Birth Weight and Future Life-span in Finnish Triplets

Johan Fellman[1,2*] and Aldur W. Eriksson[1]

[1]*Folkhälsan Institute of Genetics, Department of Genetic Epidemiology, Helsinki, Finland.*
[2]*Hanken School of Economics, Helsinki, Finland.*

Authors' contributions

This work was carried out in collaboration between all authors. Author AWE designed the study, Author JF performed the statistical analysis. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Aims: Interest in the distribution of birth weight arises because of the association between birth weight and the future health of the child. A common statistical result is that the birth weight distribution differs slightly from the Gaussian distribution.
Methods: A standard attempt has been done to split the distribution into two components, a predominant Gaussian distribution and an unspecified "residual" distribution.
Results: We considered birth weight data among triplets born in Finland in 1905-1959 and compare the birth weight among stillborn and live-born triplets. The stillbirth rates are 119.1 per 1000 births for males, 124.6 for females and 121.8 for all. The sex differences are not significant. The still birth rate for the period 1905-1930 was 119.5 and for the period 1931-1959, 124.2. We identified a strong association between birth weight of the triplets and their survival. The weight distribution for male triplets is described well by the Gaussian curve, while for females a slight deviation from the Gaussian distribution is discernible.

*Corresponding author: Email: fellman@hanken.fi;

1. INTRODUCTION

Scientists have studied the distribution of birth weight comprehensively. This interest in birth weight arises from its central role in the future health of the child. Recorded birth weight data show skewing from normal distribution [1,2,3]. The birth weight and length of triplets have been studied in several studies [4,5,6,7]. Forsén analyzed the association between fetal growth and future physical condition [8]. He also presented a thorough review of the literature, including the Barker hypothesis, which proposes that phenotypic changes occur in fetal life [9].

We studied triplets born in Finland in 1905-1959. The total number of triplets in our family study was 1944. Of these, 931 had a registered birth weight. The initial study of the triplets did not pay special attention on the birth weight. Consequently, one can suppose that the missing birth weights are randomly missing and have no marked biasing influence on the results. We present the basic characteristics of all of the triplets and group them into stillborn and live-born categories. The live-born group is further grouped according to future life-span. More detailed studies are based on the sub-set of triplets with known birth weights.

2. MATERIALS AND METHODS

2.1 Material

The triplet family data comprise triplets born in Finland in 1905–1959. During this period 723 triplet sets were registered in the official Finnish birth records. Using genealogical studies, sibships of the triplets and of their mothers and fathers were collected. The genealogical investigations, which were initiated by Miettinen [10] and continued by our group, resulted in sufficiently complete birth information for 642 sibships of triplets containing 649 triplet sets. Consequently, almost 90% of all registered triplet sets were included in our studies. Among the 1944 triplets included in our study there were five with unknown life-span and two with unknown sex. The 1942 triplets of known sex comprise 984 males and 958 females. To examine presumptive temporal effects, we split the period into two sub-periods of 1905-1930 and 1931-1959.

Birth weight data were registered for 931 triplets consisting of 473 males, 456 females and two infants of unknown sex. For this subgroup, we present more detailed analyses. One can suppose that the missing values are randomly missing and have no marked biasing influence on the results. This assumption is supported by the similar life-span distributions in the Table 1 presented and discussed. The other variables had isolated missing values, explaining the slightly different totals in the tables. We present the basic characteristics of all of the triplets and group them into stillborn and live-born categories. The live-born group is further grouped according to future life-span. More detailed studies are based on the sub-set of triplets with known birth weights. For a presentation of the family data set [10].

We compared birth weight among stillborn and live-born triplets and examined the association between birth weight and the survival of the children. The data are grouped in life-span classes and the codes used are given in Table 1. Data for infants belonging to the first two classes, stillborn and death on the same day, are precise. For the remaining infants, some were classified such that their life-span was at least of a given age. Such infants are categorized according to the highest threshold registered. In fact, some of them may have attained higher ages. The infants with exact life-spans are included here in the

corresponding survival class. Consequently, the survival of the triplets may to some extent be underestimated.

2.2 Statistical Methods

Recently, Lindsay and Liu [11] discussed how to test normal distribution by QQ (quantile-quantile) plots. In a two-dimensional co-ordinate system, the quantiles (Q_W) of the observed variable (birth weight in this study) are distributed over the horizontal axis, and the quantiles (Q_N) of the normal variable, when the parameters of the normal distribution are estimated from the sample, are distributed over the vertical axis. If the scatter points (Q_W, Q_N) are linearly distributed, then the observed variable can be assumed to be normal. Lindsay and Liu used the Kolmogorov-Smirnov goodness-of-fit test to test the normality assumption. The test statistic is the greatest standardized absolute vertical distance, $K = \sqrt{n} \sup_x |F_n(x) - F(x)|$,

where $F_n(x)$ is the observed distribution and $F(x)$ the hypothetical normal distribution, the parameters of which are estimated from the sample. The critical values for K are $K_{0.05} = 1.358$, $K_{0.01} = 1.628$ and $K_{0.001} = 1.949$ for $P = 0.05$, $P = 0.01$ and $P = 0.001$, respectively. Lindsay and Liu stressed that for large samples the normality is rejected, although the QQ plot appears quite linear in the centre [11]. This finding is attributed to the Kolmogorov-Smirnov test measuring absolute deviations, therefore being more sensitive to discrepancies in the centre than in the tails. In order to simultaneously estimate the effects of sex, condition at birth and year of birth we perform a linear regression model.

3. RESULTS

The 1942 Finnish triplet births of known sex comprised 984 males and 958 females (sex ratio = 102.7 males per 100 females).For these triplets, Miettinen registered *inter alia* the conditions live- or stillborn [10]. We obtained the stillbirth rate (SBR) 119.1 per 1000 births for males, 124.6 for females and 121.8 for all (cf. Table 1). For live-born infants, Miettinen also registered infant death data. Miettinen was unable to follow the future of all triplets because her study ended with her thesis. We added to Miettinen´s data by following the future of the children. We were especially, interested in obtaining accurate information on the proportion of the triplets reaching adult age i.e. at least 15 years.

The distribution of triplets according to sex and survival of infants is presented in Table 1. In this table, we introduce the survival codes used later in Fig. 1. Among the 1937 triplets of known sex and life-span class, the proportion obtaining ages of over 15 years was 358.5 per 1000 for males, 391.6 for females and 374.8 for all.

Table 1. Distribution of triplets of known sex in different survival groups. Codes of the classes of life-span data used in the text are introduced here. No sex differences were found ($\chi^2(6) = 5.81, P > 0.05$ **)**

Life-span	Codes		Males	Females	Total
Stillborn	A0	N	117	119	236
		per mille	119.1	124.6	121.8
Live-born; dead the same day	A1	N	132	102	234
		per mille	134.4	106.8	120.8
Life-span 1 day - 6 days	A2	N	116	99	215
		per mille	118.1	103.6	111.0
Life-span 7 - 27 days	A3	N	98	100	198
		per mille	99.8	104.7	102.2
Life-span 4 - 52 weeks	A4	N	121	120	241
		per mille	123.2	125.7	124.4
Life-span 1 year - 14 years	A5	N	46	41	87
		per mille	46.8	42.9	44.9
Life-span $\geq$ 15 years	A6	N	352	374	726
		per mille	358.5	391.6	374.8
Total		N	982	955	1937
		per mille	1000	1000	1000

The data were also grouped according to year of birth. We obtained the SBR 119.5 for the period 1905-1930 and 124.2 for the period 1931-1959. These results are given in Fig. 1. We observed that the proportion of triplets obtaining 15 years of age is markedly higher for the later sub-period being 491 vs. 262 per mille for the first one. In Table 2 we present the perinatal, neonatal and infant mortality among triplets born 1905-1930 and 1931-1959.
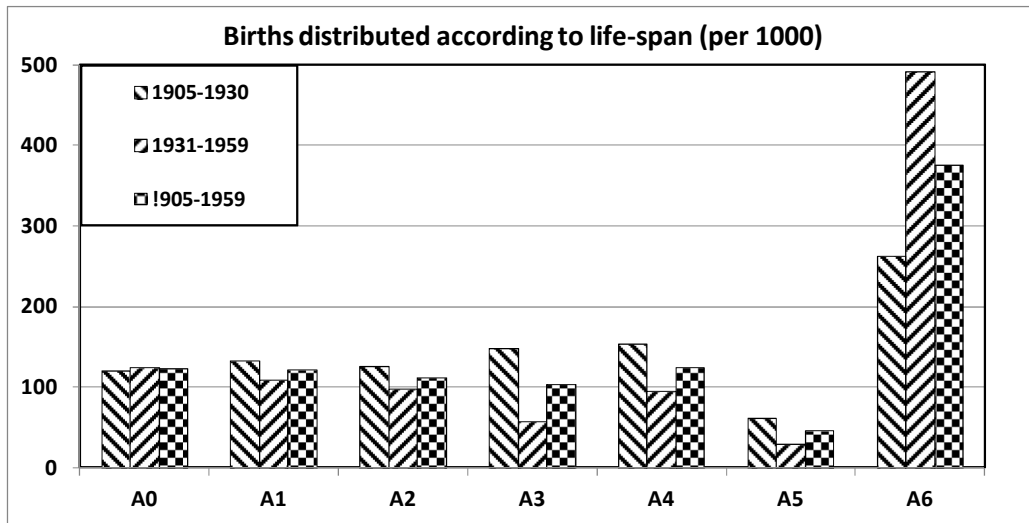

Fig. 1. Distribution of all triplets born in 1905-1930 and in 1931-1959 according to life-span. The survival codes are given in Table 1. Temporal differences were statistical significant ($\chi^2(6) = 137.6, P < 0.001$ **)**

Table 2. Perinatal, neonatal and infant mortality in the triplets according to the periods 1905-1930 and 1931-1959

Mortality		1905-30	1931-59	Total
Stillborn – life-span 27days	N	513	370	883
Total	N	979	958	1937
Perinatal mortality	per mille	524.0	386.2	455.9
Live-born - life-span 27 days	N	396	251	647
Live born	N	862	839	1701
Neonatal mortality	per mille	459.4	299.2	380.4
Life-born - 52 weeks	N	546	342	888
Live born	N	862	839	1701
Infant mortality	per mille	633.4	407.6	522.0

Table 3. Mean birth weight among 929 Finnish triplets born in 1905-1959 grouped according to sex and future survival. Significant weight differences are noted, $F(6,456) = 53.0, \quad P < 0.001$ for males, $F(6,461) = 47.9, \quad P < 0.001$ for females and $F(6,924) = 93.3, \quad P < 0.001$ for all

Life-span	Males			Females			Total		
	n	mean	SD	N	mean	SD	n	mean	SD
Stillborn	42	1284.6	896.7	55	1210.6	754.4	97	1242.7	815.4
Live-born; dead same day	57	1376.4	494.4	41	1162.8	466.1	98	1287.0	491.8
Life-span: 1 day - 6 days	43	1507.8	424.6	40	1373.8	466.0	83	1443.2	447.4
Life-span: 7 - 27 days	28	1983.6	519.4	25	1709.2	465.0	53	1854.2	508.9
Life-span: 4 - 52 weeks	45	2228.2	444.3	42	1912.9	483.9	87	2086.3	491.0
Life-span: 1 - 14 years	23	2184.4	539.0	18	2404.4	624.9	41	2281.0	581.4
Life-span $\geq$ 15 years	225	2266.8	491.4	247	2109.0	444.2	472	2242.4	487.3
Total	463	2033.9	692.9	468	1830.1	640.1	931	1931.4	674.3

Birth weight data were registered for 463 male and 468 female triplets (sex ratio = 98.9). The SBR was 90.7 per 1000 for males, 117.5 for females and 104.2 for all. A simultaneous estimation of the effects of sex, condition at birth (live- and stillborn) and year of birth can be obtained with the regression model $Weight = \alpha + \beta_S\,S + \beta_C\,C + \beta_Y\,Y + \varepsilon$, where *S* is sex (0 for males, 1 for females), *C* is the birth condition (0 for liveborn, 1 for stillborn) and *Y* is the year of birth (calendar year minus 1905). The estimated model is is $Weight = 1725.4 - 197.2\,S - 736.0\,C - 10.1\,Y$, and all parameter estimates are statistically significant. The *SE*s are $SE_{\beta_S} = 40.6$, $SE_{\beta_C} = 66.5$, $SE_{\beta_Y} = 2.0$ and the adjusted coefficient of determination is $\bar{R}^2 = 0.160$. According to this model, male triplets are on average about *197* grams heavier than female triplets, liveborn infants are about *736* grams heavier than stillborn infants and the mean weight decreases with 10 grams per year.

In Table 3 one observes that the mean birth weight is lowest among stillborn infants, increasing with increasing future life-span.

In Fig. 2, we present the birth weight distributions among male triplets (mean = 2033.9 grams) and female triplets (mean = 1830.1 grams). For the male triplets (n = 463), the normal distribution can be accepted ($K = 1.184, P > 0.05$). However, for the female triplets (n = 468) there is a slight discrepancy from the normal distribution ($K = 1.447, P < 0.05$). The QQ plots included in Fig. 2 confirm these differences between male and female triplets. When all the weight data are considered, the distribution differs from the normal distribution. The number of subjects is 931, the mean is 1931.4 and the the test result is $K = 1.362, P < 0.05$.
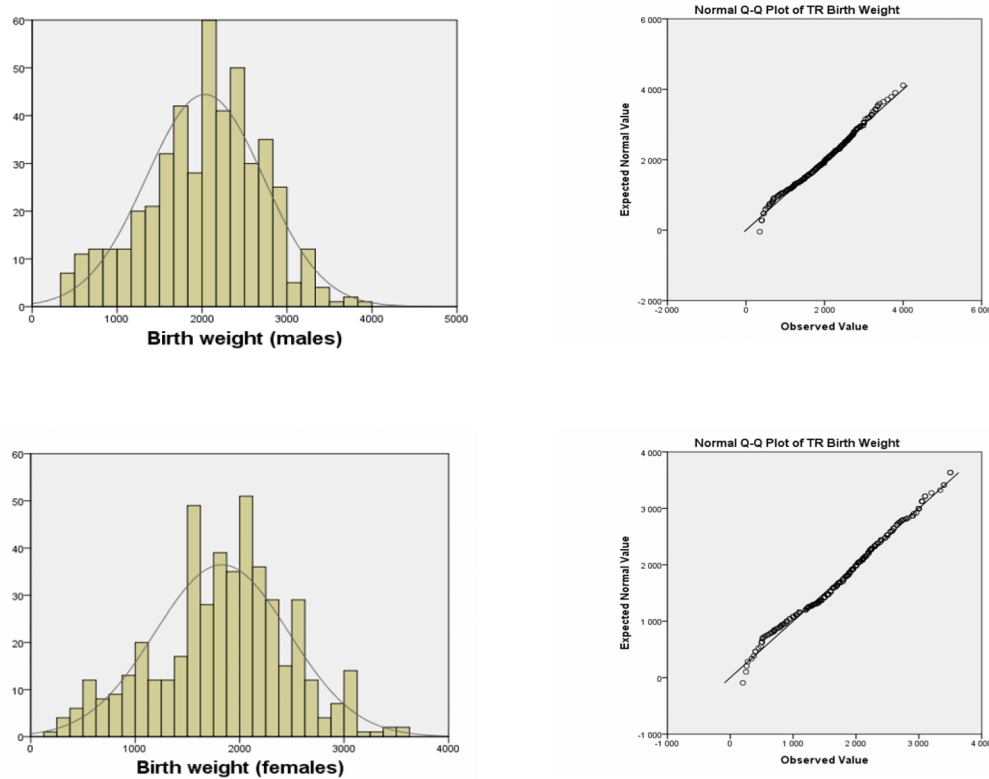

Fig. 2. Distribution of birth weight among male and female triplets. For the subgroup male triplets (n = 463), the normal distribution can be accepted ($K = 1.184, P > 0.05$), but for the female triplets (n = 468) there is a slight discrepancy from the normal distribution ($K = 1.447, P < 0.05$). The QQ plots confirm these findings

4. DISCUSSION

According to Fellman and Eriksson [12], the SBR among triplets in Sweden in 1901-1967 was 104.5. Later, Fellman and Eriksson [13] reported for triplets born in Sweden in 1869-1967 an SBR of 113.5 for males, 116.3 for females and 115.2 for all. Observing that the

Swedish SBR shows a marked decrease, as late as during the 1930s, our Finnish data are in good agreement with the Swedish findings.

Scientists have studied the distribution of birth weight extensively. Recorded birth weight data showed skewing from the normal distribution. Erkkola et al. compared perinatal and neonatal mortality rates in different birth weight groups [1]. They stated that while the neonatal mortality rates are indicators of general obstetrical and neonatal care, rates in different weight groups are extremely important for obstetricians. Wilcox and Russell discussed the frequency distribution of the birth weight and identified a predominant Gaussian distribution and a residual distribution, and the complete distribution could be characterized by three parameters: the mean and standard deviation of the Gaussian component and the proportions of births in the residual distribution [2].Umbach and Wilcox assumed that the distribution of birth weight is a Gaussian distribution contaminated within the tails by an unspecified "residual" distribution [3]. They proposed a technique for measuring certain features for birth weight distributions useful for epidemiologists; the mean and variance of the predominant distribution, the proportion of births in the high- and low-birth weight residual distributions and the boundary support for these residual distributions. In his thesis, Forsén analyzed the association between fetal growth and future physical condition [8]. He also presented a thorough review of the literature, including the Barker hypothesis that proposes that phenotypic changes occur in fetal life [9].

Newman et al. analyzed birth weight among live born triplets [4]. They found the mean weights 1959 grams among males, 1790 among females and 1864 among all. Their results concerning sex differences are supported by our results. Recently, Yokoyama et al. analyzed the relative height at birth and the growth trend among Japanese triplets [5]. They noted that the triplets are small at birth and that their height deficit compared with the general population of Japan remained between 2% and 5% until 12 years of age. Later Yokoyama et al. analyzed the weight growth among Japanese triplets [6]. Lamb et al. discussed the effect of chorionicity and zygosity on the birth weight of triplets [7]. Given that birth weight of triplets is, on average, lower than that of singletons and twins, they examined if chorionicity and zygosity influence birth weight. Their central conclusion was that having shared a chorion, rather than being monozygotic, increases the risk of low birth weight.

5. CONCLUSION

The main results concerning our birth weight project are presented in Fellman and Eriksson [14,15] and are based on a data set consisting of almost 19000 births with known birth weights and the data were collected by us for our studies. When we noted birth weights registered in the Miettinen data we were interested in additional comparative investigations. A marked association between birth weight and future life-span of the triplets is presented in Table 3. Our study of Finnish triplets indicates that for male triplets the normal distribution can be accepted, while for female triplets there is a slight discrepancy from the normal distribution. Fellman and Eriksson [14] noted that for singletons the grouping according to sex did not result in normal distributions, but for twins this grouping yielded acceptable normal distributions.

Box [16] stated that since all models are wrong the scientist cannot obtain a "correct" one by excessive elaboration. Furthermore, he stressed that, for example, in nature there is never a normal distribution or a straight line, yet with normal and linear assumptions, known to be false, one can often derive results that approximate those observed in the real world.

Consequently, following [16] and [11], the distributions of birth weight for triplets found in our studies can be considered acceptable approximations of normal distributions.

CONSENT

Consent section is not applicable for this article.

ETHICAL APPROVAL

Ethical approval section is not applicable for this article.

ACKNOWLEDGEMENTS

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1.   Erkkola R, Kero P, Seppälä A, Grönroos M, Rauramo L. Monitoring perinatal mortality by birth weight specific mortality rates. International Journal of Gynecology & Obstetrics. 1982;30:231-235.
2.   Wilcox AJ, Russell IT. Birthweight and perinatal mortality: I. On the frequency distribution of birthweight. International Journal of Epidemiology. 1983;12(3):314-318.
3.   Umbach DM, Wilcox AJ. A technique for measuring epidemiologically useful features of birthweight distributions. Statistics in Medicine. 1996;15:1333-1348.
4.   Newman RB, Jones JS, Miller MC. Influence of clinical variables on triplet birth weight. Acta Geneticae Medicae et Gemellologiae. 1991;40:173-179.
5.   Yokoyama Y, Sugimoto M, Pitkäniemi J, Kaprio J, Silventoinen K. Height growth of triplets from birth to 12 years of age in Japan. Twin Research and Human Genetics. 2011;14:468-475.
6.   Yokoyama Y, Pitkäniemi J, Kaprio J, Silventoinen K. Weight growth of triplet infants from birth to twelve years of age. Twin Research and Human Genetics. 2012;15:672-679.
7.   Lamb DJ, Vink JM, Middeldorp CM, van Beijsterveldt CEM, Haak MC, Overbeek LIH, Boomsma DI. (). Effects of chorionicity and zygosity on triplet birth weight. Twin Research and Human Genetics. 2012;15:149-157
8.   Forsén T. Early growth and adult disease.Programming of coronary heart disease, Type 2 diabetes and hypertension by fetal and childhood growth.(Thesis). University of Helsinki; 2000.
9.   Barker DJ. Mothers, Babies, and Health in Later Life. 2nd Ed. Edinburgh: Churchill and Livingstone. 1998;ix+217 pp.
10.   Miettinen M. On triplets and quadruplets in Finland.Thesis, Turku. Acta Paediatrica Scandinavica, 43, Supplement 97; 1954.

11. Lindsay B, Liu J. Model assessment tools for a model false world. Statistical Science. 2009;*24*:303-318.
12. Fellman J, Eriksson AW. Stillbirth rates in singletons, twins and triplets in Sweden, 1869 to 2001. Twin Research and Human Genetics. 2006a;9:260-265.
13. Fellman J, Eriksson AW. Stillbirths in multiple births: Test of independence. Twin Research and Human Genetics. 2006b;9:677-684.
14. Fellman J, Eriksson AW. Birth weight among single and multiple births on Åland Islands (Finland).Twin Research and Human Genetics. 2013a;16(3):739-742.
15. Fellman J, Eriksson AW. Factors influencing the birth weight on Åland Islands (Finland). JP Journal of Biostatistics. 2013b;9(2)2013:105-118.
16. Box GEP. Science and statistics. Journal of the American Statistical Association. 1976;71:573-580.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid=358&id=12&aid=2694