ARTICLE

PRENATAL DIAGNOSIS AND MANAGEMENT OF INTRAUTERINE GROWTH RESTRICTION: A LONG-TERM PROSPECTIVE STUDY ON OUTCOME AND MATERNAL STRESS

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ABSTRACT: This study examines long-term effects of antenatal management of intrauterine growth restriction (IUGR) on developmental outcome and on maternal coping using a prospective cross-sectional design. Sixty-nine families were evaluated using psychological testing and risk questionnaires. The effects of timing of diagnosis (prenatal/perinatal) and of pregnancy management [induction of labor (IL)/conservative management (CM)/none, i.e., diagnosed-at-birth (DaB)] on maternal stress were tested at 6 years' postbirth. In general, prenatal management protocols of IUGR were efficient in preventing major disabilities; however, 49% of the variance in maternal stress at 6 years' postbirth could be attributed to the child's presenting behavior and to pregnancy management of IUGR condition. Mothers who received CM treatment reported being more stressed by their child's poor emotional adjustment (ps $< .01-.002$) and distractibility ($p < .029$), and to have more difficulty in accepting them ($p < .01$). Prenatal psychological consultation to better handle stress for parents whose fetus is diagnosed with IUGR is recommended, particularly when pregnancy is managed conservatively and familial–educational resources are low.

RESUMEN: Este estudio examina los efectos a largo plazo de cómo se maneja antes del nacimiento el retardo del crecimiento intrauterino (IUGR) en el resultado del desarrollo y en el proceso materno de arreglárselas, usando un diseño probable de corte transversal. Sesenta y nueve familias fueron evaluadas usando exámenes sicológicos y cuestionarios de riesgo. Los efectos de calcular el diagnóstico (prenatal/perinatal) y del manejo del embarazo (inducción del parto [IL]/el manejo conservador [CM]/ ninguno, por ejemplo, el estrés maternal diagnosticado al momento del nacimiento [DaB] fue examinado a los 6 años después del nacimiento. En general, los protocolos del manejo prenatal del retardo del crecimiento intrauterino fueron eficientes para prevenir discapacidades serias. Sin embargo, cuarenta y seis por ciento de la discrepancia en el estrés materno a los 6 años después del nacimiento pudiera ser atribuída a la

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presentación de conducta del infante y al manejo de la condición de retardo de crecimiento intrauteirno durante el embarazo. Aquellas madres que recibieron un tratamiento de manejo conservador reportaron estar más estresadas por los débiles ajustes emocionales del infante, así como la facilidad de distracción del mismo ($p<.029$), y tener más dificultades en aceptarlos ($p<.01$). Se recomienda la consulta sicológica prenatal con el fin de sobrellevar el estrés mejor, a aquellos padres cuyo feto es diagnosticado con retardo de crecimiento intrauterino, particularmente cuando el embarazo se maneja conservadoramente y los recursos familiares y educacionales son bajos.

RÉSUMÉ: Cette étude examine les effets à long terme de la gestion prénatale du retard de croissance intra-utérine (abrégé IUGR en anglais) sur le développement et sur la manière dont les mères font face, en utilisant un modèle transversal. Soixante neuf familles ont été évaluées en utilisant des tests psychologiques et des questionnaires de risque. Les effets du moment du diagnostic (prénatal/périnatal) et de la gestion de la grossesse (déclenchement de l'accouchement [abrégé en anglais IL]/gestion conservatrice [abrégé en anglais CM]/aucune gestion, c'est-à-dire diagnostic à la naissance [abrégé en anglais DaB]) sur le stress maternel ont été testés à l'âge de six ans après la naissance. En général, les protocols de gestion prénatale de retard de croissance intra-utérine IUGR se sont avérés efficaces pour la prévention d'handicaps importants. Cependant, quarante neuf pourcent de la variance dans le stress maternel six ans après la naissance pouvaient être attribués aux raisons pour la consultation de l'enfant et à la gestion de la condition IUGR. Les mères ayant reçu un traitement CM ont estimé être plus stressées par le manque d'ajustement émotionnel de leur enfant (*p*s<,01-,002) et sa distractibilité (*p,*029) ainsi qu'ayant plus de difficulté à les accepter ($p<,01$). La consultation psychologique prénatale afin de faire face au stress, aux parents dont le fœtus est diagnostiqué comme ayant un retard de croissance intra-utérine, est recommandée, en particulier quand la grossesse est suivie de manière conservatrice et que les resources familiales en matière d'éducation sont limitées.

ZUSAMMENFASSUNG: Mittels eines prospektiven, gekreuzten Design wurde in dieser Studie die Langzeiteffekte von vorgeburtlichem Management der intrauterinen Wachstumsverzögerung (IUWV) auf die Entwicklung und die Fähigkeit der Mütter damit fertig zu werden untersucht. 69 Familien wurden mittels psychologischer Testung und Risikofragebögen untersucht. Die Auswirkungen des Zeitpunkts der Diagnose (prä- oder perinatal) und des Schwangerschaftsmanagements (Geburtseinleitung (GebE), konservative Geburt (KG), keines – das heißt Diagnose bei der Geburt) auf den mütterlichen Stress wurden sechs Jahre nach der Geburt untersucht. Generell waren pränatale Maßnahmen der IUVW imstande massivere Behinderungen zu vermeiden. Jedoch konnten 49% der Varianz des mütterlichen Stress sechs Jahre nach der Geburt dem derzeitigen Verhalten des Kindes und dem Schwangerschaftsmanagement der IUVW zugeordnet werden. Mütter bei denen konservatives Management durchgeführt wurde, berichteten über mehr Stress durch die schlechte emotionale Anpassung (ps<.01-.002) und die Ablenkbarkeit ihres Kindes ($p<.029$). Sie hatten mehr Schwierigkeiten ihre Kinder zu akzeptieren ($p<.01$). Vorgeburtliche psychologische Beratung der Eltern, deren Fetus IUVW hat, um Stress besser verarbeiten zu können wird empfohlen, insbesondere, wenn die Schwangerschaft konservativ begleitet wird und die Schulausbildung der Eltern gering ist.

抄録：この研究は、前向きの横断的研究計画を使って、子宮内胎児発育遅延 intrauterine growth retardation (IUGR) の出産前管理が、発達の結果と母親の対処に与える長期的な影響を検証する。69 家族が心理検査とリスクについての質問紙を用いて評価された。診断のタイミング（出産前／周産期）と、妊娠管理（分娩誘発 [IL] ／保存的管理 [CM] ／なし、すなわち出産時に診断された [DaB] ）が、母親のストレスに与えた影響が、出産 6 年後にテストされた。一般的に、IUGR の出産前管理プロトコールは、主要な障害の予防には有効であった。しかし、出産 6 年後の母親のストレスにおける分散の 49 %は、子どもが表している行動と、IUGR という状況に対する妊娠中の管理に帰属させることができた。CM 治療を受けた母親は、子どもの情緒的な適応の悪さ (*p*s<.

01-.002) と被転導性 (p<.029) によってよりストレスがかかること、および子どもを受け入れることがより難しいこと (p< .01) を報告した。胎児が IUGR と診断された親に対する、ストレスをよりうまく扱うための親の心理カウンセリングが推奨される。特に妊娠が保存的に管理され、家族教育の資源が乏しいときには。

* * *

INTRODUCTION

Intrauterine growth restriction (IUGR) is frequently detected in a pregnancy with a less-than-expected third-trimester weight gain [100–200 g (3.5–7 oz) per week] or as an incidental finding on ultrasound examination when fetal measurements are smaller than expected for gestational age (GA). Conditions associated with IUGR are often medical such as chronic hypertension, preeclampsia early in gestation, diabetes mellitus, infectious, syphilis, cytomegalovirus, toxoplasmosis, rubella, hepatitis B. Other factors are genetic or are related to maternal habits such as smoking, alcohol use, restricted nutrition, and so on (Vandenbosche, 1998).

An estimated fetal weight under the 5th percentile, as determined by serial ultrasound examination, strongly correlates with growth restriction (Bernstein & Gabbe, 1996; Hadlock, 1994; McCormick, 1985). Once IUGR is diagnosed, physicians commonly prescribe mothers specific protocols of pregnancy management, dependent on site-specific medical practices and on case-specific characteristics following diagnosis (Queenan, 1994). These specific characteristics may pertain predominantly to the fetus, to the mother, or to a pathogenic process affecting both. For example, maternal illness, such as pregnancy-induced hypertension, may affect both fetal and maternal health. To date, the relations between prenatal medical interventions and maternal stress in this population have not been established.

Management protocols of IUGR may be divided into two categories: active medical interventions and conservative management (CM). Active intervention, such as induction of labor (IL), is opted for in some circumstances, dependent on factors such as fetal heart rate, amniotic-fluid volume, fetal movements, and fetal maturation (Bernstein & Gabbe, 1996; Creasy & Resnik, 1994; Pardi et al., 1993; Vandenbosche, 1998). CM, such as bed rest with and without medication, also is often advised as part of the management protocol once IUGR is suspected or diagnosed (Ribbert, van Lingen, & Visser, 1991; Trudinger, Cook, Thompson, & Giles, 1988).

While the medical benefits of early diagnostic techniques are substantial, the psychological consequences of these processes are not yet fully understood. It may be particularly an issue among parents if fetuses are diagnosed with IUGR. The parents are confronted during pregnancy with distressing information about their offspring's abnormal size and growth rate (Doubilet & Benson, 1995; Hay, Thureen, & Anderson, 2001; Lee, Conner, Charafeddine, Woods, & Priore, 2001; Waugh & Kilby, 2001). Inevitably, their parental representations of themselves and their child are affected by diagnosis of IUGR.

Investigators have found that mothers of prematurely born children continue to recall distressful aspects of their infant's illness for many months and even years thereafter (Affleck, Tennen, Rowe, & Higgins, 1990; Lobel, DeVincent, Kaminer, & Meyer, 2000; Singer et al., 1999; Wells & Hobfoll, 1999; Wereszczak, Miles, & Holditch-Davis, 1997); however, it is not clear whether it is primarily infant-focused memories and/or the prenatal period that affects maternal stress for many years (Evans, Heron, Francomb, Oke, & Golding, 2001). It may be that physical and emotional processes experienced by the mother-to-be, due to a sense of inadequacy to provide her fetus with a growth-promoting inner environment and the need to rely on a

specifically tailored management protocol of the prenatal risk condition, affect representations related to herself and the IUGR fetus for years postbirth.

Presumably, IL may be perceived by the mother in two ways. On one hand, IL may represent a swift, relatively low-risk medically directed procedure that will eliminate further strain from the developing fetus and allow for accessible medical intervention. In such a case, IL should lead to a decrease in maternal stress. On the other hand, IL may be perceived by the expectant mother as an aggressive interference required to mend a grave situation that cannot be handled conservatively. If so, IL may cause an elevation of stress and a long-term anticipation of a problematic developmental course.

Analogous to the possible implications of IL, there are two conflicting hypotheses regarding expectant mothers' perception of CM. On the one hand, CM may be perceived as a gentle modification for the fetus that allows nature to take its course. If so, suggesting CM may elicit self-calming thoughts such as "then it cannot be too severe" and hence alleviate stress. On the other hand, the efficacy of CM may be comprehended as being dependent solely on the mother-to-be, thus imposing a great emotional burden on her, resulting in increased stress.

The present study examined cross-sectionally and prospectively the diagnosis timing effect (prenatal/perinatal) and the management effect (IL/CM/none) on long-term maternal stress and preoccupations, apropos to the the mother and her growing IUGR child. The main focus was on the postnatal age of 6 years, at which time many families contemplate and cope with another phase of separation from their child who is getting ready for school.

The objectives of this study were: (a) to examine the relationships between different antenatal diagnosis and pregnancy-management programs, and long-term maternal stress; (b) to examine whether stress in mothers of IUGR children is related to the child's cognitive and/or behavioral outcome; and (c) to determine whether cognitive and behavioral outcomes of IUGR children at 6 years of age are related to different timing of diagnosis and antenatal management procedures. The main hypothesis tested was that the earlier IUGR is diagnosed, the greater the severity of IUGR risk, and thus greater maternal stress.

METHOD

Subjects

The group comprised a subsample of a long-term follow-up study of factors related to IUGR (Fattal-Valevski et al., 2001; Leitner et al., 2000). The subjects, all with a birth weight under the 5th percentile for GA, were recruited from the Lis (previously Serlin) Maternity Hospital, Tel-Aviv Sourasky Medical Center, Israel, from September 1992 through June 1996. This stringent criterion was chosen to exclude as much as possible a familial small-for-age predisposition. The neonates were identified by the participating obstetricians and neonatologists, and referred to the study. GA was calculated according to the date of the last menstrual period. Antenatal management protocols were decided upon by the Obs/Gyn team. Follow-up was conducted by a psychological and pediatric neurological team blinded to group assignments. This population is further described by Leitner et al. (2000). Data regarding prenatal management protocol were available for 69 IUGR children. Neonatal, parental, and demographic descriptions are presented in Table 1.

Data in Table 1 show that generally the groups were not different on most variables related to the parents and the familial variables. As expected with regard to neonatal variables, children in the IL group were delivered earlier and therefore weighed less and had a smaller head circumference (HC) at birth. Children in the CM and diagnosed-at-birth (DaB) groups were

TABLE 1. *Neonatal, Parental, and Demographic Parameters*

Age		*Diagnosed-at-Birth* n = *28*	*CM* n = *26*	*IL* n = *15*	F	p <
Neonatal	Estimated gestational age	38.2 ± 1.7	38.5 ± 1.3	34.7 ± 1.2	6.9	.000[c]
	Birthweight	2021.61 ± 319.19	2014.00 ± 269.67	1368.67 ± 319	28.14	.000[c]
	Head circumference	31.3 ± 1.4	31.3 ± 1.3	28.3 ± 1.7	15.4	.000[c]
Maternal	Maternal birth date	59.6 ± 6.2	63.3 ± 6.1	61.6 ± 5.5	1.6	n.s.
	Maternal education	12.5 ± 2.0	12.6 ± 2.1	12.8 ± 1.6	.154	n.s.
	Maternal occupation[a]	1.12 ± 1.2	1.4 ± 1.1	1.8 ± 1.1	1.06	n.s.
	Maternal health	19.6 ± 2.04	20.0 ± 0	18.0 ± 5.6	1.8	n.s.
Paternal	Paternal birth date	55.9 ± 5.7	60.2 ± 6.1	58.0 ± 6.4	2.09	n.s.
	Paternal education	12.0 ± 2.7	12.8 ± 2.6	12.7 ± 2.5	1.12	n.s.
	Paternal occupation[a]	2.1 ± 1.2	2.2 ± 1.2	3.1 ± 1.9	7.83	.000[d]
	Paternal health	18.7 ± 4.5	19.6 ± 2.0	19.3 ± 2.6	.423	n.s.
Familial	Marital status[b]	100	100	80	93.1	n.s.
	No. of siblings	2.5 ± 1.1	2.8 ± 3.7	2.3 ± 1.0	.712	n.s.
	Birth order	2.2 ± 1.14	1.8 ± .96	1.85 ± .77	2.83	.043[d]
	%singletons	87.5	95.6	92.9	100	n.s.
	%females	60.7	42.3	60.0	48.8	n.s.

CM = conservative management; IL = induced labor; n.s. = nonsignificant.

[a]Occupation was rated according to the Duncan Socioeconomic Index (Mueller & Parcel, 1981); [b]percentage of families in which both parents are present at home;[c]Scheffe post hoc significance due to difference between induced labor group and other groups; [d]Scheffe post hoc significance due to difference between Diagnosed-at-Birth group and other groups.

not different from each other on any of the neonatal variables. With regard to parental variables, the groups did not differ on any of the maternal variables. Parental variables also were nondifferential among the groups, except for paternal occupation, which was on average higher in the IL group than the other two groups. Familial variables also were mostly nondifferential, except for the variable of birth order. Children in the DaB group were less often firstborns than children in the other groups. Therefore, it is important to note that in none of the parameters—neonatal, parental, and familial—was the CM group different from the other two groups.

Exclusion Criteria

Newborns diagnosed as suffering from genetic syndromes, major malformations, or with evidence of congenital infection were excluded. The children included in the study group all had a late-onset (mid-second–third trimester) IUGR. Diagnosis was verified clinically and/or by ultrasound, and all showed signs of the asymmetric type of IUGR (Lapillone, Peretti, Ho, & Salle, 1997). Leitner et al. (2000) discerned that the majority of children in this study had suffered a (placental) vascular-induced growth restriction. No significant differences were found between the lost-to-follow-up group (21%) and the study group in biometric, perinatal, or socioeconomic status. Data regarding maternal stress were collected 2 years after the initial protocol was developed.

Procedures

Risk parameters were assessed using three detailed questionnaires with respect to sociofamilial, obstetric, and neonatal risks (Fattal-Valevski et al., 2001; Leitner et al., 2000). From birth, the

children were followed up annually at the Institute for Child Development by a team of pediatric neurologists and psychologists. At each follow-up visit, they underwent a detailed neurodevelopmental examination, biometric measurements, and formal psychological testing. The portion of data presented in the current report is comprised of the psychological testing conducted individually at the clinic. The evaluation included the testing of general competence using the Wechsler Preschool and Primary Scale of Intelligence (WPPSI; Wechsler, 1967).

Maternal ratings of their children's concurrent behavior was evaluated using the revised Conner's Parent Rating Scales (CPRS-48; Conners, 1989). This widely used tool allows for ratings of items on six scales: Conduct problem, Learning problem, Psychometric, Impulsive-hyperactive, Anxiety, and the Hyperactivity Index. The Hyperactive Index was developed to measure empirically behaviors which are indicative of an underlying diagnosis of hyperactivity. It has been found that using the index by itself yields a general index of child psychopathology rather than a syndrome specific to the diagnosis of hyperactivity or Attention Deficit Hyperactivity Disorder (see note by the author, Conners, 1989). The 48 items comprising the six scales are rated with four optional responses (*not at all, just a little, pretty much,* and *very much*). The individual scale scores are compared to norms for appropriate age groups of children. *T*-scores of 65 or greater are considered to be clinically significant for having a behavioral problem.

Maternal anxiety and stress domains were evaluated by the third edition of the Parental Stress Index (PSI; Abidin, 1986). The index is based on ratings of 120 items that pertain to the child domain, the parent domain, and life stress. The child domain consists of six discrete scales; namely, Reinforces Parent, Distractibility/Hyperactivity, Mood, Adaptability, Demandingness, and Acceptability. In the parent domain, there are seven discrete scales: Competence, Isolation, Attachment, Health, Role Restriction, Depression, and Spouse. The respondent responds to each item by circling one of five options (*strongly agree, agree, not sure, disagree,* or *strongly disagree*). The normal range for scores is within the 15th to 80th percentile. High scores that are indicative of psychiatric consultation are considered to be scores at or above the 85th percentile. An additional scale is used for significant life-stressing events during the last year. It provides some indication of the amount of stress outside the parent–child relationship that the parent is currently experiencing (Abidin, 1995). The scale is rated binarically.

In addition, for external validity purposes, records of referrals to individually tailored intervention programs were collected with regard to special education programs and psychological, occupational, physical, and/or speech therapy referrals. These referrals are good external indicators of both clinical need and of the focus of the parental concern.

RESULTS

Parental Emotional Adjustment at 6 Years as a Function of Antenatal Management of IUGR

Multivariate ANOVA (MANOVA) demonstrated that the average responses on PSI scales varied between prenatal and postnatal diagnosis of IUGR groups, taking into account the effects of prematurity and maternal education, and were significant regarding overall stress rates and most stress scales of the PSI. PSI total scores of mothers in the CM group were significantly higher than those of the other groups. These scores were higher both in the child domain and in the parent domain (Figure 1). Frequency of scores in the abnormal range were calculated using the PSI manual guidelines. Scores that were calculated to be at the 85th percentile or higher are defined as indicative of psychiatric consultation. Such elevated scores were reported

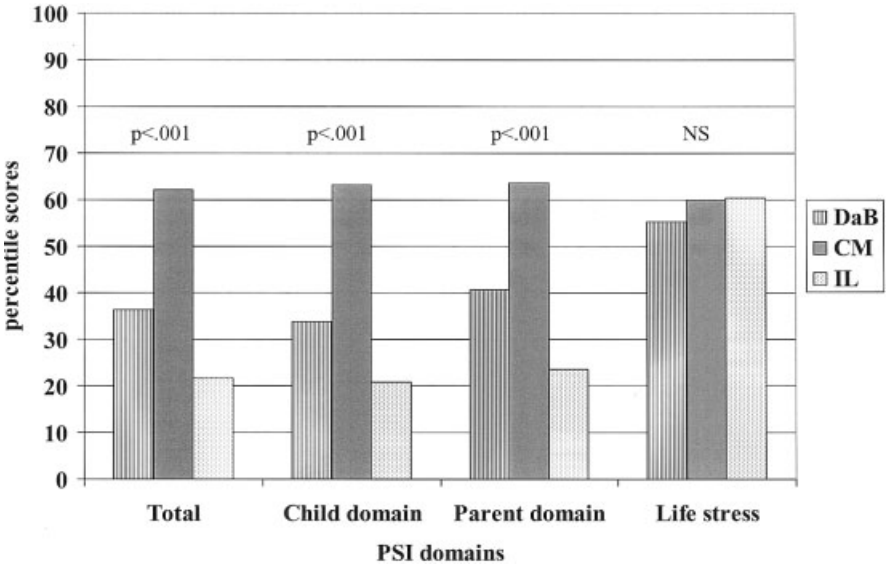

FIGURE 1. PSI percentile scores at 6 years as a function of antenatal IUGR management.

significantly more often in the CM group. It was most evident in the total stress score, where 30% of the CM group had scored higher than the 85th percentile cutoff level versus none in the IL group (Figure 2).

A similar distribution was found for most scales in the child domain, such that mothers in the CM group reported their children to be more distractible, more demanding, less adaptable, and exhibiting more mood swings than expected, and mothers had greater difficulty accepting them (Figure 3). Elevated scores in the child domain that are indicative of psychological referral (Figure 4) were noted significantly more often in the CM group, particularly with regard to

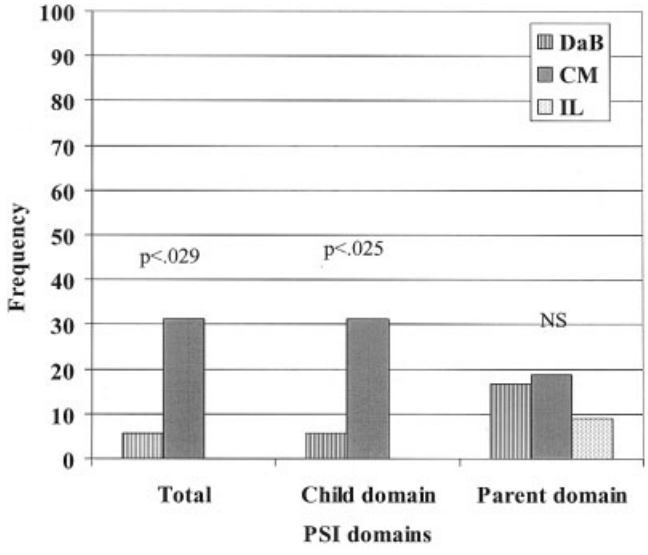

FIGURE 2. PSI percentile scores at 6 years in the abnormal range as a function of antenatal management.

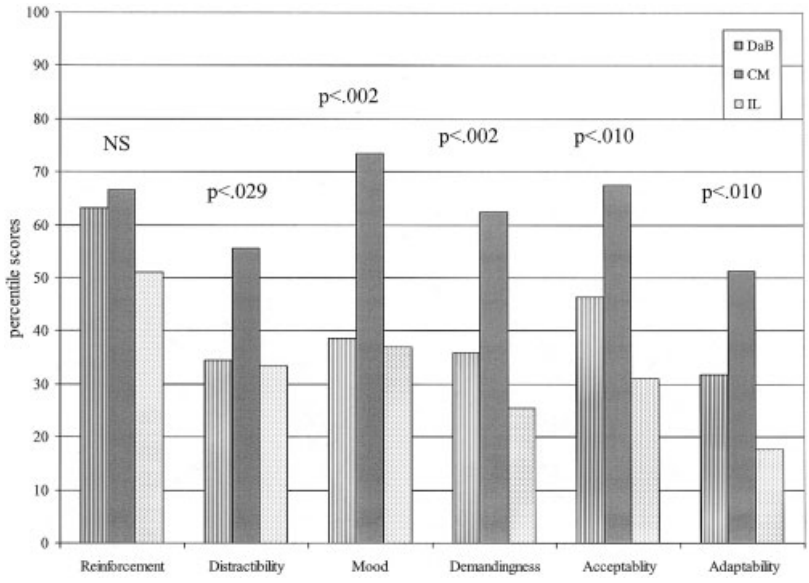

FIGURE 3. PSI child domain scores as a function of antenatal IUGR management.

stress evoked by the child's distractibility and demandingness symptoms. It was noted that the sole domain affected in the DaB group was the Reinforces Parent scale. About 40% of the parents in the DaB and the CM groups versus only 8% in the IL group experienced their children to be significantly less rewarding.

A regression analysis was conducted to find out whether some of the variance in maternal stress could be predicted based solely on fetal variables known to the mother antenatally. The

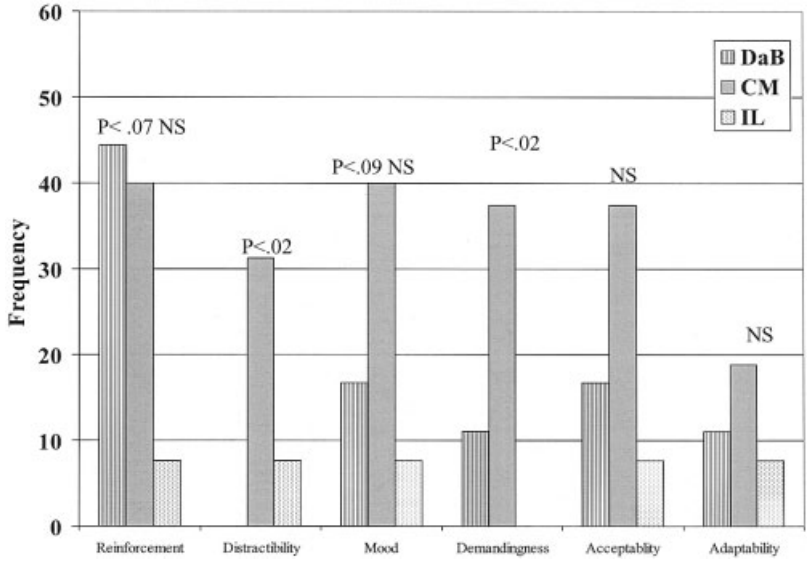

FIGURE 4. Frequency in percentage of child domain scores in the abnormal range as a function of antenatal IUGR management.

TABLE 2. *Regression for Fetal Antecedent Variables Known to the Mother Best Predicting Total Maternal Stress Levels at 6 Years*

Model	*Model Significance*	B	SE B	β	t	p <	*Adjusted* R^2
	.003						.16
(Constant)		223.34	77.76		2.87	.006	
Cephalization index		−23.35	12.04	−.30	−1.94	.057	
IUGR management		−31.90	8.45	−.46	−3.77	.000	
Estimated gestational age		−3.24	1.64	−.32	−1.97	.054	

IUGR = intrauterine growth restriction.

best predicting antecedent variables predicting maternal stress levels at 6 years are presented in Table 2.

The model comprised fetal variables available to the mother-to-be during pregnancy: the Cephalization Index (i.e., the ratio of HC to birth weight), IUGR management, and the estimated gestation age. It was found to be significant in predicting parental stress scores 6 years' postnatally. Regression for antecedent variables characterizing the family best predicting total maternal stress at 6 years was significant, but accounted for only 5% of the variance explained, and none of these variables predicted parental stress at 6 years (see Table 3).

The hierarchical regression model that combined antenatal and concurrent factors accounted for 49.1% of the variance explained (see Table 4). It includes hyperactivity, prenatal management, and child's concurrent anxiety-related symptoms as best predicting maternal stress at 6 years.

Note that stressful life events during the previous 12 months were in the upper normal range and were similar for all three IUGR groups, and thus cannot account for these group differences. Furthermore, analysis of variance with GA and maternal-education variables treated as covariates determined that neither GA nor maternal education contributed to the variance. In addition, the effects of parental age and the child's gender on all PSI variables did not emerge as contributing factors to outcome.

TABLE 3. *Regression for Antecedent Variables Characterizing the Family Best Predicting Total Maternal Stress Levels at 6 Years*

Model	*Model Significance*	p <	*Adjusted* R^2
	.055		.05
(Constant)		.001	
Maternal education		n.s.	
Maternal occupation		n.s.	
No. of children		n.s.	
Child's position in family		n.s.	

n.s. = nonsignificant.

TABLE 4. *Hierarchical Regression for Combined Antenatal and Concurrent Variables Best Predicting Total Maternal Stress Levels*

Model	*Model Significance*	B	SE B	β	t	p <	*Adjusted* R^2
Step 1	.000						.378
(Constant)		−40.40	16.86		−2.40	.021	
Hyperactivity Index		1.6	.30	.63	5.09	.000	
Step 2	.000						.443
(Constant)		−18.31	18.44		−.99	.327	
Hyperactivity Index		1.52	.31	.58	4.97	.000	
IUGR management		−21.20	8.88	−.28	−2.38	.022	
Step 3	.000						.491
(Constant)		−60.41	26.27		−2.30	.027	
Hyperactivity Index		1.22	.32	.47	3.78	.001	
IUGR management		−22.45	8.51	−.29	−2.64	.012	
Anxiety scale		1.13	.52	.26	2.16	.037	

IUGR = intrauterine growth restriction.

TABLE 5. *Hierarchical Regression for Concurrent Variables Best Predicting Total Maternal Stress Levels*

Model	*Model Significance*	B	SE B	β	t	p <	*Adjusted* R^2
Step 1	.000						.343
(Constant)		−39.41	15.61		−2.52	.015	
Hyperactivity Index		1.6	.30	.59	5.30	.000	
Step 2	.000						.449
(Constant)		−94.41	22.02		−4.28	.000	
Hyperactivity Index		1.26	.299	.46	4.24	.000	
Anxiety scale		1.41	.43	.36	3.28	.002	
Step 3	.000						.500
(Constant)		−123.87	24.15		−5.13	.000	
Hyperactivity Index		1.19	.28	.44	4.19	.000	
Anxiety scale		1.29	.41	.33	3.13	.003	
Psychosomatic scale		.77	.31	.24	2.46	.017	
Step 4	.000						.531
(Constant)		−137.61	24.27		−5.67	.000	
Hyperactivity Index		2.04	.49	.75	4.16	.000	
Anxiety scale		1.51	.41	.39	3.67	.001	
Psychosomatic scale		.84	.30	.27	2.74	.009	
Learning problem scale		−.83	.40	−.39	−2.08	.043	

Excluded variables: Conduct Problem scale and intelligence quotients.

Parental Stress at 6 Years as a Function of the Child's Outcome

To examine whether parental stress was related to concurrent cognitive and behavioral outcomes, hierarchical regression for concurrent variables best predicting total maternal stress levels is presented in Table 5.

Data presented in Table 5 show that stress was accounted for in part by concurrent behavioral outcome and was not related to cognitive aptitude. Of the behavioral outcome variables, the great majority, 34.4% of the variance in total maternal stress at 6 years, was accounted for by the Hyperactivity Index of the CPRS-48 followed by the additive contribution of the Anxiety scale, the Psychosomatic scale, and finally the Learning Problem scale, so that Step 4 accounts for 53.1% of the variance explained in maternal stress. Conducted problem and the intelligence quotients were the excluded variables.

Cognitive Outcome at 6 Years of Age as a Function of Antenatal Management of IUGR

Multivariate analysis of variance (MANOVA) of all WPPSI variables [scaled scores of all tests and the intelligence quotients (IQ)] was conducted with gestation age (GA) and maternal education as covariates. The analysis showed that the modes of management were not related to cognitive measures of children at 6 years of age. Note that there was a tendency for children in the IL group, considered a priori to be at the highest developmental risk, to experience more difficulties in solving mathematical problems than children in the other groups (Twenty-seven percent of the children in the IL group had subnormal scores on this test vs. 8 and 3% in the other IUGR groups, Pearson $\chi^2 = 5.8$, $p = .053$.)

Emotional and Behavioral Outcomes at 6 Years of Age as a Function of Antenatal Management of IUGR

Behavioral problems, reported on the CPRS-48, were similar among all the IUGR management groups. They also were not differentially related to a particular management protocol as indicated by ANOVA, except for a tendency to report more frequent and severe learning problems in children of the CM group, $F = 3.13$, $p = .06$. Mothers in the CM group reported more frequently high stress levels that required referral for consultation (i.e., >65th percentile) due to learning problems, Pearson $\chi^2 = 7.1$, $p = .028$. As expected, the learning-problem-related stress levels in all subjects correlated negatively with a wide array of cognitive measures of the WPPSI, including IQ and domain quotients (significant *r*s found in 7 of 10 WPPSI tests, *r*s = −.26–.48, *p*s = .02–.000). Overall, lower maternal education and lower paternal occupation were related to increased frequency of externalizing behavioral symptoms (i.e., Hyperactivity Index and the Conduct scale of the CPRS-48).

Individually Tailored Intervention Referrals

Thirty-one percent of the IUGR children diagnosed prenatally were referred to occupational therapy intervention programs. This rate tended to be higher than the 12.5% occupational therapy referral of IUGR children diagnosed postnatally; 11.9% of the prenatally diagnosed IUGR children were referred and/or admitted for psychological counseling versus none of the DaB IUGR children. No differences were found in other individually tailored paramedical intervention programs.

DISCUSSION

The main objective of the study was to determine which mothers-to-be of IUGR fetuses were at greatest risk for long-term stress: (a) mothers who discovered at birth, often without any forewarning, that their neonate suffered from IUGR in the womb (i.e., the DaB group); (b) mothers who knew of the growth difficulties in the early stages of pregnancy and were encouraged to undergo IL to avoid further risk on either fetus, mother, or both; or (c) mothers who knew of the IUGR condition during pregnancy and were prescribed bed rest (i.e., the CM group). Analysis showed that mothers in the CM group reported most often increased parental stress levels. This finding suggests that physical and emotional processes experienced by the mother-to-be subsequent to management of this condition are significant long-term contributors to maternal stress. This finding was unexpected and appeared counterintuitive since the IL group was originally thought to be at the highest developmental risk and potentially arousing the highest stress levels; however, CM related stress is supported by studies on short-term antenatal bed-rest effects on stress experienced by pregnant mothers. These studies showed that bed rest, because of its own special physical and psychological characteristics, compounds an already highly stressful pregnancy (Gupton, Heaman, & Ashcroft, 1997; Maloni et al., 1993). Maloni and colleagues (Maloni et al., 1993; Maloni & Kutil, 2000) found that women who were prescribed bed rest had more somatic complaints such as fatigue, indigestion, sleep disturbances, and weight loss. They also experienced increased anxiety, hostility, emotional lability, depression, and stress levels. Gupton et al. (1997) identified three types of antepartum stressors acting in the CM group: situational, environmental, and familial. Situational stress includes being cast in a "sick" role, lack of control, concern for fetal well-being, and being tired of waiting. Environmental stress includes feelings of isolation, boredom, and missing out on life. Familial stress is associated with role reallocation and anxiety about other siblings. Furthermore, in addition to physical, emotional, and familial stress, Schroeder (1996) found a correlation between CM and economic hardship due to reduced earnings and increased expenses of child care. Hence, stress may be related to the medical condition of the mother and/fetus and to the maternal adjustment process arising during pregnancy. Active medical interventions such as IL may play an important role in preventive augmentation of maternal stress. CM is efficient in conserving the child's cognitive and physical gross competencies; however, it may impose a heavy emotional burden on the mother-to-be, which is further hampered by the characteristics and difficulties of the IUGR infant, and possibly problematic mother–infant coregulation that evolves over the years.

Moreover, the data support the notion that stress was not related to absolute offspring size nor was it related to the timing of the diagnosis (i.e., a fetal maturational factor) but rather to management of the risk condition (i.e., CM/IL/DaB). Furthermore, it also was found that the timing of IUGR diagnosis does not in itself necessarily increase maternal long-term stress levels, evident by lack of variance between the DaB and the IL groups. Once IUGR is diagnosed, management protocol is an essential factor in determining long-term paternal stress levels.

The second objective of the study was to examine whether stress in mothers of IUGR children is related to the child's emotional-cognitive outcome. Of all the concurrent outcome variables, maternal stress was in part accounted for by the child's emotional and behavioral outcomes, mostly by hyperactivity which best predicted maternal stress followed by anxiety, psychosomatic symptoms, and learning difficulties. Furthermore, traces of the effects of CM are discernible years later and are only slightly related to the child's present cognitive competence. The study demonstrated that IUGR children who were prenatally diagnosed and received CM were exposed to significant parental emotional stress and were more inclined to

exhibit distractible behavior and poor emotional adjustment that required psychological and neurological management. The IUGR child was perceived by his or her CM-treated mother as exhibiting poor self-regulation of behavior. They described the children to be demanding, moody, distractible, and lacking in adjustability to changing conditions. These CM traces may reflect direct effects of prenatal experience and/or an additional interaction factor between maternal stress and her infant's development. These traces are present and are, as expected, limited. Hierarchical regression analysis that includes a range of possible predictors of long-term maternal stress, both antenatal variables known to the mother and concurrent variables reported by her, revealed that as expected the great majority of the variance is accounted for by the reports of child's concurrent behavioral symptoms (i.e., hyperactivity). However, IUGR management emerged as an additional significant factor (Table 5) even in the presence of multiple stress focuses currently perceived by the mother 6 years' postbirth.

Several trajectories may lead to this finding. One compelling explanation may be that antenatal mechanisms, poor mother–infant coregulation, and long-term maternal stress are linked and impact each other. According to this hypothesis, physiological chain reactions caused by long-term stress modify uterine environment, further undermine fetal development, and result in symptoms secondary to anxiety and stress that are evident in poor emotional reactivity, hyperactivity, and learning difficulties. This hypothesis may be further supported by the finding by Teixeira, Fisk, and Glover (1999) that antenatal maternal anxiety is associated with adverse changes in the uterine environment and by studies of long-term sequelae of early exposure to stress-related substances. Glover, Modi, and Stevenson (2004) recently showed that early exposure to high endogenous cortisol levels during pregnancy and shortly after birth has long-term effects so that hyperactivity and attention deficits may be potentiated as a response to toxic glucocorticoid exposure in utero and shortly after birth.

In view of the results, the question arises as to the possible effect of parental distress on parents' reports of their children's emotional and behavioral problems. Indeed, it has been shown that maternal depression and marital dissatisfaction (Forehand, Brody, & Smith, 1986) affect maternal perceptions of children's behavior; however, community-based epidemiological analysis of data from parents of 6-year-old children indicated that the effect of maternal distress on mothers' reports of children's emotional adjustment and behavior is negligible and accounts for 1% of the variance (Fergusson, Lynskey, & Horwood, 1993; Sawyer, Streiner, & Baghurst, 1998).

The third objective of the study was to determine whether cognitive and behavioral outcomes of IUGR children at 6 years of age were related to the various antenatal management procedures. The results showed that overall cognitive and behavioral outcomes of the three management groups of IUGR children were not related to management. This finding was in some ways unexpected since the IL group was originally thought to be the highest risk group and since the IUGR condition in the IL was diagnosed early and managed more aggressively; however, the children in this group eventually performed cognitively and behaviorally as well as the other IUGR groups. This reaffirms previous partial findings on a smaller sample size from the same cohort (Leitner et al., 2000) in respect to cognitive competence. Cognitive outcome of the IUGR children was typically within normal range. Furthermore, cognitive outcome of IUGR children was not found to be dependent upon either the timing of diagnosis (prenatal or neonatal) or on the mode of prenatal management (IL/CM). These findings fortify current custom-tailored antenatal and perinatal management of IUGR protocols for efficient prevention of gross long-term cognitive and behavioral disability (Leitner et al., 2000). Since the timing of diagnosis and management type were not related to cognitive outcome measures, cognitive competence cannot mediate maternal stress and behavioral outcome.

Maternal stress on various dimensions pertaining to the child's and the parent's domain correlates moderately well with concurrent child behavioral difficulties. From the mothers'

reports, it was established that families of low socioeconomic status and lower parental education have higher initial levels of externalizing symptoms. Furthermore, socioeconomic status also has a slight effect on the development of mother-reported externalizing behavior (Keiley, Bates, Dodge, & Pettit, 2000). The findings presented in the predictive model based on maternal and familial characteristics (Table 4) also may be viewed in light of the socioeducational-factor contribution (Dodge, Pettit, & Bates, 1994; Duncan, Brooks-Gunn, & Kebanov, 1994; Kramer, 1998; McLoyd, 1990; Ritter, Hobfoll, Lavin, Cameron, & Hulsizer, 2000).

In conclusion, inference of causality should be made with caution. We have shown that CM-treated mothers of fetuses with IUGR exhibited long-term stress while other investigators have shown that antepartum stress may interact with prenatal growth rate of the fetus (Diego, Field, & Hernandez-Reif, 2004; Sable & Wilkinson, 2000). Further study is warranted to determine the mechanism involved. One possible mechanism—a resetting in programming of the HPA axis in response to toxic levels of antenatal cortisol—has been recently proposed and needs to be studied further (Glover et al., 2004).

To summarize, data shown in this study may very well reflect the significance of the interaction between technological advances of the 1990s and parental resiliency. We suggest that this interaction is a significant factor in understanding long-term outcomes for both families and high-risk infants. The findings underscore the relationship between prenatal management of risk in pregnant women, diminished fetal growth, and long-term maternal stress, particularly when pregnancy is managed conservatively and emotional, familial, and educational resources are low.

Implications for Future Research

1. Long-term consequences of antenatal maternal anxiety and depression are not well understood (Glover et al., 2004; Teixeira et al., 1999). Future research should concentrate on prospective antepartum stress in mothers to-be of IUGR fetuses.
2. A study of antenatal and postnatal parental emotional adaptability, parental representations of their fetus, and stress responses as a function of management procedures would deepen the understanding of the mechanism involved in long-term stress (Chen, Tseng, Chou, & Wang, 2000), particularly with regard to mother–child relationships in the CM group.
3. An intervention study of CM in high-risk pregnancies is recommended to prevent long-term stress (Hernandez-Reif, Field, & Diefo, 2004; Ulman, 2000; Villar et al., 1992).
4. Further follow-up of the CM group into school age will permit examination of their behavioral outcome when required to cope with more demanding situations.

REFERENCES

Abidin, R.R. (1986). Parental Stress Index: Test manual. Charlottesville, VA: Pediatric Psychology Press.

Affleck, G., Tennen, H., Rowe, J., & Higgins, P. (1990). Mothers' remembrances of newborn intensive care: A predictive study. Journal of Pediatric Psychology, 15, 67–81.

Bernstein, I., & Gabbe, S.G. (1996). Intrauterine growth restriction. In S.G. Gabbe, J.R. Niebyl, J.L. Simpson, & G.J. Annas (Eds.), Obstetrics: Normal and problem pregnancies (3rd ed., pp. 863– 886). New York: Churchill-Livingstone.

Chen, C., Tseng, Y., Chou, F., & Wang, S. (2000). Effects of support group intervention in postnatally distressed women. A controlled study in Taiwan. Journal of Psychosomatic Research, 49, 395–399.

Conners, C.K. (1989). Manual for Conner's Rating Scales. N. Tonawanda, NY: Multi-Health Systems.

Creasy, R.K., & Resnik, R. (1994). Intrauterine growth restriction. In R.K. Creasy & R. Resnik (Eds.), Maternal–fetal medicine: Principles and practice (3rd ed., pp. 558–574). Philadelphia: Saunders.

Diego, M., Field, T., & Hernandez-Reif, M. (2004, May). Elevated cortisol as a risk factor for less optimal fetal growth. Symposium presented at the International Conference on Infant Studies, Chicago.

Dodge, K.A., Pettit, G.S., & Bates, J.E. (1994). Socialization mediators of the relation between socioeconomic status and child conduct problems. Child Development, 65, 649–665.

Doubilet, P.M., & Benson, C.B. (1995). Sonographic evaluation of intrauterine growth retardation. American Journal of Roentgenology, 164, 709–717.

Duncan, G.J., Brooks-Gunn, J., & Kebanov, P.K. (1994). Economic deprivation and early childhood development. Child Development, 65, 296–318.

Evans, J., Heron, J., Francomb, H., Oke, S., & Golding, J. (2001). Cohort study of depressed mood during pregnancy and after childbirth. British Medical Journal, 323, 257–260.

Fattal-Valevski, A., Leitner, Y., Geva, R., Bassan, H., Goez, H., Jaffa, A.J., & Harel, S. (2001). The effect of intrauterine growth restriction on the development and health of children. Nutrition & Health, 15, 169–175.

Fergusson, D.M., Lynskey, M.T., & Horwood, L.J. (1993). The effect of maternal depression on maternal ratings of child behavior. Journal of Abnormal Child Psychology, 21, 245–269.

Forehand, R., Brody, G., & Smith, K. (1986). Contributions of child behavior and marital dissatisfaction to maternal perceptions of child maladjustment. Behaviour Research and Therapy, 24, 43–48.

Glover, M., Modi, R., & Stevenson, N. (2004, May). Early exposure to high endogenous cortisol has long-term effects. Symposium presented at the International Conference on Infant Studies, Chicago.

Gupton, A., Heaman, M., & Ashcroft, T. (1997). Bed-rest from the perspective of the high-risk pregnant woman. Journal of Obstetric, Gynecologic, and Neonatal Nursing, 26, 423–430.

Hadlock, E. (1994). Ultrasound evaluation of fetal growth. In P. Callen (Ed.), Ultrasonography in obstetrics and gynecology (3rd ed., pp. 129–142). Philadelphia: Saunders.

Hay, W.W., Jr., Thureen, P.J., & Anderson, M.S. (2001). Intrauterine growth restriction. Neonatal Reviews, 2, 129–138.

Hernandez-Reif, M., Field, T., & Diego, M. (2004, May). Reducing pregnancy cortisol and prematurity. A symposium presented at the International Conference on Infant Studies, Chicago.

Keiley, M.K., Bates, J.E., Dodge, K.A., & Pettit, G.S. (2000). A cross-domain growth analysis: Externalizing and internalizing behaviors during 8 years of childhood. Journal of Abnormal Child Psychology, 28, 161–179.

Kramer, M.S. (1998). Socioeconomical determinants of intrauterine growth retardation. European Journal of Clinical Nutrition, 52, s22–s33.

Lapillone, A., Peretti, N., Ho, P.S., & Salle, B.L. (1997). Aetiology, morphology and body composition of infants born small for gestation age. Acta Paediatica, 423, 173–176.

Lee, M.J., Conner, E.L., Charafeddine, L., Woods, J.R., & Priore, G.D. (2001). A critical birth weight and other determinants of survival for infants with severe intrauterine growth restriction. Annals of the New York Academy of Sciences, 943, 326–339.

Leitner, Y., Fattal-Valevski, A., Geva, R., Posner, E., Jaffa, A.J., & Harel, S. (2000). A six-year follow up of children with intrauterine growth retardation: A long-term, prospective study. Journal of Child Neurology, 15, 781–786.

Lieblich, A. (1973). WPPSI—Wechsler Preschool and Primary Scale of Intelligence. WPPSI Manual [Hebrew version]. Jerusalem: Jerusalem Post Press.

Lobel, M., DeVincent, C.J., Kaminer, A., & Meyer, B.A. (2000). The impact of prenatal maternal stress and optimistic disposition on birth outcomes in medically high-risk women. Health Psychology, 19, 544–553.

Maloni, J., Chance, B., Zhang, C., Cohen, A., Betts, D., & Gange, S. (1993). Physical and psychosocial side effects of antepartum hospital bed-rest. Nursing Research, 42, 197–203.

Maloni, J.A., & Kutil, R.M. (2000). Antepartum support group for women hospitalized on bed-rest. American Journal of Maternal and Child Nursing, 25, 204–221.

McCormick, M.C. (1985). The contribution of low birth weight to infant mortality and childhood morbidity. New England Journal of Medicine, 312, 82–90.

McLoyd, V.C. (1990). Minority children: Introduction to the special issue. Child Development, 61, 311–346.

Mueller, C.W., & Parcel, T.L. (1981). Measures of socioeconomic status: Alternatives and recommendations. Child Development, 52, 13–30.

Pardi, G., Cetin, I., Marconi, A.M., Lanfranchi, A., Bozzetti, P., Farrazzi, E., Buscaglia, M., & Battaglia, F.C. (1993). Diagnostic value of blood sampling in fetuses with growth retardation. New England Journal of Medicine, 328, 692–696.

Queenan, J.T. (Ed.). (1994). Management of high-risk pregnancy (3rd ed.). Boston: Blackwell.

Ribbert, L.S., van Lingen, R.A., & Visser, G.H. (1991). Continuous maternal hyperoxygenation in the treatment of early fetal growth retardation. Ultrasound Obstetrics and Gynecology, 1, 331–336.

Ritter, C., Hobfoll, S.E., Lavin, J., Cameron, R.P., & Hulsizer, M.R. (2000). Stress, psychosocial resources, and depressive symptomatology during pregnancy in low-income, inner-city women. Health Psychology, 19, 576–585.

Sable, M.R., & Wilkinson, D.S. (2000). Impact of perceived stress, major life events and pregnancy attitudes on low birth weight. Family Planning Perspectives, 32, 288–294.

Sawyer, M.G., Streiner, D.L., & Baghurst, P. (1998). The influence of distress on mothers' and fathers' reports of childhood emotional and behavioral problems. Journal of Abnormal Child Psychology, 26, 407–414.

Schroeder, C. (1996). Women's experience of bed-rest in high-risk pregnancy. Image, 28, 253–258.

Singer, L.T., Salvator, A., Guo, S., Collin, M., Lilien, L., & Baley, J. (1999). Maternal psychological distress and parenting stress after the birth of a very low-birth-weight infant. Journal of the American Medical Association, 281, 799–805.

Teixeira, J.M.A., Fisk, N.M., & Glover, V. (1999). Association between maternal anxiety in pregnancy and increased uterine artery resistance index: Cohort based study. British Medical Journal, 318, 153–157.

Trudinger, B.J., Cook, C.M., Thompson, R.S., & Giles, W.B. (1988). Low-dose aspirin therapy improves fetal weight in umbilical placental insufficiency. American Journal of Obstetrics and Gynecology, 159, 681–685.

Ulman, K.H. (2000). An integrative model of stress management groups for women. International Journal of Group Psychotherapy, 50, 341–362.

Vandenbosche, R.C. (1998). Intrauterine growth retardation. American Family Physician, 58, 1384–1392.

Villar, J., Farnot, U., Barros, F., Victora, C., Langer, A., & Belizan, J.M. (1992). A randomized trial of psychosocial support during high-risk pregnancies. The Latin American Network for Perinatal and Reproductive Research. New England Journal of Medicine, 327, 1266–1271.

Waugh, J., & Kilby, M. (2001). Intrauterine growth restriction: Diagnosis and management. Hospital Medicine, 62, 214–221.

Wechsler, D. (1967). WPPSI—Wechsler Preschool and Primary Scale of Intelligence. WPPSI Manual.

New York: Psychological Corporation (Hebrew version: Lieblich, A. (1973). Jerusalem: Jerusalem Post Press.

Wells, J.D., & Hobfoll, S.E. (1999). When it rains, it pours: The greater impact of resource loss compared to gain on psychological distress. Personality and Social Psychology Bulletin, 25, 1172–1182.

Wereszczak, J., Miles, M.S., & Holditch-Davis, D. (1997). Maternal recall of the neonatal intensive care unit. Neonatal Networks, 16, 33–40.