Risk factors for mother-to-child transmission of human immunodeficiency virus-1 infection

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OBJECTIVE: Our aim was to examine maternal, obstetric, and infant characteristics of mother-to-child transmission of human immunodeficiency virus-1 in Nairobi, Kenya.

STUDY DESIGN: Proviral human immunodeficiency virus-1 was detected by polymerase chain reaction in peripheral blood samples taken between 6 weeks and 3 months of age from 107 children born to human immunodeficiency virus-1 seropositive women. The association of maternal, infant, and obstetric variables with human immunodeficiency virus-1 transmission was examined.

RESULTS: The mother-to-child transmission rate was 31% (95% confidence interval 21.6 to 40.2) as defined by the presence of proviral human immunodeficiency virus-1 in the infant. Variables associated with transmission in a univariate analysis included placental inflammation (7/12 in the transmitting group as compared with 2/22 in nontransmitters, $p = 0.006$), low maternal CD4 and high CD8 percentages (21% and 52%, respectively, in transmitting mothers and 32% and 40% in nontransmitting mothers; $p = 0.001$), and the gender of the neonate (20/29 infected neonates were female as compared with 26/65 noninfected children, $p = 0.02$). Sexually transmitted diseases were found more often in transmitting mothers but the differences were not significant. Birth weight and gestational age were not related to vertical transmission of human immunodeficiency virus-1.

CONCLUSION: Risk factors for mother-to-child transmission of human immunodeficiency virus-1 included chorioamnionitis, an impaired maternal immune status, and female gender. (Am J Obstet Gynecol 1995;172:700-5.)

Key words: Vertical transmission, human immunodeficiency virus-1, risk factors

Transmission of human immunodeficiency virus-1 (HIV-1) from an infected mother to her infant is the major route of acquisition of human immunodeficiency virus (HIV) infection in children. Over a decade of HIV-1 epidemic, estimates of transmission remain highly variable and arrange between 13% and 32% in industrialized countries and from 25% to 48% in developing countries. Several factors including methodologic and population differences, maternal HIV incidence rates, concomitant infections, maternal levels of viremia, obstetric interventions, and breast-feeding have been suggested to explain the discrepancy in vertical transmission rates between different populations.[1] Loss to follow-up is known as one of the drawbacks in prospective studies with a long follow-up period, particularly in African urban areas. Therefore we preferred to keep the length of follow-up short and to base diagnosis of HIV infection in the infant on polymerase chain reaction (PCR) testing, which is considered as a reliable diagnostic test in the first months of life.[2]

This study provides information on risk factors and risk markers for mother-to-child transmission of HIV-1 infection, as determined in a prospective study in Nairobi, Kenya.

Patients and methods

A prospective cohort study examining the impact of maternal HIV-1 infection on pregnancy outcome was initiated in Nairobi, Kenya, in 1989. The methods and results of this study have been described in detail elsewhere.[3] Initially, follow-up was planned only at 2 and 6 weeks post partum to study neonatal morbidity and mortality and to assess postpartum complications in the mother. Long-term follow-up of the infants was not considered because of the focus of this study on pregnancy outcome, because of the abundant number of perinatal transmission studies already ongoing in

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Africa, and because of the financial and logistic implications of long-term follow-up studies in urban settings with a high migration rate. Gradually it became clear that important obstetric and maternal information was missing in many perinatal transmission studies. Furthermore, the preparation and shipment of infant samples for PCR testing in Antwerp became operational after January 1991. PCR was considered appropriate for diagnosis of HIV-1 infection in the child before the age of 3 months.[2, 4, 5] Therefore we decided to follow up the children born after January 1991 and to draw blood at the ages of 6 weeks and 3 months to determine maternal and infant characteristics of vertical transmission without engaging in a long-term follow-up study. Despite the worrisome data on breast-feeding and HIV transmission[6] our patients were allowed to breast-feed, which they all did, in the absence of a safe alternative.

The PCR was done at the Institute of Tropical Medicine, Antwerp, Belgium, on primary lymphocytes of HIV-1–exposed babies. Lymphocytes were separated on a Ficoll gradient and resuspended in a lysis buffer with nonionic detergents at a concentration of 6.10^6 cells per milliliter and stored at −20° C until use. These samples were incubated for 1 hour at 56° C with proteinase K to release target deoxyribonucleic acid, followed by inactivation of the enzyme for 20 minutes at 95° C. PCR was performed in a 50 μl volume containing 1.25 units of *Taq* polymerase (Perkin Elmer, Zaventem, Belgium), 200 μmol/L of each deoxynucleoside triphosphate, 0.4 μmol/L of each primer, 0.5 μg of total cellular DNA, 0.01% gelatin, 5 mmol/L of potassium chloride, and 2.5 mmol/L magnesium chloride in 10 mmol/L tris hydrochloride buffer, pH 8.3. The reaction was overlaid with 2 drops of mineral oil. Nested oligonucleotide primers specific to the pol, env, and LTR regions of the HIV-1 virus were designed and produced in the Institute of Tropical Medicine laboratory. Thirty-five cycles of amplification were carried out in a DNA thermal cycler (Perkin Elmer/Cetus, Beaconsfield, United Kingdom) under the following conditions: 94° C for 1 minute, 50° C for 1 minute, and 72° C for 1 minute. In the last round the extension step of 72° C was held for 7 minutes. One microliter of amplified product was removed to a second amplification series in which the inner primers were used for 25 cycles under the same conditions. Ten microliters of amplified product was loaded onto a 2% agarose gel, electrophoresed, and stained with ethidium bromide. The DNA was visualized under the transilluminator and photographed. A single PCR with primers of the β_2-microglobulin gene of the cellular DNA was performed on the samples to check the DNA availability. PCR was done with both pol and env primer sets. In case of discrepancy a third PCR with the LTR set was carried out. A PCR test result was considered positive if at least two of the primers were positive. A PCR was considered negative if none of the three primers was positive and the β_2-microglobulin was positive. In all other cases PCR was considered indeterminate or not valid if β_2-microglobulin was negative. The sensitivity of the pol and env primer set was 93% and 69%, respectively, and the specificity was 100% for both primer sets as compared with serology results tested on adult Kenyan blood samples. The LTR primer has not yet been evaluated.

Maternal blood was obtained for white blood cell count and lymphocyte subsets. Whole-blood samples drawn in ethylenediaminetetraacetic acid–containing tubes were used to determine helper/inducer T lymphocytes (CD4) and suppressor/cytotoxic T lymphocytes (CD8) by direct immunofluorescence with monoclonal antibodies (Becton Dickinson, California) and with two-color flow cytometry (Becton Dickinson). Absolute numbers of CD4 and CD8 cells were calculated with the white blood cell count and differential count (Coulter Electroncis, Inc., Hialeah, Fla.) and multiplication by the appropriate factor obtained on flow cytometry. For most analyses CD4 percentage was used because it seems to be more reliable since it is determined directly from flow-cytometric measurements.[7]

Odds ratios and 95% confidence intervals were used to measure the strength of associations and the *t* test was used to compare sample means.

Results

Between January 1991 and March 1992, 139 HIV-1–exposed children were enrolled in the prospective study on HIV-1 and pregnancy outcome.[3] These mothers and children were invited to the research clinic at 6 weeks and at 3 months so that an infant blood sample could be drawn for PCR determination. Three children died in the neonatal period. Eight mothers refused to have blood drawn from their children, and 21 mother-infant pairs were lost to follow-up. One hundred seven infants had blood drawn (77%), only 16 of whom twice, because a substantial number declined frequent blood sampling of their babies. Out of 107 children, 13 were classified as having indeterminate results on PCR testing. Out of the remaining 94 infants, 29 were PCR positive and 65 were PCR negative, suggesting a vertical transmission rate of 30.9% (95% confidence interval 21.6 to 40.2). If the 13 indeterminant samples are taken into account the vertical transmission rate is situated between 27.1% and 39.1%. Out of 16 infants who were tested twice, 5 were PCR positive, 10 were PCR negative on both occasions, and one initially PCR-negative child was found to be PCR positive at the age of 3 months. This infant was considered infected for the calculation of the vertical transmission rate.

Maternal and infant characteristics are summarized

Table I. Sociodemographic, medical, and behavior characteristics of HIV-1–transmitting and HIV-1–nontransmitting mothers

Maternal characteristic	*Transmitters (n = 29)*	*Nontransmitters (n = 65)*	*Significance*	*Relative risk*	*95% Confidence interval*
Age (yr, mean and SD)	23.6 (4.7)	22.0 (3.9)	$p = 0.09$	–	–
Age at first sexual intercourse (yr, mean and SD)	15.5 (2.0)	16.4 (2.1)	$p = 0.007$	–	–
Partners last 2 yr (No., mean and SD)	1.3 (0.6	1.6 (2.4)	$p = 0.5$	–	–
History of STDs (No.)	7/29 (24.0%)	13/65 (20.0%)	$p = 0.8$	–	–
History of blood transfusion (No.)	2/29 (6.9%)	2/65 (3.1%)	$p = 0.7$	–	–
Malaria parasitemia (No.)	5/9 (55.5%)	9/28 (32.1%)	$p = 0.4$	–	–
AIDS-related signs or symptoms (No.)	8/27 (29.6%)	16/62 (25.8%)	$p = 0.9$	–	–
Genital ulcer disease (No.)	5/28 (17.9%)	2/64 (3.1%)	$p = 0.05$	2.6	0.8-8.3
Genital warts (No.)	4/28 (14.3%)	1/64 (1.6%)	$p = 0.06$	3.6	0.6-20.9
RPR and TPHA positive (No.)	2/29 (6.9%)	4/65 (6.2%)	$p = 0.7$	–	–
Neisseria gonorrhoeae (No.)	4/29 (13.8%)	1/58 (1.7%)	$p = 0.08$	3.5	0.6-20.2
Chlamydia trachomatis (No.)	1/22 (4.5%)	3/53 (5.7%)	$p = 0.7$	–	–
Postpartum endometritis (No.)	7/25 (28.0%)	11/59 (18.6%)	$p = 0.5$	–	–

STDs, Sexually transmitted diseases; *AIDS,* acquired immunodeficiency syndrome; *RPR,* reactive plasma reagin; *TPHA, treponema pallidum* hemagglutination.

in Tables I to V. Transmitting mothers were more likely to be carrying a sexually transmitted disease, particularly genital ulcer disease, warts, and gonococcal infection, although the differences were not statistically significant. They were also younger when they began sexual intercourse. Placental inflammation was a risk factor for mother-to-child transmission of HIV-1 (Table II). Unfortunately, >50% of the placentas were stored in a locally purchased formalin suspension at a low concentration of formalin and could not be analyzed on arrival in the laboratory. Therefore the sample size did not allow multivariate analysis.

No differences were observed in maternal clinical disease stage between transmitting and nontransmitting mothers, but the mean CD4 count, the mean CD4 percentage, and the CD4/CD8 ratio were significantly lower in transmitting mothers, whereas the CD8 count and percentage were significantly higher. The mean CD4 was 21.6% in transmitting mothers and 31.5% in nontransmitters ($p = 0.001$). The mother-to-child transmission rate increased with declining CD4 percentage (Table IV). There was no difference in birth weight, gestational age, and maturity score between infected and noninfected children. Most striking, however, was the high proportion of female children in the infected group (68.9% vs 40.6%, relative risk 3.2, 95% confidence interval 1.1 to 9.2, $p = 0.02$) (Table V).

Comment

A vertical HIV-1 transmission rate between 21.6% and 40.2% was found on the basis of a PCR test before the age of 3 months. Most samples were taken at the age of 6 weeks. The PCR technique as described earlier is recognized as a reliable method for diagnosing perinatal HIV infection in the first months of life by several authors,[2, 4, 5] but an error of 5% has to be taken into account. Indeed, 1 out of 16 infants who had two determinations had a positive result only on the second testing at the age of 3 months. As for the calculation of the transmission rate and the weight of the risk factors, a follow-up bias may have been introduced by the fact that 23% of the infants were not available for testing because of loss to follow-up, refusal to undergo blood sampling, or death. Nevertheless, the vertical transmission rate falls within the range of most African studies. The incidence of perinatal transmission varies between 14% (European Collaborative study)[8] and 48% (Nairobi, Kenya).[9] Methodologic differences, length of follow-up, serology incidence rates, concomitant infections, maternal levels of viremia, and breast-feeding have been proposed to explain the differences in vertical transmission rates between different populations.

Perinatal HIV transmission is undoubtedly a multifactorial process that can take place in utero, during delivery, and during lacation. In this study samples were

Table II. Obstetric characteristics of HIV-1–transmitting and HIV-1–nontransmitting mothers

Obstetric characteristic	*Transmitters (n = 29)*	*Nontransmitters (n = 65)*	*Significance*	*Relative risk*	*95% Confidence interval*
Primiparity (No.)	82/29 (27.6%)	21/65 (32.3%)	$p = 0.8$	–	–
Gestational age at delivery (wk, mean and SD)	38.4 (2.2)	38.0 (2.0)	$p = 0.4$	–	–
Length of labour (hr, mean and SD)	11.3 (5.3)	11.0 (9.4)	$p = 0.9$	–	–
Length of ROM (hr, mean and SD)	6.6 (9.5)	2.5 (7.1)	$p = 0.1$	–	–
Chorioamnionitis (No.)	6/14 (42.9%)	2/23 (8.7%)	$p = 0.04$	7.9	1.3-47.4
Funisitis (No.)	4/12 (33.3%)	1/23 (4.3%)	$p = 0.08$	3.6	0.6-21.0
Villitis (No.)	2/12 (16.7%)	0/24 (0.0%)	$p = 0.2$	–	–
Any placental inflammation (No.)	7/12 (58.3%)	2/22 (9.1%)	$p = 0.006$	14.0	2.2-89.2

ROM, Rupture of membranes.

Table III. Hematologic and immunologic characteristics of HIV-1–transmitting and HIV-1–nontransmitting mothers

Maternal characteristic	*Transmitters (n = 21)*	*Nontransmitters (n = 45)*	*Significance*
Hemoglobin (gm/L, mean and SD)	10.9 (1.3)	10.8 (1.6)	$p = 0.8$
White blood cell count (cells/ml, mean and SD)	6093 (2142)	6492 (3889)	$p = 0.6$
Lymphocyte count (cells/ml, mean and SD)	1769 (787)	1799 (653)	$p = 0.9$
CD4 count (cells/ml, mean and SD)	371 (198)	550 (289)	$p = 0.01$
CD4 percentage (%, mean and SD)	21.1 (6.8)	31.5 (9.6)	$p = 0.001$
CD8 count (cells/ml, mean and SD)	921 (462)	726 (287)	$p = 0.04$
CD8 percentage (%, mean and SD)	51.9 (8.1)	40.2 (10.6)	$p = 0.001$
CD4/CD8 ratio (mean and SD)	0.5 (0.3)	0.8 (0.5)	$p = 0.002$

taken mainly at the age of 6 weeks. In 16 children blood was drawn twice, and in one of them seroconversion had occurred at the age of 3 months. A vertical transmission rate of around 30% at the age of 6 weeks suggests a high intrauterine or intrapartum infection rate, but early postnatal infection by breast milk cannot be excluded in this study and may be a major confounder. Theoretically, there is no direct continuous exchange between maternal and fetal blood during pregnancy, but passage of cells to and from the fetal circulation can take place, depending on the morphologic characteristics of the placental barrier, which change during the course of pregnancy. Potential routes of intrauterine transmission include transfer of HIV-containing maternal lymphocytes or free virus. The two placental cell types that are most likely to be infected are the placental macrophages and the trophoblasts themselves. Although no placental lesions specific for HIV infection have been noted, several authors describe higher incidence rates of placental inflammation, particularly chorioamnionitis, in HIV-1–transmitting mothers as compared with HIV-1–seropositive nontransmitters.[10-12] Also in our study we found a higher rate of chorioamnionitis in transmitting than in nontransmitting mothers (42.9% vs 8.7%, $p = 0.04$). These findings were not typical for HIV infection, but inflammation could render the trophoblast barrier more leaky and allow freer passage of virus or infected lymphocytes to the fetus.

The clinical and/or immunologic stage of HIV disease seems to be correlated with vertical transmission. In the European Collaborative study mother-to-child transmission has been associated with antigenemia and a CD4 count of < 700 cells/ml.[8] In a study from Kinshasa, HIV-1 was cultured from cord blood in 6 of 18 women with antepartum CD4 counts of < 400 cells/ml maternal serum as compared with none of 19 deliveries of women with CD4 cell counts > 400 ($p = 0.02$). As in our study mother-to-child transmission of HIV-1 increased with declining CD4 cell counts.[10] Similar findings were reported from Rwanda.[13] This could be due to an increased viral load with advanced disease leading to more efficient transmission. Intercurrent infections may enhance HIV replication in the mother, thus increasing the risk of vertical transmission. In our group we found a trend toward sexually transmitted diseases, including maternal infections with gonococci, genital warts, or genital ulcers, in transmitting mothers, which suggests an increased risk of vertical transmission of HIV. An

Table IV. Mother-to-child transmission and maternal CD4 percentage

Maternal CD4 percentage	*Transmitters (No.)*	*Nontransmitters (No.)*	*Transmission rate*
10%-19%	9	4	69.3%
20%-29%	8	18	30.8%
≥30%	4	23	14.8%

$p = 0.002$.

Table V. Infant characteristics of HIV-1–infected and HIV-1–noninfected infants

Infant characteristic	*HIV-1–infected infants (n = 29)*	*HIV-1–noninfected infants (n = 65)*	*Significance*	*Relative risk*	*95% Confidence interval*
Birth weight (gm, mean and SD)	2984 (384)	2987 (397)	$p = 0.9$	–	–
Preterm birth (No.)	5/28 (17.9%)	14/62 (22.5%)	$p = 0.7$	–	–
Female baby (No.)	20/29 (70.0%)	26/65 (40.0%)	$p = 0.02$	3.2	1.1-9.2

independent association between mother-to-child transmission of HIV and multiple sexual partners was reported by the Butare group,[14] suggesting a role of sexually transmitted diseases in the transmission process.

Surprising is the observed association between vertical transmission and the gender of the baby. Twenty of 29 infected children were female as opposed to 26 of 65 uninfected children. Similar findings were reported by the Italian Multicentre Study where 295 of 690 (42.8%) girls were infected compared with 269 of 736 (36.5%) boys, $p < 0.02$,[15] and by the Dutch Collaborative Study where 8 of 9 infected children were female.[16] Other large studies including the European Collaborative Study did not report this finding.[8] A gender factor in perinatal transmission is difficult to explain and might be due to chance. One could hypothesize that the perinatal mortality rate in boys, especially in HIV-infected boys, might be higher than in girls but this was not the case.[3] A follow-up bias could play a role if girls were less likely to continue follow-up unless they were ill, but the number of boys and girls in the follow-up was similar. A possible explanation could be that female genitalia at birth typically exhibit evidence of maternal estrogen stimulation with prominent labia and a dull pink vaginal epithelium, resulting in a larger potential area of entry for the virus. If confirmed, this hypothesis would underline the importance of intrapartum transmission.

Birth weight and gestational age were not confirmed as risk factors for vertical transmission, which is in agreement with the Italian Register,[15] the French Collaborative study,[16] and data from Sweden,[17] whereas prematurity has been associated with an increased risk of infection in other studies.[18, 19] Further studies including larger numbers and combining sociodemographic, medical, obstetric, and infant data will be necessary to gain more knowledge on risk factors and risk markers for mother-to-child transmission. This can only be realized if different specialists, including obstetricians, pediatricians, immunologists, virologist, pathologists, and statisticians, join efforts to improve the quality of research in the field of perinatal transmission of HIV.

REFERENCES

1. Dabis F, Msellati P, Dunn D, et al. Estimating the rate of mother-to-child transmission of HIV: report of a workshop on methodological issues, Ghent (Belgium). 17-20 February 1992. AIDS 1993;7;1139-48.
2. Krivine A, Firtion G, Cao L, Francoual C, Henrion R, Lebon P. HIV replication during the first week of life. Lancet 1992;339:1187-9.
3. Temmerman M, Chomba EN, Ndinya-Achola J, Plummer FA, Coppens M, Piot P. Maternal HIV-1 infection and pregnancy outcome. Obstet Gynecol 1994;83:495-501.
4. Rogers MF, Ou C-Y, Rayfield M, et al. Use of the polymerase chain reaction for early detection of the proviral sequences of human immunodeficiency virus in infants born to seropositive mothers. N Engl J Med 1989;320: 1649-54.
5. Scarlatti G, Lombardi V, Plebani A, et al. Polymerase chain reaction, virus isolation and antigen assay in HIV-1-antibody-positive mothers and children. AIDS 1991;5:1173-8.
6. Van De Perre P, Simonon A, Msellati P, et al. Postnatal transmission of human immunodeficiency virus type I from mother to infant. N Engl J Med 1991;325:593-8.
7. Fahey JL, Taylor JMG, Detels R, et al. The prognostic value of cellular and serological markers in infection with human immunodeficiency virus type I. N Engl J Med 1990;322:166-72.
8. European collaborative study: risk factors for mother-to-child transmission of HIV-1. Lancet 1992;339:1007-12.
9. Datta P, Embree J, Plummer E, et al. Perinatal HIV-1 transmission in Nairobi: 5 years follow-up [Abstract MC3]. In: Proceedings of the seventh international conference on AIDS, Florence, Italy, June 16-21, 1991. Florence: International Conference on AIDS, 1991.
10. Ryder RW, Nsa W, Hassig SE, et al. Perinatal transmission of the human immunodeficiency virus type 1 to infants of seropositive women in Zaire. N Engl J Med 1989;320: 1637-42.
11. Bulfamante G, Muggiasca L, Conti M, et al. Placental morphological findings in HIV positive pregnancies: frequency and correlation of the clinical status of mothers and their babies [Abstract WC3228]. In: Proceedings of the seventh international conference on AIDS, Florence,

Italy, June 16-21, 1991. Florence: International Conference on AIDS, 1991.
12. St Louis ME, Kamenga M, Brown C, et al. Risk for perinatal transmission according to maternal immunologic, virologic and placental factors. JAMA 1993;269: 2853-9.
13. Hitimana DG, Lepage P, Van de Perre P, et al. Perinatal study of HIV-1 in Kigali, Rwanda: estimation of the mother-to-child transmission rate and analysis of its determinants [Abstract POC4019]. In: Proceedings of the eighth international conference on AIDS/third STD world congress, Amsterdam, The Netherlands, July 19-24, 1992. Amsterdam: International Conference on AIDS/STD World Congress, 1992.
14. Bulterys M, Chao A, Dushimimana A, et al. Multiple sexual partners and mother-to-child transmission of HIV-1. AIDS 1993;7:1639-45.
15. Gabiano C, Tovo P-A, de Martino M, et al. Mother-to-child transmission of human immunodeficiency virus type 1: risk of infection and correlates of transmission. Pediatrics 1992;90:369-74.
16. Scherpbier HJ, Kampinga GA, Boer K. Prognostic factors for vertical HIV transmission [Abstract POC4231]. In: Proceedings of the eighth international conference on AIDS/third STD world congress, Amsterdam, The Netherlands, July 19-24, 1992. Amsterdam: International Conference on AIDS/STD World Congress, 1992.
17. Blanche S, Rouzioux C, Guihard Moscato M-L, et al. A prospective study of infants born to women seropositive for human immunodeficiency virus type 1. N Engl J Med 1989;320:1634-48.
18. Lindgren S, Anzen B, Bohlin A-B, Lidman K. HIV and child-bearing: clinical outcome and aspects of mother-to-infant transmission. AIDS 1991;5:1111-6.
19. Goedert JJ, Mendez H, Drummond JE, et al. Mother-to-infant transmission of human immunodeficiency virus type 1: association with prematurity or low anti-gp 120. Lancet 1989;2:1351-4.

Gestational weight gain among average-weight and overweight women—What is excessive?

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OBJECTIVE: Our purpose was to determine the association between increased gestational weight gain and birth weight outcomes for low-income women.
STUDY DESIGN: A total of 53,541 single, live infants delivered from 1990 to 1991 to white, black, and Hispanic women in eight states were evaluated. Multiple logistic regression was used to calculate risk of low and high (>4500 gm) birth weight, adjusting for selected factors.
RESULTS: The association between gestational weight gain and birth weight varied by prepregnancy body mass index. Risk for low birth weight decreased with increasing weight gain for average-weight women. There was no reduction in risk for low birth weight, however, beyond weight gains of 30 to 34 pounds for overweight women and 15 to 19 pounds for very-overweight women. Risk for high birth weight, however, increased with increasing weight gain in all three groups.
CONCLUSION: Very-overweight women (body mass index >29 kg/m^2) may benefit from an upper guideline of 25 pounds of weight gain to help reduce risk for high birth weight. (Am J Obstet Gynecol 1995;172:705-12.)

Key words: Birth weight, weight gain, pregnancy, body mass index

Both low (LBW) and high birth weight are associated with increased mortality and other adverse outcomes. LBW infants (birth weight <2500 gm) are five to ten times more likely to die in the first year of life than are normal-birth-weight infants.[1] Those infants who survive the first year may experience impaired growth and development.[1] High-birth-weight infants (birth weight >4500 gm) are more than twice as likely to die within the first 28 days of life and to have birth trauma or be delivered by caesarean section than are normal-birth-weight infants.[2] High-birth-weight infants are also more likely to have obesity during early childhood.[3] Almost

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