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Factors Associated with Birthweight: An Application of the Multiple Skew-Normal Regression

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Abstract: In the present research, we consider birthweight as a skew-normal random variable. It is possible the birthweight relative risk factors change under the skew-normal assumption. Our results confirm that the data for groups of babies, LBW (low birthweight), normal and combined groups ($p<0.001$) are skew. It is to be noted that the relevant factors associated with birthweight for two groups of babies, LBW and normal babies, are quite different and we should not analyze them together. We also found out that the relevant risk factors for birthweight are different in the normal and skew-normal models. Such that some relevant variables that are not significant in normal assumption become significant in skew-normal and versa as. Moreover the association magnitude of risk factors in the normal and skew-normal is different.

Key words: Birthweight, multiple regression, skew-normal, relevant factors

INTRODUCTION

Birthweight is one of the most important variables in the epidemiology (Wilcox, 2001). The association between birthweight and perinatal mortality has been confirmed repeatedly (Zadkarami, 2000) and to a lesser degree, with developmental problems in childhood (Kumar *et al*., 2004; Richards *et al*., 2002; Breslau *et al*., 2006) and the risk of various diseases in adulthood (Velde *et al*., 2004; Andersen and Osler, 2004; Hediger *et al*., 2002). In the last two decades, some of relative birthweight risk factors have been investigated e.g., smoking during pregnancy, multiple births, baby's gender, pregnancy problems, parity, mother's job, mother's age, maternal height and weight, gestation, low income and crowding.

It is reported repeatedly that smoking in pregnancy is a major determinant of low birthweight (Spencer, 2006; Meis *et al*., 1997; Silva *et al*., 2001; Hosain *et al*., 2006; Johansson *et al*., 2007) and range of adverse pregnancy outcome (Andres and Day, 2000; Spencer, 2006; Teramoto *et al*., 2006). Furthermore the median birthweighted of male is heavier than that of female (Kato, 2004; Teramoto *et al*., 2006) and the median birthweighted of twin was smaller than singleton (Suzuki *et al*., 2007). Moreover the median birthweighted of first-born twin heavier than that of the second-born and it is smaller in triplets (Kato, 2004). Neighborhood socioeconomic characteristics may associates with birthweight (Pearl *et al*., 2001) and crowding (number of persons per room) was strongly (positively) related to poor pregnancy outcome (Grove and Hughes, 1983).

The most fundamental measure of the progress of a pregnancy is gestational age. It has been showed that gestational age is strongly correlated with birthweight, with shorter gestation corresponding to lower birthweight (Duncan, 2002; Cavalli and Tanaka, 2000; Hosain *et al*., 2006) and teenager mothers have highest rate of LBW, Duncan (2002).

Maternal characteristics are an important group of variables in baby's weight. It has been showed that the birthweight was lower in the case of a low maternal pre-pregnancy weight and low parity

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(Teramoto *et al*., 2006; Johansson *et al*., 2007). It is found that maternal height, pre-pregnancy weight and hospitalization before the 37th week of gestation were significantly associated with LBW, (Cavalli and Tanaka, 2000). There are significant associations with LBW were found (in decreasing order of magnitude) for low maternal weight, short maternal height (Meis *et al*., 1997; Silva *et al*., 2001), late pregnancy bleeding, early pregnancy bleeding, primiparity and older maternal age (Meis *et al*., 1997).

It is well known that maternal occupation influences negatively the health of both baby and mother during pregnancy (Macfarlane and Mugford, 1984; Zadkarami, 2000). Occupational activities of mother were significantly associated (positively) with LBW (Cavalli and Tanaka, 2000; Gisselmann and Hemstrom, 2008). It is also reported that the birthweight was lower in the case of a low income (Teramoto *et al*., 2006) and increase in the risk of low birthweight was found in association with financial problems during the current pregnancy, controlling for differences in race, certain poor health habits, complications of pregnancy and several other factors (Binsacca *et al*., 1987).

It is also reported that LBW was associated with primiparity, public insurance and preterm (Silva *et al*., 2001). Moreover it is found that there is associations between LBW and mother's age, parity, weight gain and health problems during pregnancy (Hosain *et al*., 2006; Johansson *et al*., 2007). But no such association was seen for mother's height, economic status, educational level, body mass index, mid upper arm circumference and number of antenatal care visits (Hosain *et al*., 2006).

Important birthweight risk factors are to be found in the obstetric history of the mother. Birthweight is associated (negatively) with previous stillbirth, pre-eclampsia (Meis *et al*., 1997; Johansson *et al*., 2007), previous LBW (Silva *et al*., 2001) and a history of LBW (Cavalli and Tanaka, 2000).

Although magnitude and independence of some of these risk factors have been challenged, but we consider the most of the risk factors in our analysis. The variable BMI (mother's body mass index) is used to indicate the obesity of the mother because neither mother's height nor mother's weight does this on its own.

MATERIALS AND METHODS

Epidemiological analyses often regard birthweight as a normal random variable (Kumar *et al*., 2004; Velde *et al*., 2004; Johansson *et al*., 2007) but, there always exist some skewness in the real data (Hill and Dixon, 1982). So, practically the normal assumption may deviate form the reality. In such cases, we usually use transformations, for example Box-Cox method, for solving the problem of skewness and normality of the data. However the transformation may be created other problems such as heterogeneity of the variances or generally, it is possible that search for finding a suitable transformation to normalize the data can be fruitless. In such cases, the skew-normal distribution is a powerful method.

Azzalini (1985) introduced the skew-normal distribution which extends the class of normal distributions by the addition of a shape parameter. The skew-normal distribution has properties similar to the normal distribution but more flexible. It is convenient to analyze the unimodal data, specially skew data. Therefore the skew-normal regression is the powerful method in all situations. Simple skew-normal regression was introduced by Azzalini (1985). Regression models with skew normally distributed errors are widely used in empirical studies in various fields (Arellano-Valle *et al*., 2005; Azzalini, 2005; Lachos *et al*., 2007).

The 1958 British national cohort study, the National Child Development Survey (NCDS) includes 8960 girls and 9593 boys. The data was analyzed in various aspects (Power, 1992; Bartly *et al*., 1994;

Goldstein, 1997; Joffe and Li, 1994; Wildschut *et al*., 1997). The NCDS data is used to investigate the relevant factors associated with baby's weight. We managed to use 13518 individuals who have complete information on the relevant birthweight factors.

The aims of this study were to investigate firstly, the distribution of birthweight and the secondly identify the relevant factors with birthweight. Finally, what is the results when we assume a wrong distribution for birthweight.

Statistical Analyses

Multiple linear skew-normal regression is used to assess the relationship between birthweight and the relevant factors. However, the multiple linear normal regression is used to compare between normal and skew-normal regression fitting values.

The Analyses Carried out for Both Groups

LBW babies, normal birthweight babies and combined groups. The test of normality is done by the likelihood ratio test statistics (LR). The LR show that the baby's weight for the both groups of the LBW babies, normal birthweight babies and combined groups of babies are skew-normal distribution ($p<0.001$). Then the skew-normal regression is more convenient for the data.

All analyses were carried out with R statistical Package which is designed to analysis data in new areas of statistics. The discussion of the results carried out in two ways. First, we compare the results of the skew-normal regression and normal regression. Secondly, we find out the significant relevant factor for birthweight in the skew-normal regression model.

RESULTS

Combined Groups

The results in Table 1 indicate that the level eclampsia in the variable raised mother blood pressure is significant, at level 0.05, in the skew-normal but it is not significant in the normal. The level variable smoking in variable mother's smoking is associated positively with birthweight in the normal but it is associated negatively with birthweight in the skew-normal. The magnitude of association between birthweight and risk factors are different in the two models, normal and skew-normal.

The results in Table 1 also show that the variables BMI, parity and gestation are positively associated with birthweight. However, the variables No. of person per room, No. of past stillbirth and neonatal deaths, pervious premature livebirths, baby's sex, multiple birth, abnormality during pregnancy, raised mother blood pressure, mother's smoking and mother's job are negatively associated with birthweight in the skew-normal regression.

LBW Group

Table 2 shows that the variable No. of past stillbirth and neonatal deaths and some levels of the variables abnormality during pregnancy, raised mother blood pressure, mother's smoking and mother's job have different significant level in the skew-normal and the normal fitting models.

The results in Table 2 also show that the variable gestation is positively associated with birthweight. However, the variables baby's sex and some levels of variables multiple birth, abnormality during pregnancy, raised mother blood pressure, mother's smoking and mother's job are negatively associated with birthweight in the skew-normal.

Table 1: Result of fitting models to the combined data

Variables		Normal $\hat{\beta}$(SE)	Normal p-value	Skew-normal $\hat{\beta}$(SE)	Skew-normal p-value
Constant		-2.073 (0.091)	<0.001	-2.352 (0.094)	<0.001
BMI[1] × 10		0.154 (0.012)	<0.001	0.152 (0.012)	<0.001
No. per room × 10		-0.488 (0.107)	<0.001	-0.486 (0.107)	<0.001
Gestation × 10		0.183 (0.003)	<0.001	0.184 (0.003)	<0.001
Mother's age × 100		0.134 (0.087)	0.122	0.131 (0.086)	0.128
(No. of Past stillbirths and neonatal deaths)× 10		-0.767 (0.162)	<0.001	-0.783 (0.162)	<0.001
Parity × 10		0.524 (0.046)	<0.001	0.515 (0.046)	<0.001
Previous premature livebirths		-0.221 (0.021)	<0.001	-0.218 (0.022)	<0.001
Baby's sex	Male	-	-	-	-
	Female	-0.14 (0.008)	<0.001	-0.139 (0.008)	<0.001
Multiple birth	Single	-	-	-	-
	First twin	-0.492 (0.039)	<0.001	-0.484 (0.039)	<0.001
	Second twin	-0.625 (0.04)	<0.001	-0.619 (0.04)	<0.001
	Triplet	-1.172 (0.156)	<0.001	-1.167 (0.155)	<0.001
Abnormality during pregnancy	None	-	-	-	-
	APH[2]	-0.193 (0.073)	0.008	-0.193 (0.073)	0.008
	Placenta	-0.099 (0.059)	0.092	-0.104 (0.059)	0.076
	APH+bleeding	-0.109 (0.024)	<0.001	-0.110 (0.024)	<0.001
	Others	-0.035 (0.01)	<0.001	-0.036 (0.01)	<0.001
Raised (mother) blood pressure	None	-	-	-	-
	Hypertension	0.016 (0.031)	0.601	0.017 (0.031)	0.582
	EH toxaemia	-0.152 (0.042)	<0.001	-0.159 (0.042)	<0.001
	Toxaemia	-0.038 (0.012)	0.0015	-0.040 (0.012)	<0.001
	Unclassified toxaemia	-0.037 (0.012)	0.002	-0.040 (0.012)	<0.001
	Eclampsia	-0.336 (0.191)	0.077	-0.379 (0.192)	0.048
	Others	-0.028 (0.02)	0.160	-0.028 (0.02)	0.159
Mother's smoking	None	-	-	-	-
	Medium smoking	-0.111 (0.011)	<0.001	-0.112 (0.011)	<0.001
	Heavy smoking	-0.162 (0.013)	<0.001	-0.162 (0.013)	<0.001
	Variable smoking	0.107 (0.018)	<0.001	-0.109 (0.018)	<0.001
Mother's job	None	-	-	-	-
	Social C. I and II	-0.005 (0.024)	0.834	-0.004 (0.024)	0.956
	Nurse (unqualify)	-0.041 (0.051)	0.419	-0.044 (0.051)	0.995
	Clerks, typists,	-0.051 (0.013)	<0.001	-0.051 (0.013)	<0.001
	Other S. C. III	-0.051 (0.017)	0.0025	-0.053 (0.017)	0.001
	Social C. IV	-0.050 (0.015)	<0.001	-0.051 (0.015)	<0.001
	Social C. V	-0.093 (0.026)	<0.001	-0.092 (0.026)	<0.001
	Teachers	-0.010 (0.032)	0.749	-0.013 (0.032)	0.680
Past complication of pregnancy	None	-	-	-	-
	Toxaemia	-0.003 (0.017)	0.869	-0.004(0.017)	0.810
	Antepartum haemorrhage	0.037 (0.033)	0.256	0.039 (0.032)	0.238
	Ceasearean	0.012 (0.048)	0.800	0.012 (0.048)	0.802
	Others	-0.041 (0.051)	0.431	-0.047 (0.051)	0.368

[1]BMI (Body mass index = (Mother's weight (kg)/(square of mother's height(m))), [2]APH: Accidental antepartum haemorrhage, [3]EH: Essential hypertension

Normal Birthweight Group

Table 3 shows that some levels of the variables abnormality during pregnancy, raised mother blood pressure and mother's job have different significant level in the skew-normal and normal fitting models.

The results in Table 3 also show that the variables BMI, gestation and parity are positively associated with birthweight. However, the variables No. of person per room, previous premature livebirths, baby's sex and some levels of variables multiple birth, abnormality during pregnancy, raised mother blood pressure, mother's smoking and mother's job are negatively associated with birthweight in the skew-normal.

Table 2: Results of fitting model to the LBW babies

Variables		Normal		Skew-normal	
		$\hat{\beta}$(SE)	p-value	$\hat{\beta}$(SE)	p-value
Constant		-0.929 (0.162)	<0.001	-0.511 (0.216)	0.017
BMI × 10		-0.037 (0.034)	0.279	0.032 (0.031)	0.292
No. per room × 10		0.113 (0.268)	0.674	0.347 (0.239)	0.147
Gestation × 10		0.125 (0.005)	<0.001	0.113 (0.008)	<0.001
Mother's age × 100		-0.071 (0.233)	0.760	0.061 (0.200)	0.764
(No. of Past stillbirths and neonatal deaths) × 10		-0.751 (0.338)	0.026	-0.531 (0.303)	0.080
Parity × 10		0. 147 (0.131)	0.263	0.173 (0.116)	0.126
Previous premature livebirths		0.006 (0.019)	0.806	-0.001 (0.017)	0.688
Baby's sex	Male	-	-	-	-
	Female	-0.067 (0.022)	0.002	-0.063 (0.019)	<0.001
Multiple birth	Single	-	-	-	-
	First twin	-0.007 (0.044)	0.88	-0.016 (0.038)	0.689
	Second twin	-0.043 (0.04)	0.28	-0.023 (0.035)	0.409
	Triplet	-0.545 (0.127)	<0.001	-0.600 (0.116)	<0.001
Abnormality during pregnancy	None	-	-	-	-
	APH	0.072 (0.09)	0.424	0.068 (0.077)	0.373
	Placenta	-0.188 (0.098)	0.054	-0.184 (0.083)	0.026
	APH+bleeding	-0.179 (0.045)	<0.001	-0.145 (0.038)	<0.001
	Others	-0.081 (0.029)	0.006	-0.029 (0.026)	0.258
Raised (mother) blood pressure	None	-	-	-	-
	Hypertension	-0.195 (0.137)	0.155	-0.202 (0.117)	0.095
	EH toxaemia	-0.201 (0.075)	0.007	-0.188 (0.066)	0.005
	Toxaemia	-0.107 (0.032)	<0.001	-0.093 (0.028)	<0.001
	Unclassified toxaemia	-0.098 (0.030)	0.001	-0.067 (0.027)	0.014
	Eclampsia	-0.481 (0.192)	0.012	-0.489 (0.195)	0.012
	Others	0.058 (0.046)	0.208	-0.053 (0.040)	0.186
Mother's smoking	None	-	-	-	-
	Medium smoking	-0.070 (0.028)	0.016	-0.064 (0.025)	0.010
	Heavy smoking	-0.038 (0.030)	0.218	-0.053 (0.026)	0.022
	Variable smoking	-0.018 (0.047)	0.700	-0.012 (0.042)	0.779
Mother's job	None	-	-	-	-
	Social C. I and II	0.028 (0.065)	0.666	0.005 (0.057)	0.918
	Nurse (unqualify)	0.077 (0.105)	0.465	-0.064 (0.099)	0.515
	Clerks, typists,	-	0.023	-0.051 (0.029)	0.078
	Other S. C. III	0.076 (0.033)	0.186	-0.036 (0.038)	0.326
	Social C. IV	-0.060 (0.046)	0.480	0.024 (0.036)	0.308
	Social C. V	-0.028 (0.040)	0.010	-0.135 (0.050)	0.007
	Teachers	-0.154 (0.060)	0.591	-0.056 (0.095)	0.555
		0.060 (0.112)			
Past complication of pregnancy	None	-	-	-	-
	Toxaemia	0.065 (0.046)	0.156	0.036 (0.040)	0.373
	Antepartum haemorrhage	0.106 (0.083)	0.203	0.075 (0.079)	0.312
	Ceasearean	-0.092 (0.148)	0.537	-0.093 (0.127)	0.465
	Others	0.010 (0.115)	0.926	-0.004 (0.108)	0.968

Table 3: Result of fitting models to the normal babies

Variables	Normal		Skew-normal	
	$\hat{\beta}$(SE)	p-value	$\hat{\beta}$(SE)	p-value
Constant	0.347 (0.104)	<0.001	0.186 (0.097)	0.056
BMI × 10	0.147 (0.011)	<0.001	0.130 (0.011)	<0.001
No. per room × 10	-0.388 (0.100)	<0.001	-0.363 (0.095)	<0.001
Gestation × 10	0.104 (0.003)	<0.001	0.096 (0.003)	<0.001
Mother's age × 100	0.099 (0.080)	0.218	0.054 (0.075)	0.478
(No. of Past stillbirths and neonatal deaths) × 10	-0.199 (0.157)	0.205	-0.245 (0.149)	0.099
Parity × 10	0.592 (0.043)	<0.001	0.539 (0.040)	<0.001
Previous premature livebirths	-0.189 (0.011)	<0.001	-0.178 (0.011)	<0.001

Table 3: Continued

Variables		Normal $\hat{\beta}$(SE)	Normal p-value	Skew-normal $\hat{\beta}$(SE)	Skew-normal p-value
Baby's sex	Male	-	-	-	-
	Female	-0.129 (0.007)	<0.001	-0.117 (0.007)	<0.001
Multiple birth	Single	-	-	-	-
	First twin	-0.429 (0.046)	<0.001	-0.389 (0.044)	<0.001
	Second twin	-0.513 (0.053)	<0.001	-0.452 (0.050)	<0.001
	Triplet	-0.861 (0.296)	<0.001	-0.745 (0.275)	<0.001
Abnormality during pregnancy	None	-	-	-	-
	APH	-0.078 (0.08)	0.331	-0.072 (0.076)	0.342
	Placenta	-0.037 (0.059)	0.532	-0.034 (0.056)	0.542
	APH+bleeding	-0.054 (0.023)	0.018	-0.045 (0.022)	0.038
	Others	-0.028 (0.009)	0.002	-0.028 (0.009)	0.001
Raised (mother) blood pressure	None	-	-	-	-
	Hypertension	0.003 (0.028)	0.907	-0.003 (0.027)	0.912
	EH toxaemia	-0.044 (0.041)	0.278	-0.054 (0.039)	0.159
	Toxaemia	-0.005 (0.011)	0.662	-0.010 (0.011)	0.368
	Unclassified toxaemia	0.001 (0.001)	0.946	-0.008 (0.011)	0.452
	Eclampsia	0.461 (0.242)	0.056	-0.456 (0.223)	0.040
	Others	-0.014 (0.019)	0.450	-0.015 (0.018)	0.400
Mother's smoking	None	-	-	-	-
	Medium smoke	-0.088 (0.01)	<0.001	-0.086 (0.010)	<0.001
	Heavy smoking	-0.140 (0.012)	<0.001	-0.129 (0.011)	<0.001
	Variable smoke	-0.087 (0.016)	<0.001	-0.089 (0.015)	<0.001
Mother's job	None	-	-	-	-
	Social C. I and II	0.002 (0.023)	0.939	-0.001 (0.021)	0.966
	Nurse (unqualify)	-0.009 (0.049)	0.851	-0.016 (0.046)	0.712
	Clerks, typists,	-0.030 (0.012)	0.013	-0.024 (0.011)	0.032
	Other S. C. III	-0.040 (0.016)	0.010	-0.048 (0.015)	<0.001
	Social C. IV	-0.040 (0.013)	0.003	-0.040 (0.013)	0.003
	Social C. V	-0.066 (0.024)	0.007	-0.054 (0.023)	0.019
	Teachers	0.012 (0.029)	0.666	-0.024 (0.028)	0.394
Past complication of pregnancy	None	-	-	-	-
	Toxaemia	0.008 (0.016)	0.641	0.004 (0.015)	0.771
	Antepartum hemorrhage	0.040 (0.031)	0.196	0.042 (0.029)	0.128
	Ceasearean	-0.012 (0.044)	0.789	-0.013 (0.042)	0.787
	Others	-0.027 (0.049)	0.573	-0.072 (0.046)	0.112

DISCUSSION

The object of this study was, firstly, to investigate the relevant factor associated with baby's weight. The importance of birthweight for the foetal outcome has been known for many years and a birthweight less than 2,500 g has been classified internationally as that of a LBW. This type of baby in the group of high risk babies has been the subject of great interest (Breslau *et al*., 2006; Meis *et al*., 1997; Silva *et al*., 2001; Hosain *et al*., 2006; Binsacca *et al*., 1987). We found that we can not be satisfied with analyzing the combined groups (low-birthweight and normal), because two groups have different relevant factors associated with birthweight. Secondly, we consider the effect of wrong distribution assumption for birthweight. We observed that using normal regression instead skew-normal regression would have led to misleading results.

Now, we investigate the results of multiple skew-normal regression. The present study has been showed that the variables BMI, gestation and parity are positively associated with birthweight but the variables number of persons per room and previous premature livebirths are associated negatively with birthweight in the group of normal babies. However, in LBW group, only variable gestation was associated positively with birthweight. It has been showed that gestational age is strongly correlated with birthweight, with shorter gestation corresponding to lower birthweight (Duncan, 2002; Cavalli and Tanaka, 2000; Hosain *et al*., 2006).

Some studies have addressed different relationship between birthweight and maternal age (Duncan, 2002; Meis *et al*., 1997), but our results confirmed that mother's age does not statistical associated with birthweight in both groups LBW and normal babies.

We observed that female babies have lower birthweight as our review was indicated (Spencer, 2006; Meis *et al*., 1997; Silva *et al*., 2001; Hosain *et al*., 2006). Multiple birth babies have weight less than single babies (Kato, 2004). Present results showed that twins and triplet babies have lower weight in the normal group of babies. But only triple babies has lower weight in LBW babies.

We found that the variables abnormality during pregnancy and raised mother blood pressure have negatively associated with birthweight but the association patterns with birthweight and those variables in the two groups normal and LBW are different.

Systematic reviews have been supported that mother's smoking during pregnancy have negatively associated with birthweight (Meis *et al*., 1997; Silva *et al*., 2001; Spencer, 2006; Hosain *et al*., 2006; Johansson *et al*., 2007). We observed that all level of variable mother's smoking are negatively associated with birthweight in normal group of babies. But the medium and heavy smoking levels are the only levels that are negatively associated with birthweight in LBW group.

Occupational activities of mother were significantly associated (positively) with LBW (Cavalli and Tanaka, 2000; Gisselmann and Hemstrom, 2008). We observed that mothers who worked in the low social classes (social classes III, IV and V) have been expected to have smaller baby than mothers that have no job during pregnancy in LBW group. But only mothers who worked in the low social class V have been associated (negatively) with birthweight in normal group babies.

The results in Table 2 and 3 also confirmed that mother who suffered from difficulty during pregnancy has high risk of the low birthweight infant.

Birthweight is associated (negatively) with previous stillbirth, pre-eclampsia (Meis *et al*., 1997; Nault, 1997), previous LBW (Silva *et al*., 2001) and a history of LBW (Cavalli and Tanaka, 2000). However we found that the statistical associated between birthweight and variable past complication of pregnancy is not significant for two groups, normal and LBW, of babies.

Finally, the present study indicated that the distribution of birthweight is skew-normal and consider birthweight as normal distribution results in misleading outcomes.

CONCLUSIONS

In group of LBW babies, the variable gestation is positively associated with birthweight. However, the variables female baby and some levels of variables multiple birth, abnormality during pregnancy, raised mother blood pressure, mother's smoking and mother's job are negatively associated with birthweight.

In group of the normal babies, the variables BMI, gestation and parity are positively associated with birthweight. However, the variables No. of person per room, previous premature livebirths, female baby and some levels of variables multiple birth, abnormality during pregnancy, raised mother blood pressure, mother's smoking and mother's job are negatively associated with birthweight. Then two groups have different relevant factors associated with birthweight and we can not be satisfied with analyzing the combined groups (LBW and normal).

We found that the birthweight for groups of babies, LBW and normal is the skew-normal variable. Wrong distribution assumption would have led to misleading results.

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