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Original contribution

Multicentre prospective study of perinatal depression in Japan: incidence and correlates of antenatal and postnatal depression

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Summary

A multicentre study on the epidemiology of perinatal depression was conducted among Japanese women expecting the first baby (N = 290). The incidence rate of the onset of the DSM-III-R Major Depressive Episode during pregnancy (antenatal depression) and within 3 months after delivery (postnatal depression) were 5.6% and 5.0%, respectively. Women with antenatal depression were characterised by young age and negative attitude towards the current pregnancy, whereas women with postnatal depression were characterised by poor accommodation, dissatisfaction with sex of the newborn baby and with the emotional undermining. Antenatal depression was a major risk factor for postnatal depression.

Keywords: Antenatal depression; postnatal depression; epidemiology.

Introduction

Concerns for the mental health of women during pregnancy and after childbirth have promoted a series of investigations into perinatal depression. This is an issue concerning not only the women themselves but also children they look after (e.g., Murray & Cooper, 1997;

O'Connor et al, 2002, 2003). It has attracted attention from medical, nursing, social welfare and policy making perspectives. The incidence (O'Hara & Swain, 1996; O'Hara & Zekoski, 1988) and correlates (Austin & Lumley, 2002; Brugha et al, 2000; Buist et al, 1999; Cooper et al, 1996) of perinatal depression have been studied intensively in Western countries but very little in Asian countries. The classical study of Kumar & Robson (1984) reported about 10% of pregnant women experiencing the onset of depression during the current pregnancy. This finding was replicated in an interview study (Kitamura et al, 1993) as well as a large scale questionnaire survey (Kitamura et al, 1996b) in Japan. In contrast to the risk factor studies of postnatal depression, causes of antenatal depression have been little investigated (Kitamura et al, 1996a; Ross et al, 2004). Psychosocial correlates of antenatal depression have been reported by Kitamura et al (1993, 1996b) in Japan. However, these studies were conducted in a single hospital, and are thus

subject to selection bias. There is scarcity of reports about the incidence of postnatal depression in Japan.

This paper reports the incident and psychosocial correlates of antenatal and postnatal depressions among primiparous women in a nation-wide, multicentre, follow-up study in Japan. Like Kumar & Robson (1984), we used women who were expecting their first baby because we thought psychosocial environments would be substantially different between women who had and those who had not yet delivered babies. In addition, it would have been difficult to invite women with more than one child to visit a hospital at 3 months and 12 months after the delivery. The primary research question is the incidence of antenatal (during pregnancy) and postnatal (three months after delivery) depression in a Japanese female population. Despite many reports about the psychosocial correlates of perinatal depression in Western countries, we know little about them in Japan. Transcultural studies on perinatal depression such as the Transcultural Study of Postnatal Depression (TCS-PND: Asten et al, 2004) rarely include Japan. Thus the second aim of this study is to give a rough sketch of the psychosocial correlates of both antenatal and postnatal depressions in order to give perspectives to future studies.

Methods

Participants

Out of a total of 1159 women attending the antenatal clinics of the five university hospitals within a specified period (that differed between hospitals shown in brackets) – Saitama Medical School Comprehensive Medical Centre (June 1998 to October 1998), Mie University Hospital (May 1999 to January 2000), Okayama University Hospital (October 1997 to June 1999), Kyushu University Hospital (October 1997 to April 1999), and Ryukyu University Hospital (April 1999 to March 2000), 756 (65.2%) were expecting their first baby. Of these 756 pregnant women, 20 (2.6%) were planning to give birth in a clinic other than the university clinic they were currently attending and thus were excluded from the study. We solicited participation in the follow-up study of mental health related to pregnancy and childbirth to the remaining 736 women. Of these 433 (58.8%) declined while 303 (41.2%) agreed to do so. However, 13 of these 303 women failed to be followed up in the subsequent interviews thus leaving 290 women for examination. As compared to the other women expecting their first baby ($n=466$), these 290 women did not differ in terms of marital status (married vs. single), education, and the time of menarche. However, the participating women were more likely to be employed (35.7% vs. 25.6%, $P<0.01$). The majority of women (277, 96%) were married and living with their spouses, whereas seven women (2%) were married but not living with their spouses and six (2%) were single. About half of the women (42%) had a full-time job while 20% of them had a part-time job and 38% were home makers.

Antenatal depression group vs. antenatal control group: Of the above 290 women, three were excluded from the statistical analyses of identification of risk factors of antenatal depression because they had been suffering from Major Depressive Episode (MDE) when they became pregnant and one was excluded because she had a longstanding history of schizophrenia. Further analyses about antenatal depression were performed for these 286 women.

Postnatal depression group vs. postnatal control group: Of the above 290 women, nine were excluded from the statistical analyses because they were suffering from MDE when they gave birth and one was excluded because she had a longstanding history of schizophrenia. Further analyses about postnatal depression were performed for these 280 women.

Data collection

After obtaining informed consent, one midwife was dispatched to each woman as the responsible midwife. The interview was conducted by the same midwife in late pregnancy, and 1 month, 3 months and 12 months after childbirth. During each interview, a set of questionnaires was distributed to the participating women. The information regarding the husband was thus obtained from the woman.

Instruments

Psychiatric diagnoses: The midwives conducted an *ad hoc* structured diagnostic interview to compile a manual like the Diagnostic and Statistical Manual for Psychiatric Disorders (3rd ed. revised) (DSM-III-R; American Psychiatric Association, 1994). This interview guide was developed as a short structured interview for psychiatric disorders often observed during pregnancy and after childbirth – Major Depressive Episode, Dysthymic Disorder, Manic Episode, Hypomanic Episode, Panic Disorder, Generalized Anxiety Disorder, Agoraphobia, Social Phobia, Specific Phobia, and Obsessive Compulsive Disorder, and suicidal behaviour. Some of the wordings of questions used followed a Japanese draft of the Composite International Diagnostic Interview (World Health Organization, 1990) and the Schedule for Affective Disorders and Schizophrenia (SADS: Endicott & Spitzer, 1978). Although Agoraphobia is not a codable disorder of the DSM-III-R, this interview enables diagnosable Panic Disorder with Agoraphobia and Agoraphobia without history of Panic Disorder by combining the chronological data. It covers not only present but also past episodes when used in late pregnancy. In the subsequent interviews, the questions cover the time frame since the previous interview. When an interview was missed (e.g., the one three months after the delivery), its subsequent interview (e.g., the one 12 months after the delivery) covers the time frame since the last interview but one (e.g., the duration since one month postnatally to the time of the 12-month interview). When a psychiatric episode was identified, the interviewer questioned the onset of each episode. The interviewing midwives were lectured and trained by one of us (T.K.) in a series of lectures and by role playing. Using 29 case vignettes of different types of psychiatric disorders, we examined the midwives' agreement (kappa coefficient, Cohen,

1960) with the diagnoses made by the expert as moderate to almost perfect (0.64 to 0.83).

Demographic variables: We examined the ages of the women and their husbands, their education (1, elementary; 2, junior high school; 3, high school; 4, college; 5, university; 6, Master degree or over), and their annual income.

Marital condition: In the late pregnancy questionnaire we measured the women's marital status (single, married but living separately, and married and living together), the age when married, and single question items tapping marital satisfaction (1, very dissatisfied; to 5, very satisfied) and marital agreement (1, rarely; to 5, almost always). In addition, we included the Intimate Bond Measure (IBM, Wilhelm & Parker, 1988), a self-report measure assessing the current intimate relationship with the spouse in terms of two subscales – care and control. Each subscale consists of 12 items. The care and control correspond to the care and overprotection of perceived rearing respectively measured by the Parental Bonding Instrument (PBI; Parker et al, 1979). Psychometric properties of the IBM (Wilhelm & Parker, 1988) and its Japanese version (Inomata, 1994) were reported.

Accommodational condition: In the late pregnancy questionnaire the woman was asked whether she lived in rented accommodation (rented house or flat), the degree of satisfaction with her accommodation (1, very satisfied; to 5, very dissatisfied), whether she felt that the accommodation would be crowded after the birth of the child (1, never; to 3, very much so), and whether she planned to go back to the home of origin after childbirth (*Satogaeri*). Because the first three variables were substantially correlated with each other, we added the Z-score transformed scores of them as a new variable Poor Accommodation. We treated *Satogaeri* separately because it reflects the Japanese cultural characteristic of baby rearing.

Occupational condition: The woman was also asked in the late pregnancy questionnaire about her current job (home maker vs. part-time worker vs. full-time worker) and, if working, her plan for employment after childbirth (continue working vs. return to work when the child had grown up vs. relinquish the job for good). In the questionnaire 3 months after the delivery, we asked how many days a week the women and husbands respectively spent on home making and, separately, the time spent on home making before and after the birth of the child.

Obstetric variables: The numbers of pregnancies, abortions, still births, and termination of pregnancies and the menarche age were enquired about in the late pregnancy questionnaire. A single item (Sugawara et al, 1997) examined the presence and degree of premenstrual tension with a 4-point scale (1, always; to 4, never). Psychological response to the current pregnancy was examined for the woman and husband separately. The woman was asked if the sex of the baby was important (definite sex vs. "either will do"). The woman was also asked whether she had desired the pregnancy. In the late pregnancy questionnaire, the preparedness and readiness to be a mother was measured in terms of participation in a maternity class (group), taking maternity lessons (individual), use of telephone consultation, maternity-bics/maternity swimming, conversation with other pregnant women, books about pregnancy/child rearing, having heard about maternity blues and postnatal depression, confidence in pregnancy (1, very weak; to 4, strong), and past experience of holding a baby of another woman (1, never; to 4, many times). Healthy living during pregnancy was also

asked about in the questionnaire and dealt with drinking (number of times per week) and smoking (number of cigarettes per day).

Social support, coping, and life events after the delivery: Barrera (1986) distinguished between the functional aspects of social relationships and divided them into (1) perceived support (i.e., the perception that social support would be available should an individual desire it) and (2) received support (i.e. actual enactment of social support). Perceived social support includes both availability and satisfaction. In the late pregnancy questionnaire, the number (total number of people available and, if so, who they are) and satisfaction (1, dissatisfied; to 4, satisfied) of perceived social support were measured in terms of the three domains – emotional, informational and instrument supports. In the questionnaire three months after the delivery we asked about the amount and satisfaction (dissatisfaction) of enacted social support, social undermining, and disappointment about support (absence of expected support when it was needed) in three domains – emotional, informational and instrumental.

The coping style was measured by 14 items from the Ways of Coping Check List (WCCL; Folkman & Lazarus, 1980) selected according to Kendler et al (1991). The WCCL has three subscales – turning to others, problem solving and denial.

In the questionnaire three months after delivery the woman was asked as to whether she had experienced each of 45 different events for the one-month period after delivery. These include somatic conditions (e.g., insomnia and pain), changes of life pattern (e.g., relocation and *Satogaeri*), physical changes (e.g., obesity), financial difficulties (e.g., excessive expenses), families and in-laws (e.g., attitudes of in-laws), extra-familial relationships (e.g., hobbies), occupation (e.g., change of job content), child-rearing (e.g., difficulty in feeding), baby (e.g., infection), and others. If they reported having experienced any of them, they were further asked to rate the impact of each event either in positive (desirable) or negative (undesirable) deprecation from 0 to 100. The positive and negative event scores were calculated by adding all the positive and negative scores respectively.

Early parental loss, perceived rearing, and child abuse: Early parental loss was defined as either death of or separation from a parent for 12 months or longer before the subject was 16 years of age (Brown et al, 1987).

Perceived parenting was measured by the Parental Bonding Instrument (PBI; Parker et al, 1979). This is to assess retrospectively the perceived parental rearing before the subject was 16 years of age. The PBI is a self-report of 25 items with a 4-point scale anchored from 1: very likely to 4: very unlikely. The PBI consists of two subscales – care and overprotection. The care score indicates how affectionate the parent was towards the child whereas the overprotection score indicates what control the parent exercised over the child's activities and decisions. The reliability and validity was reported for both English (Parker, 1981, 1983) and Japanese versions (Kitamura & Suzuki, 1993). The participants who had reported parental loss before 16 years of age were excluded from the analyses using the PBI because they might have found it difficult to describe parental behaviour for such a short period.

In the late pregnancy questionnaire the woman was asked whether she had experienced any of eight categories of abusive behaviour on the part of the father or the mother before the age of 16: They include (a) emotional neglect; e.g., saying "you are

not my child"; (b) threat; e.g. of not giving meals and destroying cherished pets or toys; (c) shamed; e.g. scolding cruelly and making fun of the child in front of others; (d) slapping; (e) punching with a fist; (f) hitting with an object; e.g. a club; (g) kicking; and (h) burning; e.g. with a cigarette. Each category of abusive behaviour was rated for its frequency (when it was most frequent) from both parents separately with a 6-point scale; 1: never, 2: once or twice in the lifetime, 3: several times a year, 4: several times a month, 5: several times a week, and 6: almost everyday. The father's and mother's abuse scores were calculated by adding the scores of these eight abuse categories.

Past life events: The woman was questioned as to whether she had experienced each of the 28 different events during her lifetime. The list of life events includes 12 items that Brugha et al (1985) recognized as most likely to precede depression as well as other items we thought appropriate in the Japanese cultural setting. If a woman reported having experienced any of them, she was further asked how many times they occurred as well as how old she was when the event occurred.

Social desirability: Because the recall of past experiences may be subject to the response style of the subject towards socially acceptable bias, the Social Desirability Scale (SDS; Crowne & Marlowe, 1960; Kitamura & Suzuki, 1986) was administered as part of the questionnaire. We selected ten items appropriate for a Japanese population (Kitamura & Suzuki, 1986).

Statistical analysis

In order to identify risk variables of antenatal and postnatal depression, we compared those women who developed DSM-III-R MDE during the current pregnancy (antenatal depression

group, $n = 16$) and within three months after the delivery (postnatal depression group, $n = 14$) with those who did not (control groups, $n = 270$ antenatally and $n = 266$ postnatally) in terms of the demographic, marital, accommodational, occupational, obstetric, social support, coping and early life experiences. Because of the multiple comparisons we performed, we set the statistical significance level at the alpha value of 0.05 divided by the number of items of each domain. For example, because we studied a total of 28 types of past life events, we set the significance level of this domain at $P < 0.002$ ($0.05/28$). Only a few women had missing values for several variables (the number of the participants is noted in Tables where there are missing data). The mean SDS score did not differ between antenatal depression (16.9 SD = 4.0) and its control groups (16.2 SD = 3.1) nor between postnatal (16.0 SD = 4.4) and its control groups (16.2 SD = 3.1).

Results

Antenatal and postnatal depression

During the present pregnancy period, 16 (5.5%) women had an onset of MDE, 12 (4.1%) of Depressive Disorder Not Otherwise Specified, 0 (0%) of Manic Episode, 8 (2.8%) of Generalized Anxiety Disorder, 0 (0%) of Panic Disorder, 1 (0.3%) of Social Phobia, and 2 (0.7%) of Specific Phobia, and 2 (0.7%) of Obsessive Compulsive Disorder. A total of 35 (12.1%) women reported having an onset of any of the above disorders. The incidence of antenatal depression was 5.6% (16/286).

Table 1. Demographic variables, accommodational conditions, and response to the current pregnancy in the antenatal and postnatal depression groups and their control groups

	Antenatal			Postnatal		
	Control ($n = 270$)	MDE ($n = 16$)	<i>P</i> T-test or chi-squared	Control ($n = 266$)	MDE ($n = 14$)	<i>P</i> T-test or chi-squared
Demographics						
Age	29.7 (4.7) ($n = 263$)	26.1 (4.0)	0.003	29.7 (4.8) ($n = 259$)	27.3 (4.0)	0.069
Husband's age	28.7 (5.0) ($n = 262$)	25.9 (3.4)	0.030	28.6 (4.9) ($n = 258$)	27.1 (5.0)	0.266
Age when married	26.7 (3.9) ($n = 262$)	24.5 (3.9)	0.030	26.7 (4.0) ($n = 258$)	24.7 (3.2)	0.068
Accommodational condition						
Poor accommodation	-0.05 (2.17)	0.88 (2.07)	0.096	-0.09 (2.15)	1.79 (2.13)	0.002
Response to the current pregnancy and delivery						
Own negative attitude towards the pregnancy	14/262 (5.3%)	4/15 (26.7%)	FE = 0.011	14/257 (5.4%)	3/14 (21.4%)	FE = 0.049
Husband's negative attitude towards the pregnancy	15/260 (5.7%)	2/15 (13.3%)	FE = 0.235	15/255 (5.9%)	1/14 (7.1%)	FE = 0.585
The current pregnancy not desired	63/262 (24.0%)	6/15 (40.0%)	0.279	87/260 (33.5%)	9/14 (64.3%)	0.040
Woman's dissatisfaction about the sex of baby	-	-	-	39/217 (18.0%)	6/11 (54.5%)	0.010
Husband's dissatisfaction about the sex of baby	-	-	-	174/215 (80.9%)	7/11 (63.6%)	FE = 0.236

FE, Fischer exact probability test; () percentage or S.D.

After delivery, 14 (4.8%) women had an onset of MDE, 14 (5.0%) of Depressive Disorder Not Otherwise Specified, 1 (0.3%) of Manic Episode, 2 (0.7%) of Generalized Anxiety Disorder, 3 (0.1%) of Panic Disorder, 1 (0.3%) of Social Phobia, and 2 (0.7%) of Specific Phobia, and 5 (1.7%) of Obsessive Compulsive Disorder. Thirty-four (11.7%) women reported experiencing the onset of any of the above disorders. The incidence of postnatal depression was 5.0% (14/280).

Demographics

Women in the antenatal depression group were significantly younger than those in its control group (Table 1). The husbands of the antenatal depression group were also significantly younger than those husbands in the control group. As expected, the mean age of the women when they married was younger in the antenatal depression group. The level of education of the women and their husbands did not differ between the antenatal depression group and its control group. Nor did the mean annual income differ between the two.

Unlike those women with antenatal depression, women in the postnatal depression group did not differ from those in its control group in terms of their age and that of their husband when married, the women's and their husbands' level of education, or the annual income (Table 1).

Marital condition

The antenatal depression and control groups did not differ in terms of the marital condition (married and living with spouses, married but not living with spouses, and single), two subscales of the Intimate Bond Measure, or two subscales of the marital adjustment. This was also the case for the postnatal depression.

Accommodational condition

The women in the antenatal depression group lived in poorer accommodation than the control women but this did not reach statistical significance. About half of the women (55%) of the control group planned *Satogaeri* (going to the home of origin after childbirth) and a similar proportion of women of the antenatal depression group (69%) did so.

Unlike the antenatal depression group, the mean poor accommodation score was significantly higher in the women in the postnatal depression group than its control group (Table 1). The proportion of *Satogaeri* did not differ between the two groups.

Occupational condition

The antenatal depression and control groups did not differ in terms of their occupational conditions (full-time vs. part-time workers vs. home maker). Among the full-time and part-time workers, 75 (42%) planned to continue working after childbirth; 76 (43%) planned to return to work when the child had grown up; and 27 (15%) planned to relinquish their job in order to take care of the child. The proportion of those choosing to work after childbirth did not differ between the two groups. These findings were also the case for postnatal depression.

Obstetric variables

The experiences and numbers of past pregnancies, abortions, still births, and termination of pregnancy, menarche age, or premenstrual tension did not differ between antenatal depression and control groups or between postnatal depression and control groups.

The rate of the woman's negative attitude towards the current pregnancy (i.e., perplexed vs. glad/no feeling) was significantly higher in the antenatal group than the control group (Table 1). This was not the case for postnatal depression. The rate of husbands' negative attitude towards the current pregnancy or the unwanted pregnancy did not differ either between antenatal depression and its control groups, or between postnatal depression and its control groups (Table 1).

The difference in parental education and readiness for motherhood, the rate of alcohol consumption or smoking did not differ between antenatal depression and control groups or between postnatal depression and control groups.

Regarding the current delivery, the women in the postnatal depression group were more likely to be dissatisfied with the sex of the newborn baby (Table 1). In contrast, their husbands did not differ between the two groups in terms of dissatisfaction with the sex of the newborn baby. The two groups did not differ in terms of the mode of delivery (spontaneous vs. Caesarean vs. others), the number of babies born (singleton vs. twins vs. triplet), delivery time, blood lost, or subjective severity of delivery.

Social support, coping behaviour, and life events after delivery

Antenatal depression and control groups did not differ in terms of the number of individuals who could give three

Table 2. Social support, coping behaviour, and postnatal life events in the antenatal and postnatal depression groups and their control groups

	Antenatal			Postnatal		
	Control (n = 270)	MDE (n = 16)	P T-test or chi-squared	Control (n = 266)	MDE (n = 14)	P T-test or chi-squared
Satisfaction with social support during pregnancy						
Emotional support	3.5 (0.6) (n = 260)	3.6 (0.5) (n = 15)	0.245	3.5 (0.6) (n = 255)	3.6 (0.7)	0.816
Informational support	3.5 (0.6) (n = 259)	3.6 (0.5) (n = 15)	0.470	3.5 (0.6) (n = 254)	3.6 (0.6)	0.486
Instrumental support	3.4 (0.7) (n = 260)	3.4 (0.9) (n = 15)	0.982	3.4 (0.7) (n = 255)	3.4 (0.8)	0.884
Life events (LE) after childbirth						
Total positive LE score	–	–	–	346.1 (408.3)	240.4 (293.3)	0.340
Total negative LE score	–	–	–	–419.3 (402.6)	–636.5 (638.3)	0.229
Satisfaction with social support after childbirth						
Emotional support	–	–	–	3.5 (0.8) (n = 214)	3.2 (0.8) (n = 11)	0.162
Informational support	–	–	–	3.5 (0.7) (n = 212)	3.6 (0.7) (n = 11)	0.695
Instrumental support	–	–	–	3.6 (0.6) (n = 214)	3.2 (1.0) (n = 11)	0.175
Satisfaction with social undermining after childbirth						
Emotional undermining	–	–	–	3.4 (1.1)	2.4 (1.3)	0.001
Informational undermining	–	–	–	3.4 (1.2)	3.1 (1.3)	0.381
Instrumental undermining	–	–	–	3.4 (1.0)	3.3 (1.0)	0.656
Coping styles after childbirth						
Turning to others	–	–	–	6.7 (3.5) (n = 207)	7.9 (2.4) (n = 11)	0.276
Problem solving	–	–	–	6.6 (3.6) (n = 204)	6.3 (3.4) (n = 11)	0.761
Denial	–	–	–	6.7 (3.1) (n = 209)	5.9 (2.1) (n = 11)	0.385

FE, Fischer exact probability test; () percentage or S.D.

types (emotional, informational, and instrumental) of support when necessary (perceived social support) and their satisfaction.

The mean total scores of both the positive and negative life events occurring for the one month period after childbirth showed no difference between the postnatal and control groups (Table 2).

After childbirth, the women in the postnatal depression group did not differ from those in its control group in terms of the number and satisfaction of all the three types of enacted social support, social undermining, or disappointment except for the (dis)satisfaction of the emotional undermining. Thus, those women in the postnatal depression group were more likely to be dissatisfied with the emotional undermining (Table 2). Postnatal depression women did not differ from the control group women in terms of the use of any of the enacted coping behaviour categories.

Early parental loss and perceived rearing

The rate of the father's or mother's death, or separation of 1 month or longer, or one year or longer before the age of 16 did not differ between antenatal depression

and control groups. The father's or mother's PBI and abuse scores did not differ between the antenatal and control groups. This was also the case for postnatal depression.

Past life events

Among 27 life events, the rate of women who experienced a death of a sibling was 3.0% (8/270) in the control group whereas it was 18.8% (3/16) in the antenatal depression group. This, however, did not reach statistical significance.

The rates of women who had experienced peer victimization, hospitalization and death of a sibling were higher among the women with postnatal depression than among the control women, but they failed to reach statistical significance.

Past of psychiatric disorders

Because the number of some of the past episodes of DSM-III-R categories was very small in the 290 women, we combined for the purpose of comparison with the antenatal and postnatal depression the cases of Panic

Disorder ($n=7$), Generalized Anxiety Disorder ($n=19$), and Obsessive Compulsive Disorder ($n=9$) as Non-phobic Anxiety Disorder ($n=31$), Major Depressive Disorder ($n=44$) and Dysthymic Disorder ($n=3$) as Depressive Disorder ($n=47$), Manic Episode ($n=5$) and Hypomanic Episode ($n=2$) as Manic/Hypomanic Disorder ($n=7$), and Agoraphobia ($n=9$), Social Phobia ($n=4$), and Specific Phobia ($n=32$) as Phobic Disorder ($n=39$). It should be noted that there are some women who experienced episodes of more than one DSM-III-R categories.

The rate of any of the past DSM-III-R groups did not differ between the antenatal depression and control groups. More women in the postnatal depression group ($5/14=35.7\%$) reported having experienced an episode of Phobic Disorder than the women in the control group ($33/266=12.4\%$) but this barely failed to reach statistical significance ($P=0.028$).

The antenatal depression as a risk factor of the postnatal depression

Among the women ($n=14$) who developed postnatal depression 4 (28.6%) had experienced antenatal depression during the current pregnancy while 7 of 266 (2.6%) of the women without postnatal depression did so (Fischer exact probability = 0.001).

Discussion

The incidence of antenatal depression was 6% in this study. The rate of depression during pregnancy varied in the past investigations between 2.6% and 27.6% possibly due to the differences in the definition of depression (O'Hara et al, 1988). Using the DSM-III criteria of Major Depression Cutrona (1983) reported a rate of 3.5% but this study covered only the third trimester. More data may be needed for the rate of antenatal depression and its timing during the pregnancy when considering its aetiology and treatment. The findings that approximately six percent of women expecting the first baby would have a new episode of Major Depression during the current pregnancy echoes the reports of past investigations (Kitamura et al, 1993, 1996b; Kumar & Robson, 1984). Popular belief that pregnancy represents a period of happiness and joy was not supported in Japan either. More attention should be given to mental health intervention for such women. In Japan it is still exceptional rather than routine care to dispatch a responsible midwife to a pregnant woman. Taking into account that psychological intervention can prevent the onset of post-

natal depression (Jané-Llopis et al, 2003 for review), we will have to conduct a vigorous study about whether individualised psychological care by a midwife can alleviate negative affectivity of pregnant woman.

A negative attitude towards a current pregnancy is a risk factor for antenatal depression as has been ascertained in previous investigations. Obviously, an unwanted or unplanned pregnancy may represent a greater negative stressful event for women (While, 1990). Of clinical importance is that these women are shocked by the news of pregnancy and yet still plan to give birth to the baby. A very high rate of elective abortion among Japanese women suggests that they have "free hand" to do so. Thus the attitude of the women in this study may be very ambivalent. Some women may have desired a baby but the timing of the pregnancy may have been premature (for example, they might have wanted to continue their job a little longer). Alternatively, they may not have desired a baby but the unexpected news of pregnancy may have elicited subtle coercion from the people who wanted a baby (e.g., in-laws). Even women who choose abortion need mental health support (Kishida, 2001; Major et al, 1998, 2000; Soderberg et al, 1998; Turell et al, 2002). Women who did not desire pregnancy yet who are determined to give birth may need even more psychological support from perinatal health professionals.

The incidence of postnatal depression in this study was 5%. This seems to be lower than that reported in western countries (Cooper & Murray, 1998; O'Hara & Zekoski, 1988). However, another 5% of women had an episode that met the criteria of MDE partially but failed to do so. This is categorised as Depressive Disorder Not Otherwise Classified according to the DSM-III-R. Past investigations occasionally used a definition of postnatal depression that may be more over-inclusive. For example, using the Research Diagnostic Criteria (RDC: Spitzer et al, 1978), Kumar & Robson (1984) and O'Hara et al (1984) reported about 10% to 15% of incidence of both Major and Minor Depressive Disorders. The RDC Major Depressive Disorder corresponds to the DSM-III-R Major Depressive Episode and the RDC Minor Depressive Disorder (of a duration as short as a few weeks) to the DSM-III-R Depressive Disorder Not Otherwise Classified. Therefore, we consider that the incidence of postnatal depression reported in our study was compatible with that reported in the previous investigations.

Poor accommodation was found to be a risk factor for antenatal depression. This variable consists of rented accommodation, dissatisfaction about accommodation,

and feeling that the accommodation will be crowded after the birth of the child. Using Japanese pregnant women, Kitamura et al (1993, 1996b) reported that rented accommodation was linked to the onset of antenatal depression. The actual housing condition may affect mental health (Booth & Cowell, 1976; Kellet, 1989; Magaziner, 1988; Platt et al, 1989). Women expecting a baby may wish to rearrange and decorate the rooms as they desire but this can be done only when they live in their own house or flat. This interpretation may be supported by the findings of no difference between the postnatal and its control groups in terms of the number of people living together.

The association between unhappiness about the sex of the newborn and postnatal depression was a unique finding of this report. This may be an aspect of mixed feelings on the part of the women towards the pregnancy and the newborn baby. In bivariate analyses, postnatal depression was, though not reaching a statistical significance level, linked to the women's negative attitude towards current pregnancy, and undesired pregnancy (Table 1). Thus such women, though they continued their pregnancy up to childbirth, had an ambivalent feeling towards pregnancy. Kumar (1982) listed the "mixed feelings and worries about baby" as a correlate of postnatal depression. Dissatisfaction about the sex of the newborn baby may be a reflection of refusal of the baby, resulting in bonding failure. We did not measure bonding failure in these women. Future studies should focus on the relationship between the bonding failure and postnatal depression.

Although there were no differences between postnatal depression and control women in the negative life events or coping behaviour, the women with postnatal depression were more likely to be dissatisfied with the social *undermining* while the two groups did not differ in the degree of social *support*. Compared with the women without depression these women may be more sensitive to negative interpersonal approaches. The effects of social undermining has been studied less than those of social support but recent investigations have emphasized the importance of social undermining on psychological adjustment (Burg et al, 1994; Lakey et al, 1994; Lepore, 1992; Riemsma et al, 2000; Symister & Friend, 2003; Vinokur & Van Ryn, 1993).

A risk factor for postnatal depression in this study was antenatal depression. Past experiences of depression were reported as a risk factor for postnatal depression (Areias et al, 1996; Verkerk et al, 2003). Antenatal depression was also reported as a risk factor for post-

natal depression (Hobfoll et al, 1995; Verkerk et al, 2003). These and our results on the risk factor for postnatal depression are in line with the fact that past experience of the disorder is a well known risk for depression in general. Nevertheless, the risk factors related to antenatal depression (rented accommodation and negative response towards the current pregnancy) were not identical with those related to postnatal depression. Thus, though women with depression during pregnancy are more vulnerable to (re)develop depression after childbirth, there may be some other factors putting them at higher risk. Ross et al (2004) reported that the biopsychosocial model predicting the onset of antenatal depression failed to predict the onset of postnatal depression. Risks factors specific to the time of the onset of perinatal depression may be a very important topic in future studies.

Considering the prevalence of perinatal depression, health professionals caring for pregnant women should pay more attention to the mental health issues and establish a more systematic mental health support and care system. It may not be psychiatrists or obstetricians but midwives and antenatal clinic nurses that should take such responsibility. They have the advantage of easy access to pregnant women and are thus in a position to provide them with psychological support. Because their graduate and postgraduate education places greater emphasis on somatic care, there should be a shift towards providing a knowledge of perinatal mental illnesses and teaching therapeutic skills such as psychotherapy and counselling techniques (Stuart et al, 2003).

Methodological drawbacks may merit consideration. Although this is a prospective follow-up study, it commenced in late pregnancy; thus, the recall of symptoms in the first trimester is a subject of recall bias. Because antenatal depression is more likely to have its onset in the first trimester (Kitamura et al, 1993), our research design was subjected to the bias of the mental condition on the response style to the questionnaire. Therefore the results related to antenatal depression call for great caution in interpretation. Secondly, we studied only women who were expecting their first baby. Therefore the findings cannot be generalised to women with children. Thirdly, the number of women studied was relatively small. A larger population should be investigated in order to confirm the present findings. Fourthly, the representativeness of the sample may be questioned because although widespread over the country, the participating antenatal clinics were all affiliated with medical schools. Future studies should include women attending non-

university antenatal clinics. Finally, our study failed to examine the interactions between variables on the onset of perinatal depression. With a larger number of participants, we will approach this issue using a multivariate analysis such as the structural equation modelling techniques (e.g., Bernazzani et al, 1997; Ross et al, 2004).

In short, this study has shown that among Japanese women, both antenatal and postnatal depression was as prevalent as reported in Western countries and that they are associated with different psychosocial correlates.

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双胎妊娠

—母体妊娠前BMI, 妊娠中体重増加率と児出生体重との相関—

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双胎妊娠における至適な母体体重増加を明らかにするため、母体の妊娠前BMI, 妊娠中体重増加率と児の出生体重との相関について解析した。低出生体重児を生まないための母体の体重増加率について、単胎妊娠におけるような明確な情報を導き出すことは困難であった。しかし、少なくとも妊娠前BMIが正常ないし肥満に属する妊婦については、低出生体重児、さらには2,000 g未満の児を生まないための母体体重の管理に有用な情報が得られたと思われる。

たがって、日本人の双胎妊娠における適正な母体体重増加を明らかにするためには、日本人を対象とした検討が必要と考えられるが、そのような報告はいまだ見当たらない。

本研究では、双胎妊娠における至適な母体体重増加を明らかにするため、母体の妊娠前BMI, 妊娠中体重増加率と児の出生体重との相関について解析した。

対象と方法

琉球大学医学部附属病院とその教育関連病院で1992年1月から2004年11月の間に、妊娠36週以降で分娩となった双胎妊娠158例のうち、児の体重増加に明らかに影響を及ぼしたと判断される因子、すなわち胎児奇形、妊娠高血圧症候群、TTTS、臍帯付着異常のあった23例を除外した135例を対象とした。なお、超音波断層診断および娩出付属物所見を含む臨床的卵性診断によると、一卵性双胎23例、二卵性双胎110例、不明2例であった。

診療録から、母体の体重因子として、妊娠前BMI, 妊娠全期間を通じての体重増加率、各三半期の体重増加率を調べ、児の体重因子として、大きいほうの児(大児)の出生体重、小さい児(小児)の出生体重を調べた。解析項目としては、(1)全対象について、各々の母体体重因子と児出生体重因子の相関を統計学的に解析した。次に、(2)対象を妊娠前BMIによる日本産婦人科学会分類に基づき、BMI 18未満をunder-weight: U群, 18

はじめに

単胎妊娠においては、母体の妊娠前体型指数(body mass index: BMI) および妊娠中体重増加が児の出生体重と正の相関を示すとされており、児出生体重からみた望ましい母体体重増加に関する多くの臨床研究が報告されている。一方、双胎妊娠における至適な母体体重増加に関しても、欧米ではいくつかの臨床研究が報告されているが、日本人と欧米人との間には身長、体重の分布に差異があり、母体の妊娠中体重増加について、その増加率やパターンに違いがあると推測される。し

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表1 母体および児の体重関連因子 [n = 135]

妊娠前体重 (kg)	52.8 ± 10.0 (36.0 ~ 115.0)
妊娠前BMI	21.6 ± 3.8 (16.7 ~ 43.8)
母体体重増加率 (kg/週)	
第1三半期	0.19 ± 0.33 (-1.05 ~ 1.10) ^a
第2三半期	0.52 ± 0.18 (0.06 ~ 0.93) ^a
第3三半期	0.48 ± 0.28 (-0.22 ~ 2.13) ^a
妊娠全期	0.43 ± 0.14 (0.07 ~ 0.76)
児出生体重 (g)	
大児	2,607.8 ± 295.5 (1,666 ~ 3,400) ^b
小児	2,352.1 ± 305.7 (1,426 ~ 3,170) ^b

() 内は範囲. a, b: p < 0.001

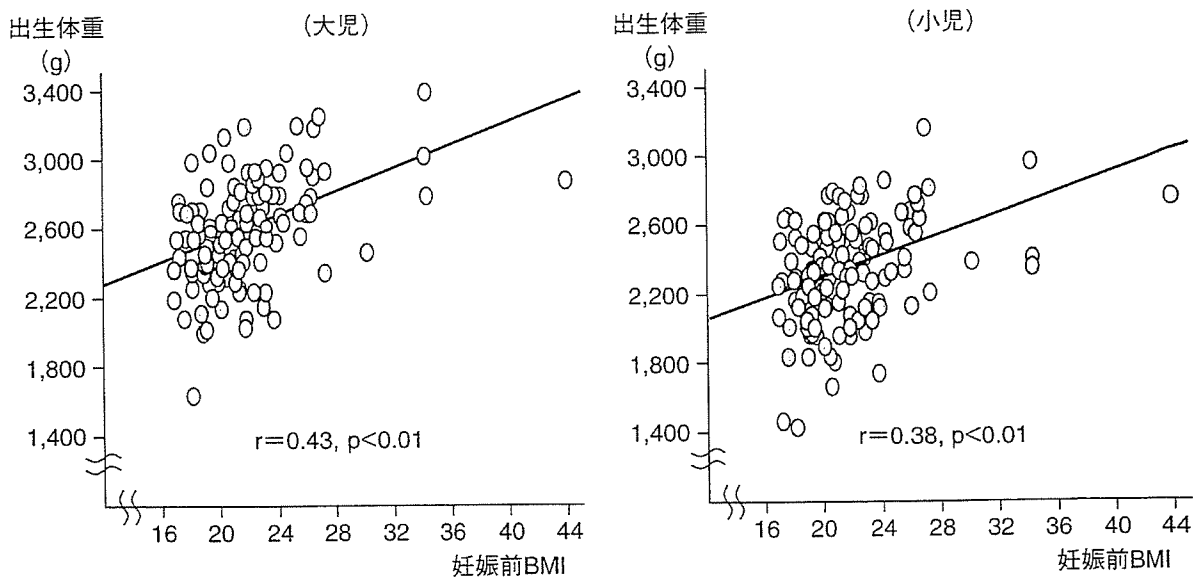


図1 母体妊娠前BMIと児出生体重との相関分析

～24をnormal-weight: N群, 24超をover-weight: O群に分け, 同様に母体体重因子と児出生体重因子の相関を解析した.

統計学的解析は, 3群間の比較についてはKruskal-Wallis検定を行い, $p < 0.05$ をもって有意とした. 母体体重因子と児出生体重因子の相関についてはPearson相関係数を用いた分析を行い, 相関係数 $r > 0.40$, かつ $p < 0.05$ をもって有意と判定した.

結果

1. 全対象135例に関する解析

全135例について, 年齢 31.7 ± 5.2 (18 ~ 45) 歳, 経妊 0.2 ± 1.2 (0 ~ 5回), 経産 0.7 ± 0.8 (0 ~ 4) 回

であった.

表1に, 母体および児の体重関連因子について示した. 妊娠前BMIは 21.6 ± 3.8 であった. 母体の体重増加率は全期間で平均 0.43 kg/週であり, 第2三半期の増加率は第1, 第3三半期に比較して有意に高かった ($p < 0.0001$, $p < 0.0001$). 児の出生体重は, 大児が平均 $2,607.8 \pm 295.5$ g, 小児が平均 $2,352.1 \pm 305.7$ gであり, 両者間に有意差があった ($p < 0.0001$).

図1に, 妊娠前BMIと大児および小児の出生体重との相関分析を示した. 妊娠前BMIと大児出生体重との相関は $r = 0.43$ かつ $p < 0.01$ であり, 両者間に有意な相関が認められた. 一方, 小児出生体重との相関は $r = 0.38$, $p < 0.01$ であり, 有意

表2 母体体重増加率と児出生体重との相関分析

	大児		小児	
	相関係数r	p値	相関係数r	p値
第1三半期	0.11	0.22	0.11	0.23
第2三半期	0.03	0.73	0.06	0.49
第3三半期	0.16	0.05	0.23	0.01
妊娠全期	0.15	0.07	0.21	0.01

有意の相関なし。

表3 BMI群別の母体および児の体重関連因子

	U群 [n=14]	N群 [n=99]	O群 [n=22]
母体体重増加率 (kg/週)			
第1三半期	0.32 ± 0.26 (-0.12 ~ 0.83) ^a	0.13 ± 0.31 (-1.05 ~ 0.85) ^a	0.12 ± 0.53 (-1.40 ~ 1.10) ^a
第2三半期	0.58 ± 0.11 (0.36 ~ 0.69) ^b	0.53 ± 0.17 (0.25 ~ 0.93) ^b	0.45 ± 0.21 (0.06 ~ 0.89) ^b
第3三半期	0.56 ± 0.36 (-0.12 ~ 1.60) ^c	0.49 ± 0.30 (-0.22 ~ 2.13) ^c	0.39 ± 0.21 (-0.01 ~ 0.84) ^c
妊娠全期	0.46 ± 0.10 (0.29 ~ 0.67) ^d	0.43 ± 0.13 (0.07 ~ 0.76) ^d	0.36 ± 0.16 (0.07 ~ 0.64) ^d
児出生体重 (g)			
大児	2,478.7 ± 333.0 (1,666 ~ 3,002) ^e	2,552.0 ± 268.7 (2,008 ~ 3,198) ^e	2,827.0 ± 293.4 (2,180 ~ 3,400) ^e
小児	2,181.0 ± 394.8 (1,426 ~ 2,672) ^f	2,303.8 ± 277.4 (1,670 ~ 2,814) ^f	2,583.5 ± 268.8 (2,104 ~ 3,170) ^f

() 内は範囲。 a, b, c, d : p > 0.05. e, f : p < 0.001.

な相関は認められなかった。

表2に、妊娠各三半期、妊娠全期の母体体重増加率と児出生体重との相関関係についてまとめたが、いずれにおいても有意な相関は認められなかった。

2. BMI群別による解析

表3に、BMI群別の母体および児の体重関連因子について示した。妊娠の各三半期および全期を通じ、母体体重増加率には3群間で有意差を認めなかったが、U群に高く、O群に低い傾向があった。児出生体重については、大児においても小児においても3群間で有意差を認め ($p < 0.001$, $p < 0.001$), O群で最も重かった。

表4に、BMI群別の妊娠各三半期、妊娠全期の母体体重増加率と児出生体重との相関関係についてまとめた。U群では、いずれの妊娠期間におい

ても体重増加率と出生体重との間に有意の相関は認められなかったが、N群では、妊娠全期における体重増加率と大児および小児の出生体重との間に、O群では、第2三半期および妊娠全期の体重増加率と小児の出生体重との間に有意の相関が認められた。

以上の結果を踏まえ、母体体重増加率と児出生体重との間に有意の相関が認められたN群およびO群について、低出生体重児 (2,500 g未満) を予防するために必要な母体の体重増加率を試算した。

図2に、N群における妊娠全期の体重増加率と出生体重との相関に関する単回帰直線を示した。本群では、妊娠36週以降に2,500 g未満の児を生まなため妊娠全期を通じた体重増加率は、小児について最低0.65 kg/週と算出された。実際の

表4 BMI群別の母体体重増加率と児出生体重との相関分析

	大児		小児	
	相関係数r	p値	相関係数r	p値
U群 [n = 14]				
第1三半期	-0.38	0.29	-0.20	0.59
第2三半期	-0.16	0.66	-0.12	0.73
第3三半期	0.48	0.08	0.43	0.13
妊娠全期	-0.39	0.17	-0.31	0.28
N群 [n = 99]				
第1三半期	0.07	0.59	0.07	0.60
第2三半期	0.30	<0.01	0.28	<0.02
第3三半期	0.24	<0.03	0.28	<0.01
妊娠全期	<u>0.41</u>	<u><0.001</u>	<u>0.42</u>	<u><0.001</u>
O群 [n = 22]				
第1三半期	0.09	0.71	0.03	0.90
第2三半期	0.37	0.10	<u>0.64</u>	<u>0.001</u>
第3三半期	-0.14	0.55	0.05	0.83
妊娠全期	0.25	0.27	<u>0.54</u>	<u><0.01</u>

下線は有意の相関を示す。

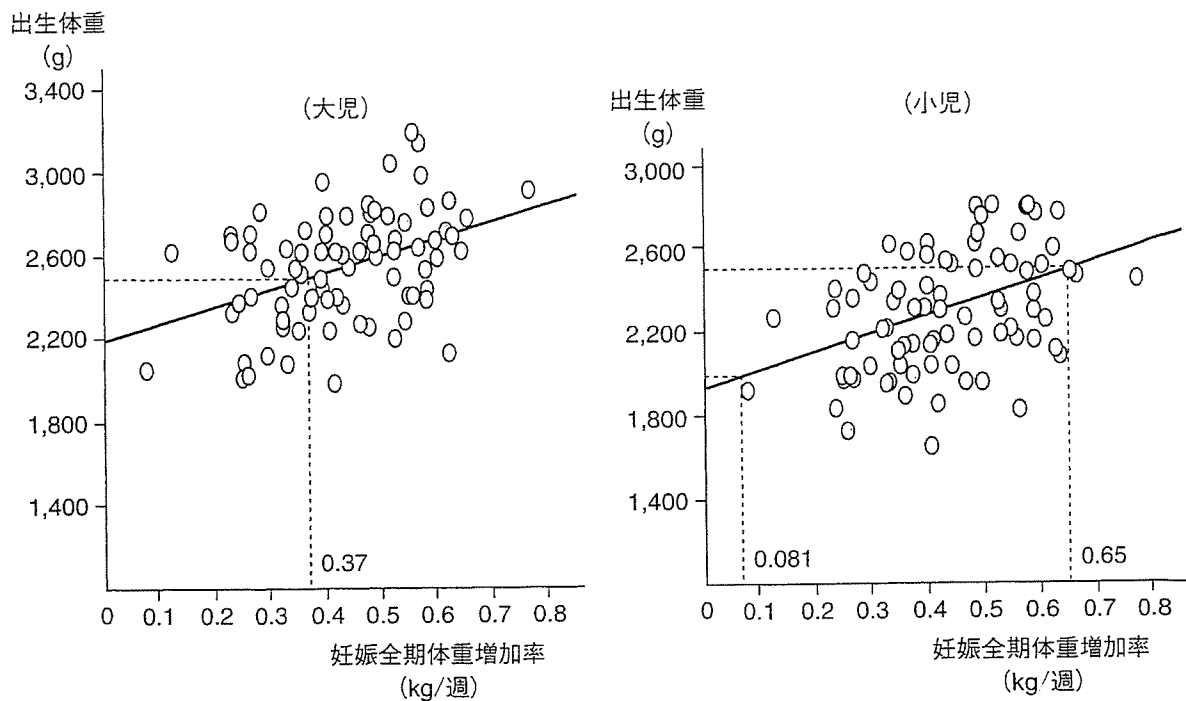


図2 N群：妊娠全期の母体体重増加率と児出生体重との相関分析

臨床で保育器収容，チューブ栄養などの管理が必要となる2,000 g未満の児を生まないための妊娠全期を通じた体重増加率は，小児について最低0.081 kg/週と算出された。次に，図3に，O群における第2三半期，妊娠全期の体重増加率と出生体重の相関に関する単回帰直線を示した。本群で

は，すべての児が2,000 g超であり，妊娠36週以降に2,500 g未満の児を生まないための第2三半期および妊娠全期を通じた体重増加率は，小児についてそれぞれ最低0.35 kg/週，最低0.27 kg/週と算出された。

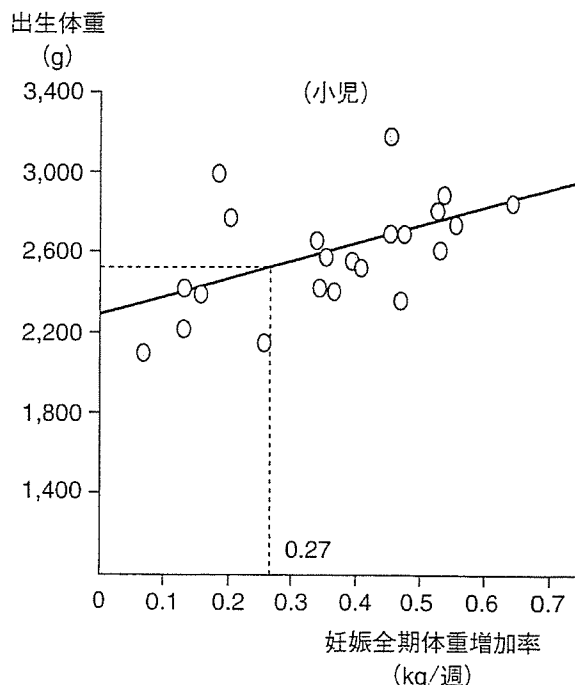
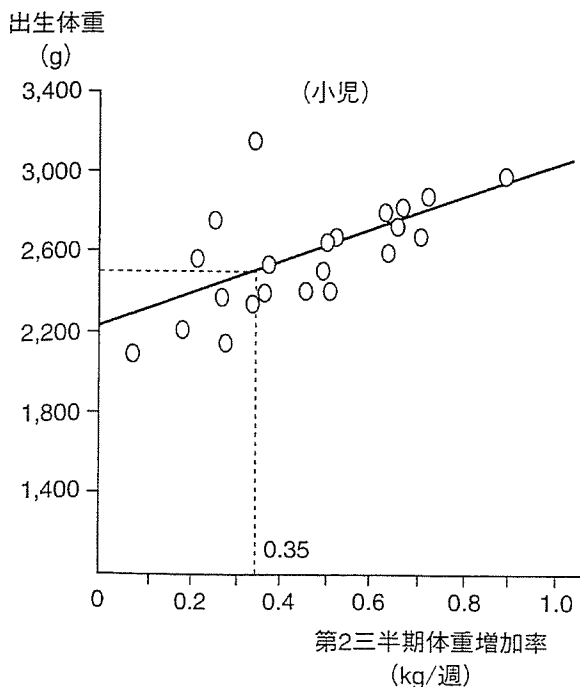


図3 O群：第2三半期および妊娠全期の母体体重増加率と小児出生体重との相関

考 察

母体は、妊娠中期まで摂取した栄養を脂質として同化するが、後期には逆に異化亢進を示すことが知られており、単胎妊娠では第2三半期の母体体重増加率が第1、第3三半期に比べて高いとされている。双胎妊娠を対象とした今回の解析においても、第2三半期の母体体重増加率は第1、第3三半期に比較して有意に高く、単胎と同様、妊娠中期の脂肪蓄積が活発に行われることを示している。

今回の解析では、母体の妊娠前BMIと児出生体重、特に大児の出生体重とに有意な正の相関を認めた。単胎妊娠では、母体の妊娠前BMIと児出生体重に有意な相関があることがすでに示されているが¹⁻³⁾、双胎妊婦においても妊娠前BMI、すなわち妊娠前の栄養状態や脂肪蓄積量が児出生体重に影響することが示された。小児の出生体重についても相関係数は0.38と高く、今後、症例を重ねることで有意の相関を示せるかもしれない。

対象全体として解析した場合、母体の妊娠前BMIと児の出生体重とには有意の相関を認めた

が、妊娠各三半期および妊娠全期の母体体重増加率と児の出生体重とには有意な相関を認めなかった。そこで、母体を妊娠前BMIによりU群、N群、O群に分けて解析した。まず、妊娠中の母体体重増加率は、有意ではないがU群で最も高く、O群で最も低かった。一方で、児の出生体重は3群間で有意差を認め、大児および小児とも逆にU群で最も小さく、O群で最も大きかった。特にO群では、母体体重増加率が低いにもかかわらず、すべての出生児が2,100 g以上であった。単胎妊娠を対象とした検討では、吉松ら⁴⁾が母体の妊娠中体重増加量は妊娠前BMIが高いほど少ない傾向にあったと報告している。また、Copperら³⁾、今井ら⁵⁾は、肥満群では、標準群や痩せ群に比較して有意に母体体重増加量が少なかったにもかかわらず、児出生体重は逆に最も重かったと報告している。今回の結果から、双胎妊娠においても単胎妊娠と同様、肥満婦人では妊娠中の体重増加が少なくても、妊娠前に十分な蓄積脂肪があることにより、低出生体重児の割合が低下すると考えられた。

次に、妊娠各三半期および全期における母体体

重増加率と児出生体重との相関についてU群, N群, O群別に解析した結果, U群ではいずれの期間においても相関を認めなかったが, N群とO群では全期の母体体重増加率と小児の出生体重とに有意の相関を認めることができた. また, O群では第2三半期の母体体重増加率と小児の出生体重とも有意の相関を認めることができた. したがって, N群とO群の妊婦においては, 少なくとも小児が低出生体重児にならないような妊娠中体重増加の目標値を設定することが可能であると思われる. 今後は, 例えば二絨毛膜二羊膜性双胎のみに限定するなど, 背景因子を均一化し, 十分な症例数を集積して解析することにより, より明確な所見が得られるかもしれない.

文献上, 児出生体重からみた双胎妊娠における至適な母体体重増加に関する報告はほとんど見当たらない. Lantzら⁶⁾の189妊婦の報告では, 両児とも2,500 g以上の出生体重であった妊婦とそうでなかった妊婦を比較検討した結果, 2,500 g以上の出生体重を得るために必要な妊娠20週から分娩までの母体体重増加率は, 妊娠前BMI<19.8の婦人では1.75 lb (0.79 kg) /週以上, 妊娠前BMI 19.8~26.0の婦人では1.50 lb (0.68 kg) /週以上であるとしている. すなわち, BMI 19.8~26.0については, 今回のN群とO群の一部に相当しており, 2,500 g以上の児出生体重を得るための母体体重増加率としてほぼ近い値となっている. 一方, Lukeら⁷⁾の2,324例を対象とした検討では, 両児とも2,850~2,950 g (妊娠36週) の出生体重を得るための母体体重増加率が詳細に検討されているが, 目標とする児体重が大きすぎるため今回のデータと比較することは困難である.

低出生体重児に関しては, 新生児管理の進歩によりその短期的予後が飛躍的に向上し, 極低出生体重児以外はさほど問題視されない傾向もあるが, なお長期的予後解析は不十分であり, 多くの解決されるべき重大な問題点が残されている. また近年, 低出生体重児は, 将来の肥満, 成人病のハイリスクとなることが指摘されている^{8~11)}. 一方で, 妊娠中の母体体重増加について, 例えば妊娠高血圧症候群の増加という危惧がある. 今回

の調査と同一期間中に当科で扱った妊娠36週以降で分娩となった妊娠高血圧症候群合併の双胎妊娠14例について, 妊娠前BMI, 妊娠第1, 第2, 第3三半期, 妊娠全期の母体体重増率を非合併症例と比較解析したが, 有意な差は認められず, 少なくとも妊娠高血圧症候群合併群において妊娠中母体体重増加がより高いというエビデンスはなかった.

結論として, 双胎妊娠における低出生体重児を生まないための母体の体重増加率について, 単胎妊娠におけるような明確な情報を導き出すことは困難であった. しかし, 少なくとも妊娠前BMIが正常ないし肥満に属する妊婦については, 低出生体重児, さらには2,000 g未満の児を生まないための母体体重の管理に有用な情報が得られたと思われる.

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MEDICAL BOOK INFORMATION

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わが国、救急医学のメッカ川崎医科大学が総力あげて完成させた本格的なマニュアルの大改訂版。全篇にわたり内容を検討。いっそう読みやすくなった、救急の「百科全書」ともいえる1冊。新薬の新技术。法改正に伴う、ここ10年の時代に沿って内容を充実させた。

原著論文

アロマセラピーに用いられる芳香物質の HIV 感染に及ぼす影響

—MAGIC-5 細胞を用いた *in vitro* での検討—

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本多三男⁴, 陳 旺全⁵, 鄭 瑞棠⁶

Anti-HIV-1 (human immunodeficiency virus type 1) activities of essential oil preparations commonly employed for aromatherapy

—*In vitro* screening with MAGIC-5 cell assay—

Abstract

AIDS/HIV infection is one of the most serious and widespread viral infections which emerged during the 20th century. Recently, the morbidity and mortality associated with AIDS are declining with the use of highly active anti-retroviral therapy (HAART). On the other hand, patients are requested to take multiple anti-retroviral drugs and often suffer from various side effects. The emergence of drug-resistance caused by frequent mutation of HIV genomes is another important clinical problem. There are several reports suggesting the clinical usefulness of alternative/complementary medical therapy on HIV infection and AIDS patients, although most of them lack a scientific background.

In the present study, we screened 35 representative essential oils and tinctures employed in aromatherapy for anti-HIV-1 activity using a highly sensitive MAGIC-5 assay. MAGIC-5 cells were delivered from MAGI (HeLa-CD4-LTR- β -gal) cells by transfection of the human CCR5 gene and were sensitive to both X4 and R5 HIV-1 substrains. Cells were treated with/without various concentrations (0.01–1000 ppm) of sample preparations for 24 hours before exposure to HIV-1. Cells cultured in the presence of HIV were stained with X-gal to identify HIV replication after 48 hours of culture.

It was found that most of the herb representative essential oils and tinctures elicit strong inhibition of HIV-1 infectivity. The effective concentrations of the essential oils and tinctures were 100 to 1000 times lower than cytotoxic concentrations. Among 35 samples, we identified strong anti-HIV-1 activity in bergamot, lemon, lemongrass, myrrh, milk thistle and rose-otto preparations. Noteworthy is the fact that most essential oil samples did not show effectiveness with a maximal dose suggesting the presence of multiple agonists with different pharmacological modes or the co-existence of agonist(s) and antagonist(s) in the same preparations. In conclusion, we identified strong anti-HIV-1 activities in the essential oil and tincture preparations employed for aromatherapy.

Key words: HIV, aromatherapy, MAGIC-5

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1. はじめに

エイズは、レトロウイルスの一つである HIV の感染により生体防御系の荒廃と日和見感染から致命的な経過をたどる疾患である。1981 年、米国で最初の症例が報告され 1983 年に、Montaignir と Gallo により HIV が同定されてから 22 年になる。その間 HIV 感染者は世界中に広まり、2003 年末の時点で感染者は 4200 万人、年間の死亡者は 250~350 万人に達している。しかしながら他方では、分子生物学ならびに免疫学の進歩により、HIV の感染機構とエイズ発症のメカニズムが明らかにされ、さらには多剤併用療法 (highly active antiretroviral therapy: HAART) により、感染者あるいはエイズを発症した患者でも免疫機能の再構築と予後の改善が可能となってきた。我が国では今日のところ幸いなことに全人口中の HIV 感染者が多発国と比較して少数である。しかし、先進国の中では唯一感染者が増加している国であり、社会的な対応が求められている。HIV は感染 2 週間前後に頭痛、発疹、筋肉痛、関節痛などの急性期症状を発症するが、その後は長い無症候期に入る。この間 HIV は、生体内で活発に増殖するが、血中の CD4 陽性リンパ球数も代償的に増殖するので自覚症状や他覚症状を欠き、通常の臨床検査では感染症として診断できない症例が多い。しかし、感染後平均 10 年間を経過して細胞性免疫不全が進行し、CD4 陽性リンパ球数が 300 個/ μ l 前後になると、表在リンパ節の腫脹のほか、発熱、下痢、体重減少などの症状が見られ、さらに減少して 200 個/ μ l 以下となると、日和見感染の発症頻度が高くなる。

現在では、いったん免疫系が荒廃した患者でも HAART により免疫能の再構築が可能であるが、強い副作用や耐性ウイルス出現の問題があり、HAART の開始時期や薬剤の選択にはいまだ議論のあるところである。

一方、代替医療により AIDS 患者の自覚症状ならびに他覚症状を軽減したり、合併症を予防する可能性が報告されている。すなわち Styles は、HIV 陽性の小児に、エッセンシャルオイルマッサージを施すことにより、苦痛と不安を取り除き、全身状態を改善できる可能性があるとして述べており¹⁾、Buckle はアロマテラピーが HIV 陽性者および AIDS 患者に真菌、原虫による日和見感染を防止すると報告している²⁾。

しかしながら、その効果の科学的根拠についての基礎的研究は少なく、アロマテラピーそのものが HIV の複製に何らかの影響を与えるや否やについての研究

もない。アロマテラピーの効果を確認する医学者の間でも直接的な効果については疑問視されている。

我々は、*in vitro* において効率的に、HIV 感染に及ぼす薬剤の効果をスクリーニングできる MAGIC-5 法を用いて、アロマテラピーに用いられるエッセンシャルオイルおよびチンキ剤の抗 HIV 活性を検討し、複数のエッセンシャルオイルおよびチンキ剤にその活性を認めたので報告する。

2. 対象と方法

株式会社グリーンフラスコより提供された 35 種類のエッセンシャルオイルおよびチンキ剤を用いて検討した。サンプルのうち、エッセンシャルオイル (Table 1, #1~#31) は DMSO にいったん溶解して、チンキ剤はそのまま培養液に加え検討を行った。

HIV 感染阻害の効果は MAGIC-5 アッセイによって検討した³⁾。MAGIC-5 は、HIV 非感受性である Hela 細胞に、HIV 感染するためのレセプターである CD4、さらに感染する細胞の指向性を決定するレセプターである CXCR4 および CCR5 を強制発現させた細胞株である。そのため R5 (マクロファージ指向性)、X4 (T 細胞指向性) 両ウイルスに感受性である。これまでに、HIV 複製の指標としては、培養液中に放出される HIVp24 の定量が多く用いられてきたが、ウイルス蛋白質量と感染効率とが必ずしも相関しないことが報告されている。

原法である blue focus assay⁴⁾ では、MAGI 細胞 (Hela-CD4-LTR, Gal) を HIV 存在下で一定時間培養した後、1% formaldehyde と 0.2% glutaraldehyde とを含む生理食塩水で固定し、X-gal で染色することにより感染細胞は青色に染色される。また MAGIC-5 では、さらに CCR5 を発現させ、R5 ウイルスでも X4 ウイルスと同様に検討できるという利点がある。

本実験では 96 穴マイクロプレートを用い、5%CO₂ の存在下で、37°C の環境において各ウェルに 10⁴ 個の MAGIC-5 細胞を 2.5% FCS 加 Dulbecco MEM [DMEM] 液中で培養した。この細胞を用いて、一定の濃度のエッセンシャルオイルおよびチンキ剤を含む培養液で 24 時間培養した後、一定量の HIV/LAI 株 (X4 ウイルス: 2×10² bfu/ウェル) を感染させた。対照としてサンプルを含まない培養液での染色細胞数を 100 とし、サンプルを含む培養液で染色数の逆数を阻害効果 (%) とし、阻害効果 50% の濃度 ppm (ID₅₀) を算出した。

また、この効果が細胞毒性によるものかどうかクリスタルバイオレット染色法により培養したウェル基底