

An experimental design to obtain nonlinear model for fitting intrauterine growth curve using Microsoft Excel spread sheet program

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Abstract

Background: Mathematical modeling and establishing the relationship between gestational age and biometric parameter is an important method of studying biological growth pattern of foetuses. The alterations seen in growth mechanism are the basis of further investigation for foetal growth aberrations.

Materials and Methods: In a hypothetical setting, we have studied Bipariteal Diameter (BPD) at various gestational ages from 12 to 40 weeks of gestation at 6 different intervals. The scatter diagram of these values has been plotted using Microsoft Excel 2010 suite.

Results: Using the trend-line future of excel graph, we have determined the relationship between gestational age and biometric parameter in question and extrapolated this equation to obtain the BPD values from 12th to 40th week of gestation at 1 week interval.

Discussion: Ideally whenever one has to construct intrauterine growth pattern using ultrasound, the patient is supposed to report for scan at specific interval. However in clinical practice, it is difficult to give scheduled appointment because of several constraints. Hence establishing a method which is independent of these factors to obtain growth curves has been possible using spread sheet program.

Conclusion: A detailed methodology to obtain intrauterine growth curve has been explained. This will further facilitate research to establish customised growth curve to serve for the local population.

Keywords: Growth curve, Trend line, Microsoft Excel, Intrauterine growth restriction

1. Introduction

Foetal growth in humans like any other biological developmental process is complex and requires complete understanding of growth kinetics [1]. The intrauterine foetal growth in length and weight is characterized by a rapid increase in number of cells in first and early second trimester (phase of hyperplasia), a combination of hyperplasia and hypertrophy in the late second trimester and finally rapid increase in the weight in the third trimester (phase of hypertrophy) [2].

Studying intrauterine growth curves is of utmost importance because it gives insight into fetal development and nutritional status [3]. The information obtained helps practicing obstetrician to greatly improve antenatal foetal surveillance and develop strategic plans for appropriate management of the pregnancy. Any deviation from the growth curve in the upper range makes the suspicion of foetal macrosomia and guides the treating doctor to investigate the pregnancy for conditions such as gestational diabetes or overt diabetes, and on the other hand, lower range values indicate foetal growth restriction which has serious effect on the foetal survival and it prompts not only further evaluation to rule out causes of intrauterine growth restriction and also design a plan for optimal timing for delivery.

The developing countries like India rely more on western growth charts to assess intrauterine foetal growth. But the foetal growth is influenced by several factors such as race, country of origin, religion, altitude, access to basic nutrition etc. The growth potential of Indian babies is definitely lesser

than that of western counter part and decision based on comparison with their growth curves is likely to end up on erroneous decisions [4, 5]. It is sad to state that a country with more than a billion population has not developed growth standards for its population. The literature search indicated that there are only few studies done in India in this regard. The largest study has come from Mediscan center, Chennai, but the information is available to those who have purchased Sonocare software. In additions, the data derived are based upon findings of cross-sectional cohort which may not truly depict the actual growth trajectory of the foetus. The longitudinal study in this aspect greatly and actually determines the intrauterine status, but it requires patients to be recruited at correct time interval (say every two weeks) and at exact gestational age range (for example, 12, 16, 20,...40 completed weeks), which in actual practice may be difficult to call the patient at exact dates, keeping in mind nonworking days, non-availability of appointments etc. These difficulties can be overcome, if we have a method to consider fractional weeks. The present treatise focusses upon generating a growth curves in such scenarios. In fact, only few ultrasound scan reports spanned throughout the pregnancy are generally enough to extrapolate interval values by generating a computerised trend lines for these data, finding an equation which describes the relationship between biometric parameter in question and gestational age and finding intermediate values at desired gestational age ranges. The growth pattern such obtained will form a basis for establishing reference standards for local population. In

addition, customised growth curves can be developed for different maternal BMI (body mass index), religion, education, economic status and even fetal gender.

2. Materials and Methods

Most of the antenatal centers now are equipped with ultrasound machine and it has become a custom to perform fetal biometry between 11 to 14 weeks (for aneuploidy screening), 18 to 20 weeks for detecting foetal anomaly and there after assessing interval growth at 4 to 8 week intervals. It is now usual to find pregnant women who have been assessed at least 5 to 6 times by ultrasound scan. The biometric parameters usually include BPD (Bi Parietal Diameter), HC (Head Circumference), AC (Abdominal Circumference), FL (Femur length) and EFW (Estimated Foetal Weight). In the following section, we will describe a method to fit a growth curve for BPD in a hypothetical patient using features available in Microsoft Excel Spreadsheet program (bundled with Office 2010 suite).

3. Results

Ms X underwent biometric measurement at 12 weeks 3 days, 20 weeks, 23 weeks 6 days, 29 weeks 6 days, 33 weeks 6 days and 37 weeks 5 days of gestation (X axis) and corresponding BPD values were 22 mm, 44.3 mm, 55 mm, 68 mm, 80 mm and 84 mm respectively (Table 1). As such the week and day cannot be directly entered as values for X axis, first they have to be converted to corresponding decimal values (Table 1. second column).

Table 1: BPD values at different periods of pregnancy

Gestational age in weeks and days	Gestational age in decimals	BPD values in mm
12W 3D	12.4	22
16 W 1D	16.1	33
20W 0D	20.0	44.3
23W 6D	23.8	55
29W 2D	29.3	68
33W 4D	33.6	80
37W 5D	37.7	84

After obtaining values for *x axis* (gestational age of fetus in question) and values for *y axis* (BPD in mm), one can use XY scatter gram feature which is inbuilt in Microsoft Excel to plot a graph. The Fig 1 indicates the scatter plot for the data in Table 1.

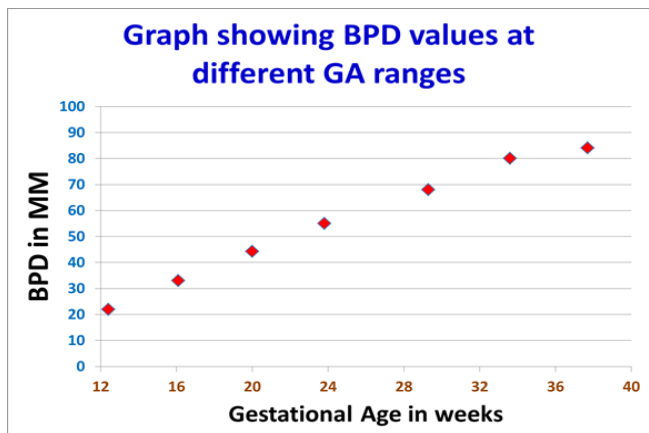


Fig 1: Graph showing XY scattered diagram graph for BPD at various gestational age.

Now excel trend line function is used to visualise the data (Fig 2). This pop up box can be invoked by right clicking on chart elements (Fig 3). This function has several other sub functions such as type of fit, deriving the suitable equation and finding out R squared value to determine the degree of fit (values closer to 1 indicate the perfect fit).

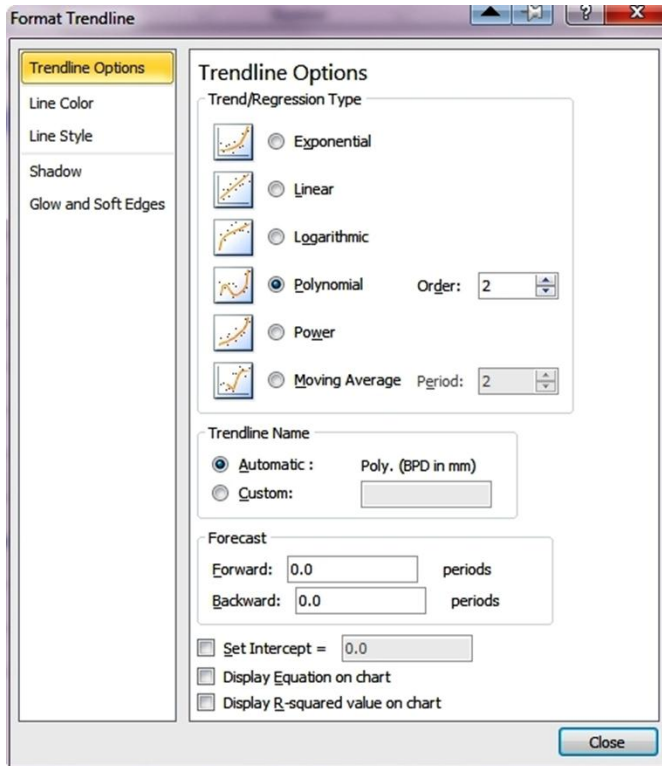


Fig 2: Excel trend line function to determine the best fit.

After setting the desired functions, the output as shown in the fig 3, can be obtained. The relationship between X and Y axis is shown as an equation within the chart, which can be further used for generating BPD table across various gestational age (Table 2).

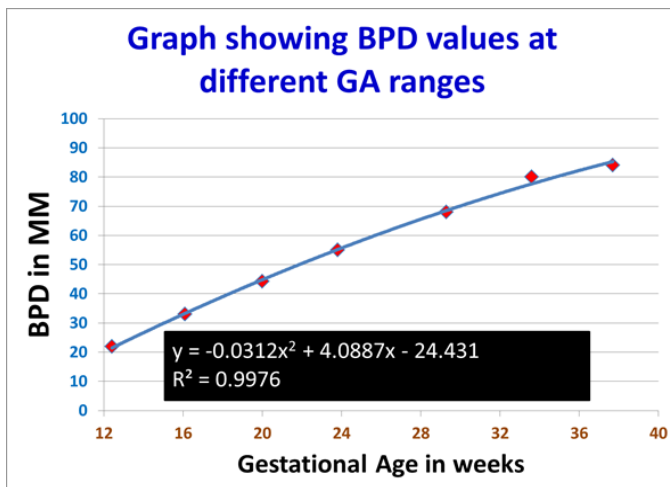


Fig 3: Shows trend line which passes closely through the BPD values. Regression equation is typed in the box.

We have used second degree polynomial function ($y = a + bx + cx^2$) to derive the equation. For example, the formula in the fig 3 can be interpreted as

BPD in mm = - 24.431 + 4.0887 X GA - 0.0312 X GA², wherein GA is the gestational age ranging from 12 weeks to 42 weeks (duration of gestation where BPD is measurable).

In fact it is possible to generate BPD table at any given interval (even one week or a day also), however most of the time, one week interval will suffice (Table 2).

Table 2: BPD values across various gestational age intervals

Gestational Weeks	BPD in mm
12	20.1
13	23.4
14	26.7
15	29.9
16	33
17	36.1
18	39.1
19	42
20	44.9
21	47.7
22	50.4
23	53.1
24	55.7
25	58.3
26	60.8
27	63.2
28	65.6
29	67.9
30	70.2
31	72.3
32	74.5
33	76.5
34	78.5
35	80.5
36	82.3
37	84.1
38	85.9
39	87.6
40	89.2
41	90.8
42	92.3

The above exercise suits one biometric parameter and one patient. The same can be extended to other biometric parameters and multiple numbers of patients. Finally values at given Gestational Age can be averaged to find the mean value and also the standard deviation can be calculated. Using Z statistics, it is also possible to derive centile charts; however this aspect is out of the scope of present paper.

4. Discussion

Improved models for intra uterine fetal growth are needed for more accurate assessment of IUGR (Intra Uterine Growth Restriction) and macrosomia^[6]. Though the actual meaning of IUGR refers to a newborn which has not achieved its genetic growth potential in utero, at present there are no appropriate diagnostic tools to determine the same. Many studies which involve IUGR babies have defined the condition as a foetus whose weight falls below the 10th centile (so called, small for Gestational Age – SGA babies). But this cut off value differs from country to country and has many influencing factors. The only workaround is establishing population based customised growth charts^[7].

The growth patterns are well established in animal husbandry to determine the suitable slaughter weight in order to obtain the good quality meat. However in human beings, this information is required to determine the optimal gestational age at delivery in order to improve the neonatal survival rate. Though these curve estimation can be done with a help of advanced statistical software, they need to be purchased for reasonably high price and also the learning period is time consuming.

There are several papers which have used Microsoft Excel Program for generation of growth charts^[8, 9, 10]. Microsoft Excel added trend line to its chart from year 2000 onwards. But it was further refined and more functions have been added recently. One of the easiest methods for guessing a general trend in data is to add a trend line to a chart. A trend line represents all the data as close as possible to the original data. This means that minor exceptions or statistical errors won't distract Excel when it comes to finding the right formula. In additions to finding intermediate values which were not originally present, in some cases, one can also use the trend line to forecast future data. The learning period to understand these features is reasonably short unlike professional curve fitting programs.

Microsoft Excel also provides five other different curve estimation methods for the given data, which include exponential, logarithmic, polynomial, power and moving average, and any model which has highest R squared value can be chosen for preparing biometric chart.

Once the individual growth curves are obtained, the extrapolated values at each gestational week can be further analysed to find mean and standard deviation. Using this information once can calculate percentile charts. Referring these charts, one can differentiate between normal and abnormal foetal growth trend and can institute necessary interventions to salvage the baby.

5. References

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