Eur J Med Res (2009) 14: 216-222

Impact of Maternal Body Mass Index on Neonatal Outcome

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Abstract

Introduction: Maternal body mass index has an impact on maternal and fetal pregnancy outcome. An increased maternal BMI is known to be associated with admission of the newborn to a neonatal care unit. The reasons and impact of this admission on fetal outcome, however, are unknown so far.

Objective: The aim of our study was to investigate the impact of maternal BMI on maternal and fetal pregnancy outcome with special focus on the children admitted to a neonatal care unit.

Methods: A cohort of 2049 non-diabetic mothers giving birth in the Charite university hospital was prospectively studied. The impact of maternal BMI on maternal and fetal outcome parameters was tested using multivariate regression analysis. Outcome of children admitted to a neonatal ward (n = 505) was analysed.

Results: Increased maternal BMI was associated with an increased risk for hypertensive complications, peripheral edema, caesarean section, fetal macrosomia and admission of the newborn to a neonatal care unit, whereas decreased BMI was associated with preterm birth and lower birthweight. In the neonatal ward children from obese mothers are characterized by hypoglycaemia. They need less oxygen, and exhibit a shorter stay on the neonatal ward compared to children from normal weight mothers, whereas children from underweight mothers are characterized by lower umbilical blood pH and increased incidence of death corresponding to increased prevalence of preterm birth.

Conclusion: Pregnancy outcome is worst in babies from mothers with low body mass index as compared to healthy weight mothers with respect to increased incidence of preterm birth, lower birth weight and increased neonate mortality on the neonatal ward. We demonstrate that the increased risk for neonatal admission in children from obese mothers does not necessarily indicate severe fetal impairment.

Key words: maternal BMI, fetal outcome

Introduction

The overall prevalence among adults being overweight or obese in the US is up to 65%; the prevalence for obese and extremely obese adults is 30% and 5 % [Hedley et al. 2004]. Interestingly, in the female population from age 20-39 years prevalence of overweight and obesity is 54.5 %. Despite the high prevalence in this population of potential mothers, the impact of body weight on maternal and fetal pregnancy outcome remains under-investigated when compared to the extent of research in its cardiovascular implications.

It is well established that an abnormal maternal body mass index (BMI) has deleterious effects on maternal and fetal pregnancy outcome: Overweight/obese mothers are known to bear an increased risk of hypertensive complications, gestational diabetes, caesarean section, postpartum hemorrhage, and fetal macrosomia [Bergmann et al. 2003; Cnattingius et al. 1998; Doherty et al. 2006; Barau et al. 2006], whereas underweight mothers bear a risk of preterm delivery and small-for-gestational-age infants [Kramer et al. 1995]. However, there are fewer studies describing increased maternal BMI as a risk factor for admission of the newborn to a neonatal unit [Abenhaim et al. 2007; Usha Kiran et al. 2005; Callaway et al. 2006; Raatikainen et al. 2006]. But data on subsequently investigated neonates on the neonatal ward with respect to diagnosis, outcome parameters and complications is scarce. This is crucial because admission to a neonatal unit can bear diametrically different meanings for the health status of the newborn: If the admission is mainly based on surveillance reasons, f. e. because of the well-known risk for hypoglycaemia in children from obese mothers [Doherty et al. 2006], one would expect those neonates to have a much better overall health status compared to an admission based on severe neonatal impairment.

Therefore the objective of our study was to determine the impact of maternal body mass index (BMI) in a large, non-diabetic study population on neonatal outcome with special attention to admission and outcome in the neonatal unit.

Methods

Study Design

After written consent was obtained a total of 2234 women delivering consecutively at the Charite obstetrics department in Berlin/Germany from January 2000 to December 2003 were included in our database. The local ethics committee approved the study. A structured medical history was taken. German guidelines for medical follow-up in pregnancy comprise the so-called "Mutterpass" (mother pass) containing essential data about the pregnancy. The following data were extracted into our database: age, body height, weight before and during pregnancy, parity, gestational age at delivery, urine dipstick results, evaluation of oedema and blood pressure readings at all follow-up visits. Biometric data of the newborn were routinely measured right after delivery. Body mass index (BMI) was calculated as maternal weight [kg]/ maternal height [m]^2. Children exhibiting a birthweight below the 10th percentile of the German reference population [Voigt et al. 1996] were denoted as small for gestational age (SGA), children above the 90th percentile were denoted as large for gestational age (LGA). As we included singleton pregnancies only and excluded all mothers with pregestational diabetes or missing data about diabetes 2049 mother/child pairs remained for analysis.

As a significant portion of the children was admitted to a specialized neonatal ward (with full ICU capacities) after birth (505 children/24.7% of all newborns), we collected data from their medical records regarding diagnosis, complications and treatment modalities such as oxygen application, antibiotics, mechanical ventilation etc.

Statistical Analysis

Data were analyzed using SPSS version 12 (Chicago, IL, USA). Initial analysis of the study population was performed using chi^2-test (categorical data) or unpaired T-Test (continuous data). Associations of maternal BMI with quantitative maternal parameters were assessed by multivariate linear regression analysis with adjustment for age, smoking and parity. Associations of maternal BMI with quantitative fetal parameters were likewise assessed after adjusting for child sex and gestational age on top of the above mentioned parameters. These covariates were chosen based on literature describing an influence of these parameters on pregnancy outcome [Pfab et al. 2006; Cnattingius et al. 1992; Jacobsson et al. 2004] and our own analysis (see Table 1). Whenever association of maternal BMI with a binary (yes/no) parameter was investigated multivariate logistic regression analysis was performed after adjusting for the same covariates as described above. Whenever appropriate mothers were grouped according to their BMI following official dietary guidelines [US Department of Agriculture and US Department of Health and Human Services, 2000]: BMI < 18.5 kg/m^2: "underweight", BMI 18.5 – 24.9 kg/m^2: "healthy weight", BMI 25- 29,9 kg/m^2: "overweight", BMI > 30 kg/m^2: "obese". The odds ratios given are using healthy weight mothers as reference.

Children admitted to the neonatal unit were grouped according to maternal BMI (see above). In order to detect differences regarding diagnosis or treatment modalities between groups the chi^2-test (categorical data) or T-Test (continuous data) were applied. Statistical significance was assumed with a probability error $p < 0.05$.

Results

Descriptive data of the study population are shown in Table 1.

The univariate analysis using T-Test (continuous data) and chi^2-test (categorical data) revealed significant differences between maternal body weight groups with respect to various maternal and fetal outcome parameters such as hypertensive complications, edema, preterm delivery, incidence of section, fetal morphology, neonatal death and fetal risk of being admitted to a neonatal ward.

Taken together, the results presented in Table 1 indicate that increased maternal BMI was associated with an increased blood pressure and increased incidence of peripheral edema, caesarean section, fetal macrosomia and admission of the newborn to a neonatal care unit, whereas decreased BMI was associated with preterm birth and lower birthweight.

Based on those findings multivariate regression analysis adjusting for possible confounders was performed to verify the results.

Impact of Maternal BMI on Maternal and Fetal Pregnancy Outcome and Complications

The results of the multivariate logistic regression analysis are illustrated in Table 2.

There was a significant impact of maternal BMI on the incidence of peripheral edema: When compared to healthy weight mothers, overweight/obese mothers have more than doubled/tripled their incidence of acquiring peripheral edema (odds ratio (OR) about 2.5/3.5) in every trimester of pregnancy. The risk for overweight/obese mothers to develop new peripheral edema in the third trimester is likewise markedly enhanced, whereas the risk for underweight mothers is reduced.

The incidence of hypertensive complications (pregnancy induced hypertension and preeclampsia) was also related to maternal body mass index: Overweight/obese mothers had a 3/4-fold increased risk for hypertensive complications; for underweight mothers there was no significant difference compared to healthy weight mothers.

Regarding obstetric outcomes overweight and obese mothers exhibited an increased risk of delivering via caesarean section in comparison to healthy weight mothers, whereas for underweight mothers no such association was detected (see Table 2).

Fetal presentation was divided into cephalic presentation versus adverse presentations such as breech presentation and transverse lie. No association between maternal BMI and fetal presentation was detected.

Furthermore, overweight or obese mothers have a significantly increased risk of macrosomic (birth weight > 4000g) children (OR about 1.5 and 2), whereas underweight mothers are not at risk. Similar results were obtained when the variable "large for gestational age" (LGA) - which is independent from child sex and gestational age - was used instead (Table 2). Correspondingly, there was a decreased risk for overweight mothers for having a small for gestational age infant.

Table 1. Descriptive data of the study population (n = 2049).

	healthy weight (n = 1446)	underweight (n = 163)	overweight (n = 309)	obese (n = 126)
age (years)	30.2 ± 5.4	27.9 ± 6.1**	30.7 ± 5.9	29.5 ± 5.9
parity	1.5 ± 0.8	1.5 ± 0.9	1.6 ± 0.9*	2.0 ± 1.2**
primipara (%)	64.8	67.9	58.3*	43.9**
weight gain during pregnancy (kg)	15.9 ± 5.4	15.7 ± 5.1	15.5 ± 6.5	12.8 ± 6.9**
maternal BMI	21.4 ± 1.7	17.6 ± 0.7**	26.9 ± 1.3**	33.9 ± 3.3**
smoking during pregnancy (%)	16.3	25.2*	16.5	14.3
preterm delivery (%)	7.6	16.8**	12.2*	8.9
gestational age (weeks)	39.0 ± 2.1	38.6 ± 2.6(*)	38.8 ± 2.5	39.0 ± 1.9
section (%)	25.2	24.2	35.9**	32.5
RR sys. In 1st half of pregnancy (mmHg)	114.3 ± 11.1	109.7 ± 10.4**	119.4 ± 11.8**	125.9 ± 11.7**
RR sys. In 2nd half of pregnancy (mmHg)	115.3 ± 10.0	111.4 ± 9.6**	120.8 ± 11.9**	125.9 ± 10.6**
RR dia. In 1st half of pregnancy (mmHg)	67.7 ± 7.5	65.2 ± 6.6**	71.8 ± 7.9**	75.1 ± 7.4**
RR dia. In 2nd half of pregnancy (mmHg)	69.1 ± 6.9	66.8 ± 6.8**	72.9 ± 7.8**	75.4 ± 6.9**
hypertensive complications (%)	5.7	2.5	13.2**	16.7**
proteinuria 2nd half of pregnancy (%)	37.4	31.6	41.6	45.0
periph. edema 2nd half of pregnancy (%)	34.6	19.1**	55.9**	59.3**
child sex (male %)	52.5	52.8	58.9*	52.4
birth weight (g)	3347.1 ± 607.8	3209.9 ± 666.7*	3452.5 ± 644.2*	3587.4 ± 617.5**
child length (cm)	50.8 ± 3.0	50.0 ± 3.7*	51.2 ± 2.9*	51.3 ± 2.9
child head circumference (cm)	34.7 ± 2.0	34.3 ± 2.9*	34.9 ± 2.4*	35.2 ± 1.7*
ponderalindex	25.4 ± 3.2	25.6 ± 2.9	25.7 ± 2.5	26.7 ± 4.9**
LGA (%)	10.8	7.8	17.2*	27.6**
SGA (%)	11.6	14.9	6.4*	8.9
APGAR 5 min	9.4 ± 0.9	9.3 ± 0.9	9.3 ± 1.0	9.3 ± 0.9
APGAR 10 min	9.7 ± 0.6	9.7 ± 0.6	9.6 ± 0.6	9.6 ± 0.7
umbilical vein blood pH	7.28 ± 0.08	7.26 ± 0.08*	7.28 ± 0.07	7.27 ± 0.07
admission to neonatal-ICU (%)	22.9	20.2	30.4*	37.3**

*/**: p< 0.05/0.001 vs. healthy weight group. (*): p = 0.05 vs healthy weight group. LGA/SGA: Large/small for gestational age. Data are given as mean ± SD, metric data are analyzed using T-Test, categorical data were analyzed using chi^2-test

Regarding preterm delivery there was a markedly elevated risk for underweight mothers (OR 2.4), whereas for elevated maternal BMI only in the overweight group a moderate association (OR 1.65) and no association in the obese groups with preterm delivery was detected.

Elevated maternal BMI was associated with increased admission to neonatal care (OR 1.5/2.2 for overweight/obese mothers), whereas for children from underweight mothers exhibited no such association.

Impact of Maternal BMI on Fetal Phenotype

Linear regression analysis was applied to detect significant associations between maternal BMI and fetal morphologic and functional parameters (see Table 3).

Table 2. Logistic regression analysis of maternal and obstetric outcomes.

Dependent variables	healthy weight	underweight OR (95%-CI)	overweight OR (95%-CI)	obese OR (95%CI)
peripheral edema 1st Trimester	1	NS	2.62(1.14-6.00)*	3.47(1.22-9.87)*
peripheral edema 2nd Trimester	1	NS	2.56(1.83-3.59)**	3.59(2.27-5.70)**
peripheral edema 3rd Trimester	1	0.50(0.32-0.77)*	2.53(1.94-3.28)**	3.23(2.17-4.80)**
new-onset periph. edema 3rd Tr.	1	0.47(0.29-0.76)*	2.43(1.85-3.20)**	2.86(1.90-4.30)**
hypertensive complications	1	NS	2.72(1.74-4.25)**	3.99(2.14-7.44)**
caesarean section	1	NS	1.73(1.31-2.28)**	1.82(1.20-2.77)*
adverse fetal presentation	1	NS	NS	NS
fetal macrosomia (>4000g)&	1	NS	1.54(1.06-2.24)*	2.07(1.25-3.42)*
preterm delivery (<37 week)	1	2.39(1.46-3.89)**	1.65(1.10-2.49)*	NS
LGA	1	NS	1.62(1.14-2.32)*	2.57(1.64-4.04)**
SGA	1	NS	0.49(0.29-0.83)*	NS
admission to neonatal unit&	1	NS	1.47(1.09-1.99)*	2.22(1.47-3.36)**

* : $p< 0.05$
**: $p< 0.001$
&: adjusted for child sex and gestational age on top of the covariates mentioned below
LGA/SGA: Large/small for gestational age
Maternal incidence of peripheral edema, hypertensive complications (pregnancy induced hypertension and pre-eclampsia) as well as a various parameters affecting obstetric outcome were analyzed using logistic regression analysis. Mothers with pregestational diabetes and multiple pregnancies were excluded, mothers were grouped according to their BMI, healthy weight mothers were used as reference. Maternal age, smoking and parity were used as covariates in all analyses.

Table 3. Linear regression analysis of fetal morphologic and functional outcome.

Dependent variables	Regression coefficient	95% confidence interval	p
birthweight (g)	18.29	13.16-23.42	< 0.001
body length (cm)	0.05	0.02-0.08	< 0.001
head circumference (cm)	0.05	0.03-0.07	< 0.001
ponderal index	0.07	0.04-0.11	< 0.001
APGAR after 5 min	-	-	NS
APGAR after 10 min	-	-	NS
umbilical blood pH	-	-	NS

Fetal morphologic and functional outcome parameters were analyzed using linear regression analysis. Mothers with pregestational diabetes and multiple pregnancies were excluded, maternal BMI was the independent variable. Maternal age, smoking, parity, child sex and gestational age were used as covariates.

A highly significant positive correlation between maternal BMI and all morphologic parameters such as birth weight, length, head circumference and ponderal index was detected, whereas functional parameters such as APGAR values at 5 and 10 minutes or pH value of umbilical blood were not influenced by maternal BMI (see Table 3).

Investigation of Children Admitted to the Neonatal Unit

A total of 505 children (24.7%) were admitted to the neonatal ward. Subsequently, those children were allocated to groups according to maternal BMI (underweight, healthy weight, overweight and obese mothers) and chi^2-test or T-Test was applied to assess differences between the groups regarding their diagnoses, interventions such as mechanical ventilation or functional parameters such as APGAR values. The results are given in Table 4.

Children on the neonatal ward exhibited a partially significant tendency towards increasing/decreasing values in morphologic parameters such as birthweight, length, head circumference according to maternal elevated/decreased BMI.

Correspondingly, children from obese mothers were significantly more often denoted as LGA and less often as SGA when compared to children from normal weight mothers. Regarding diagnoses we found that in children from obese mothers hypoglycaemia was diagnosed far more frequently compared to children from healthy weight mothers (26% vs 9%), whereas children

Table 4. Diagnoses/parameters of children admitted to neonatal ward (n = 505/24.7%)

Parameter	healthy weight mothers	under-weight mothers	over-weight mothers	obese mothers
n (abs./%)	331/65.5	33/6.5	94/18.6	47/9.3
birth weight (g)	3058+/-857	2669+/-959*	3223+/-907	3626+/-724**
length (cm)	49+/-4	47+/-5*	50+/-4	51+/-3**
head circumference (cm)	34+/-3	33+/-3	35+/-2*	35+/-2*
LGA (%)	13.4	6.3	20.2	38.3**
SGA (%)	21.5	25	5.3**	8.5*
preterm birth (%)	23	53*	32	17
birth in gestational week	38+/-3	36+/-4*	37+/-3	39+/-2
Hypoglycaemia (%)	9	6	9	26*
IRDS (%)	5	12	6	0
Sepsis (%)	5	6	5	0
Death (%)	0.6	6.1*	0	0
Antibiotics Administration (%)	34	39	32	26
Mechanical Ventilation (%)	11	21	10	2
Oxygen Administration (%)	19	30	16	4*
neonatal trauma (%)	2	0	1	2
Neonatal Ward-Stay (days)	11+/-17	13+/-16	10+/-18	6+/-5**
APGAR (5 min)	9.0+/-1.2	8.9+/-1.2	8.8+/-1.3	9.1+/-1.0
APGAR (10 min)	9.4+/-1.0	9.4+/-1.0	9.3+/-1.0	9.5+/-1.0
umbilical blood pH	7.29+/-0.09	7.25+/-0.09*	7.28+/-0.08	7.29+/-0.07

*/** p< 0.05/0.001 vs. healthy weight group
IRDS: Infant respiratory distress syndrome; LGA: large for gestational age; SGA: small for gestational age
Metric data is given as means +/-SD. Children admitted to the neonatal ward were grouped according to maternal BMI. Data were analyzed using chi^2-test (categorical data) and T-Test (metric data).

from underweight mothers showed a significant higher incidence of preterm birth (53% vs 23%). Children from underweight mothers were further characterized by significantly lower umbilical vein pH and an increased incidence of death. Corresponding to those findings children from underweight mothers exhibited a trend to be more frequently diagnosed as having Infant Respiratory Distress Syndrome (IRDS) (12% vs 5% in the healthy weight group; p = 0.08). Children from obese mothers were characterized by a decreased need for oxygen administration and a shorter ICU-Stay. (6 versus 11 days in healthy weight reference, see Table 4).

Discussion

This study demonstrates the impact of maternal BMI on pregnancy outcome. Pregnancy outcome is worst in babies from mothers with decreased body mass index as compared to healthy weight mothers with respect to increased incidence of preterm birth, lower birth weight and increased neonate morbidity and mortality on the neonatal ward. Our study demonstrates for the first time that the increased risk for neonatal admission in children from obese mothers does not necessarily indicate severe fetal impairment in this group in contrast to other maternal BMI groups. Maternal outcome with respect to blood pressure control, development of edema and incidence of section was worst in obese mothers.

Earlier studies report an increased risk for children from mothers with increased BMI to be admitted to neonatal care after birth [Abenhaim et al. 2007; Usha Kiran et al. 2005; Callaway et al. 2006; Raatikainen et al. 2006]. As admission to the neonatal ward can have two main reasons -severe illness or surveillance- which bear diametrically opposed meanings for the fetal health status we designed our study in a sequential way: First, we assessed the impact of maternal BMI on maternal and fetal outcome in a large, non-diabetic German study population in order to confirm known associations of maternal BMI and pregnancy outcome and thus ensure comparability to other studies. Second, we focused on the subgroup of children in our cohort who were admitted to a neonatal unit to elucidate the impact of maternal BMI on the outcome of those children.

Comparison to other European [Cnattingius et al. 1998; Ricart et al. 2005] studies revealed similar maternal BMI, age, smoking during pregnancy or gestational age at delivery of our study population thus indicating our cohort to be representative for an European population. We detected in our study the association of maternal BMI with adverse maternal and fetal pregnancy outcome: Increased maternal BMI is associated with increased risk of peripheral edema and hypertensive complications of pregnancy. The association of hypertensive complications with maternal BMI is supported by recent literature [Doherty et al. 2006], whereas to our knowledge the association of peripheral edema with maternal BMI has not yet been reported.

With respect to fetal outcome we found higher maternal BMI to be associated with higher incidence of caesarean section, which is in line with several recent studies [Barau et al. 2006; Abenhaim et al. 2007; Stepan et al. 2006; Cedergren 2006; Dempsey et al. 2005], whereas there was no impact of maternal BMI on fetal presentation. Thus we suggest the higher incidence of caesarean section in overweight/obese mothers to be most likely due to fetal macrosomia, which was found to be likewise associated with increased maternal BMI in our study as well as in the literature [Usha Kiran et al. 2005; Clausen et al. 2005]. Furthermore, we demonstrated that a decreased maternal BMI is linked to a higher risk of preterm birth and lower birthweight which is in line with the literature [Doherty et al. 2006; Kramer et al. 1995]. Increased maternal BMI was only found to be associated with preterm birth in overweight mothers and no such association was seen in obese mothers. Most likely, this is simply due to inadequate power/sample size of the obese mother group.

In our study children from overweight/obese mothers exhibited a significantly increased risk of being admitted to a neonatal ward. Interestingly, we demonstrated that maternal BMI had no impact on fetal clinical parameters such as APGAR and umbilical blood pH, thus making admission due to severe fetal impairment unlikely. This was supported by our observations in the neonatal cohort: Children from obese mothers were characterized by less oxygen administration and a shorter total ICU-stay (6 versus 12 days versus healthy weight reference, see Table 4). Only the incidence of hypoglycaemia was increased in babies from obese mothers.

Furthermore, in the group of neonatal ward children from obese mothers there was no case of infant respiratory distress syndrome (IRDS), sepsis or death. We thus conclude that admission of children from obese mothers to neonatal care was indeed due to surveillance rather than due to severe illness. On the contrary, children from underweight mothers admitted to neonatal care had significantly higher incidence of preterm birth accompanied by lower umbilical blood pH , increased incidence of death and exhibited a trend to be more often diagnosed for IRDS and subsequent mechanical ventilation.

We thus conclude maternal BMI to have a differential impact in our study population with regard to outcome: Children from underweight mothers are admitted to neonatal care due to preterm birth and subsequent IRDS which is a severe and life-threatening condition. On the other hand children from obese mothers are admitted because of an impaired glucose homeostasis, which requires surveillance, but within the neonatal ward-cohort they seem to be the healthiest with respect to oxygen administration and length of stay.

Those data are in contradiction with the limited number of studies assessing neonatal care admission in overweight/obese mothers, because those studies linked the admission of those infants to severe illness as indicated by lower APGAR, increased risk of neonatal trauma, fetal death, need for tube feeding and incubator [Abenhaim et al. 2007; Usha Kiran et al. 2005; Callaway et al. 2006; Raatikainen et al. 2006]. The study population used by Usha Kiran et al. is highly selected as they included only primigravid women with a singleton uncomplicated pregnancy with cephalic presentation of 37 or more weeks of gestation, and thus their cohort is possibly not comparable to our study population. Other studies are more comparable to our open approach, but they differ from our study by indicating an increased incidence of preterm birth at least in subgroups of obese mothers, which sufficiently explains fetal sickness and subsequent neonatal care admission in their cohort. Moreover, admission rates to neonatal care differ dramatically between the studies: In the study of Raatikainen et al. about 10% of the children were admitted to a neonatal care unit, whereas in the study of Callaway et al. it was about 4-5% and in our study it was 25%. These large differences possibly reflect a different selection of the patients which bears an important impact on interpretations of neonatal care data in general: We suggest that studies exhibiting a high percentage of neonatal care admissions contain a higher amount of surveillance-patients, whereas low percentage of neonatal care admission possibly reflects a more seriously impaired study population as the surveillance-patients might be covered elsewhere.

As a conclusion our study demonstrated the detrimental impact of an altered maternal BMI on maternal and fetal pregnancy outcome in a large, non-diabetic, German population. Low and high maternal BMI have different effects on maternal as well as fetal outcomes: Adverse effects of low BMI are preferentially targeting the fetus, whereas high BMI has a higher impact on maternal health. We demonstrated for the first time that the increased risk for neonatal admission in children from mothers with increased BMI does not necessarily indicate severe fetal impairment in this group.

Acknowledgements: The study was supported by grants from the Deutsche Forschungsgemeinschaft to Dr. Hocher
Conflict of interest: None for any of the authors

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Received: January 22, 2009 / Accepted: February 23, 2009

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