.

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ABSTRACT(IN KOREAN)

미국 내 다른 인종 간의 최적 출생체중과 사망률 분석

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전 지 현

배경: 건강한 신생아를 평가하는데 가장 일반적인 기준이 임신나이와 출생체중이다. 임신나이는 동일하나, 출생체중은 다른 경우가 많다. 우리나라도 다문화가정이 10% 대로 증가하면서 동일한 임신나이에 불구하고 부모의 인종에 따라 신생아 출생체중이 차이를 경험하고 있다. 나라별로 보고된 신생아 출생체중 차이가 있는 것을 보고, 인종 간의 출생체중 차이가 있을 것이라고 생각하였다. 이에 인종에 따른 신생아 출생체중과 사망률이 유전적 요인 때문인지 후천적 환경적영향 때문인지 알아보고, 각 인종마다 사망률이 가장 낮은 최적의 신생아 출생체중을 알아보고자 하였다. 저자들은 같은 지리적 환경과 사회 환경을 동일시 한 상태에서 다른 인종 간의 차이를 보고자 다민족으로 구성된 미국 출생 자료를 분석하였다.

방법: 1995년부터 2006년까지 미국 출생자료에서 37주 이상, 42주 미만의 단일아 출생 중에서 생존환아(n=28,876,197)를 대상으로 하였다. 부모가 같은 인종일 경우만 같은 그룹으로 분류하여 5개 그룹으로 나누어 그 그룹에서 출생한 생존 단일아를 대상으로 분석하였다.

- 1) WW 군(n=19,018,822): 부모 양쪽의 인종이 히스패닉이 아닌 백인그룹,
- 2) BB 군(n=3,086,435): 부모 양쪽의 인종이 히스패닉이 아닌 흑인그룹,
- 3) HH 군(n=5,905,096): 부모 양쪽의 인종이 히스패닉인 그룹, 4) KJC 군(n=357,926): 양쪽 부모가 한국인(K), 일본인(J), 중국인(C) 인 그룹,

5) FVA 군($n=507,918$): 양쪽 부모가 필리핀인(F), 베트남인(V), 아시안 인디언인(A)인 그룹으로 나누었다. 각 군의 사망률과 특징, 사망률의 위험요인, 최적 출생체중, WW 군과 비교하였을 때 신생아 사망률의 위험도 (Odds Ratio: OR), 신생아 출생체중과 사망률과의 관계를 그래프로 비교 분석하였다.

결과: WW 군이 평균 출생체중 3,475 g으로 가장 컸고, FVA 군이 3,228 g으로 평균 출생체중이 가장 작았다. KJC 군은 평균 재태주령(39.2 주)이 가장 길었고, FVA 군의 재태주령(39.0 주)이 가장 짧았다.

산모의 교육정도가 12 년 이상 길수록 부모의 나이가 많았으며, 결혼한 부부의 비율이 높았다. 산모의 임신 중 흡연 및 음주 빈도는 두 요인이 같이 높거나 낮았으며, WW 군이 흡연 10.7%, 음주 0.8%로 5 그룹 중에 가장 높은 비율을 보였다. 신생아 사망률은 KJC 군이 0.36 (신생아 출생 1,000 명 당 사망자수)으로 가장 낮았고, BB 군이 0.98 (신생아 출생 1,000 명 당 사망자수)로 가장 높았다. WW 군과 비교하였을 때, 신생아 사망률의 위험도가 부모의 사회 경제적 요인들을 보정을 해도, KJC 군 (OR, 0.49; 95% CI 0.41-0.59)으로 가장 낮고, BB 군이 여전히 위험도가 1.17(95% CI 1.12-1.22)로 유의하게 높았다.

사망률이 가장 낮은 최적 출생체중은 WW 군이 3,890 g, HH 군이 3,745 g, KJC 군이 3,666 g, BB 군이 3,650 g, FVA 이 3,491 g 이었다. 각 군의 평균 출생체중, 최적출생체중, 출생체중별 사망률이 각 군 간에 유의한 차이가 있었다.

결론: 만삭아 단일아에서 평균 출생체중, 최적 출생체중, 출생체중 별 사망률이 인종 간 차이가 유의하게 있었다. 그러므로, 한 나라에서 국가 보건 지표 설정할 때 획일적으로 동일한 기준을 세우기 보다는 각 인종별, 사회 경제적 환경을 고려하여 정책 결정해야 한다고 사료된다.

핵심되는 말: 최적 출생체중, 출생체중, 신생아사망률, 인종적차이

PUBLICATION LIST

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