CLIN. CHEM. 27/1, 133-134 (1981)

Relation between Maternal Weight and Serum Alpha-Fetoprotein Concentration during the Second Trimester

James E. Haddow, Edward M. Kloza, George J. Knight, and Dwight E. Smith

Maternal serum alpha-fetoprotein concentrations are influenced by maternal weight during the second trimester. Heavier pregnant women have lower median values, apparently as a result of a diluting effect of larger blood volume. This phenomenon is of clinical interest because alpha-fetoprotein concentration in a pregnant woman's serum is one of the factors considered in assessing risk of poor outcome. A revision of the reference interval for alpha-fetoprotein to take body weight into account might improve its use as a diagnostic aid, especially in heavier women.

Additional Keyphrases: *fetal status · birth defects · screening · reference intervals · cutoff value*

Measurement of alpha-fetoprotein (AFP) in maternal serum during the second trimester is currently being used as a screening test in a few centers in the United States (*1*), primarily to identify women at high risk for carrying fetuses with open neural tube defects. Ultrasonography and amniocentesis can then be performed for diagnostic purposes. Other less common fetal lesions, such as omphalocele and congenital nephrosis, as well as multiple gestations and pregnancies at high risk for poor outcome have also been diagnosed by measuring serum AFP (*2, 3*).

Each laboratory measuring AFP chooses its own cutoff values to segregate high-risk pregnancies for further study. This line is generally selected on the basis of the percentage of open neural tube defects that the screening program wishes to identify, given the prevalence in that population. This cutoff value is also a major factor in defining the ratio of amniocenteses performed to lesions diagnosed. Data for making these calculations have been presented in the First and Second U.K. Collaborative Studies and are generally applicable (*2, 4*).

In an effort to refine further the classification of high-risk pregnancies, we studied the effect of maternal weight on serum AFP values, reasoning that the small but varying amounts of AFP that diffuse from amniotic fluid into the mother may then be diluted according to blood volume (*5*). Thus, heavier women generally should have lower concentrations of circulating AFP, and vice versa. We found this to be the case, the effect being sufficiently large to suggest that body weight might be taken into account when AFP results are being interpreted, especially in larger women.

Materials and Methods

Subjects. Women in Maine are offered AFP serum screening as part of routine prenatal care during the second trimester in more than 100 physicians' offices. Those choosing to be tested fill out a requisition which includes a space for maternal weight. Information about ethnic origin is not requested, but the population of the state is approximately 99% white. Gestation is routinely dated from the first day of the last menstrual period, but dating by ultrasound or physical examination is used occasionally. All samples are processed at the Foundation for Blood Research. The weights are thus on record for 1644 of 4500 women screened between 14 and 20 weeks of gestation, and it is this group on whom the present study is based. Only first serum sample results are included here, and all samples associated with multiple gestations and major fetal malformations have been excluded. Four weight groups have been arbitrarily defined.

AFP in maternal serum was measured by a standard double-antibody radioimmunoassay, with use of reagents produced on-site. Within- and between-batch CVs in the diagnostic range are 3–5 and 4–6%, respectively. AFP values are expressed as a multiple of the median (MOM) value established for each gestational week by our screening program, according to U.K. Collaborative Study recommendations (*2*). The impact of outlying values on analysis of the AFP population distribution, resulting from non-symmetrical distribution of AFP values, is minimized by use of MOM. Of equal importance, MOM calculations normalize the data from various gestational weeks, allowing them to be considered collectively.

Results

Table 1 summarizes our results. Mean gestational ages are similar for the four weight groups, but median AFP concentrations decrease steadily as weight increases, although the difference is not statistically significant between the last two groups. Table 1 includes the median AFP value for each of the four weight categories as a multiple of the entire group's median.

Table 1. Median Values for Maternal Serum AFP for Four Weight Classes of Pregnant Women in the Second Trimester

Maternal wt, lb.	No. observations	Weeks gestation,[a] mean ± SE	AFP concn, μg/L, median ± SE
>170	159	16.1 ± 0.12	27.0 ± 1.4 (0.75)[b]
141–170	431	16.2 ± 0.07	34.0 ± 0.9 (0.94)
111–140	925	16.2 ± 0.05	38.0 ± 0.6 (1.06)
<111	129	16.3 ± 0.12	40.0 ± 1.4 (1.11)
All groups	1644	16.2 ± 0.03	36.0 ± 0.6 (1.0)

[a] No significant difference exists among the four groups for this variable.

[b] Numbers in parentheses represent the median value as a multiple of the combined median of 36.0. Comparisons between adjacent weight classes gave $p = <0.001$ between the first and second class and between the second and third class. The difference between the third and fourth class was nonsignificant.

Foundation for Blood Research, P.O. Box 426, Scarborough, ME 04074.

Received July 14, 1980; accepted Oct. 17, 1980.

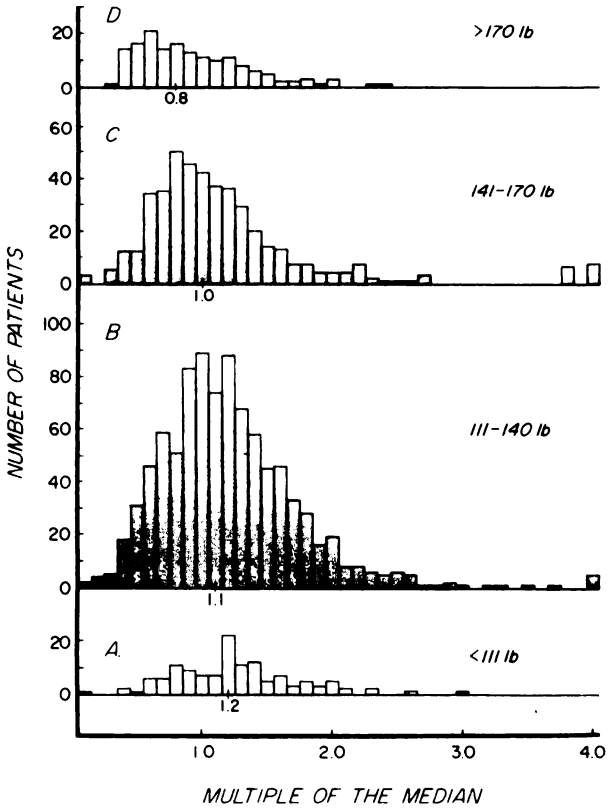

Fig. 1. Distributions of values for maternal serum alpha-fetoprotein during the second trimester in women segregated according to weight

Mass units have been converted to multiples of the median before plotting, to correct for gestational age. The median value for each group is indicated on the corresponding abscissa

A series of histograms (Figure 1) display the actual distributions of AFP values in each weight category. For this analysis, we converted each concentration to MOM before plotting, thus normalizing it individually according to its corresponding gestational week. This more refined statistical expression correlates closely with the results displayed in Table 1, showing a downward progression of median values with increasing weight. The differences in median AFP values among the four groups also follow a similar pattern of statistical significance. For interpreting clinical laboratory results, these normalized data would be more meaningful.

Discussion

Under normal conditions, most AFP appears to diffuse into the maternal circulation, directly across the amnion from the amniotic fluid; the actual amount that diffuses varies considerably from pregnancy to pregnancy, based on the amnion's porosity (5). Nevertheless, under normal conditions, even the most porous amnion allows only a relatively small percentage of AFP to cross. This is an important variable influencing AFP concentrations, and maternal weight evidently is a second such variable. Maternal weight is assumed to reflect maternal blood volume, although direct evidence for this is not available.

This second variable, in contrast to the first, can be applied clinically to refine interpretations of serum AFP concentrations in pregnancy screening programs. Currently, our screening program classifies women with serum AFP values >2 MOM as being at sufficiently high risk to warrant further testing. In light of the present results, women in the lowest weight group can be assigned a substantially higher cutoff value (2.4 the group median), and those in the highest weight group can be assigned a lower cutoff value (1.6 the group median). Although the total proportion of women considered to be at high risk is unlikely to change significantly, we hope that the assignment of risk will be more appropriate, especially in very large women. Further refinements, such as using surface area calculations, may be possible in the future.

This work has been carried out, in part, under grants from the Maine Department of Human Services.

References

1. Macri, J. N., Haddow, J. E., and Weiss, R. R., Screening for neural tube defects in the United States. A summary of the Scarborough Conference. *Am. J. Obstet. Gynecol.* **133,** 119–125 (1979).

2. U.K. Collaborative Study on alpha-fetoprotein in relation to neural tube defects: Maternal serum alpha-fetoprotein measurement in antenatal screening for anencephaly and spina bifida in early pregnancy. *Lancet* **i,** 1323–1332 (1977).

3. Brock, D. J. H., Barron, L., Duncan, P., et al., Significance of elevated mid-trimester maternal plasma alpha-fetoprotein values. *Lancet* **i,** 1281–1282 (1979).

4. Amniotic fluid alpha-fetoprotein measurement in antenatal diagnosis of anencephaly and open spina bifida in early pregnancy: Second report of the U.K. Collaborative Study on alpha-fetoprotein in relation to neural tube defects. *Lancet* **ii,** 651–662 (1979).

5. Haddow, J. E., Macri, J. N., and Munson, M., The amnion regulates movement of fetally derived alpha-fetoprotein into maternal blood. *J. Lab. Clin. Med.* **94,** 344–347 (1979).