Original Article

The effect of body mass index on the outcome of pregnancy in women with recurrent miscarriage

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ABSTRACT

Background: Maternal obesity is associated with menstrual disorders, infertility and sporadic miscarriages. Recurrent miscarriage (RM) affects at least 1% of couples trying to conceive. In over 50% of cases, the cause of the loss of pregnancy remains unexplained. The aim of this study was to determine the relationship between maternal Body Mass Index (BMI) and future outcomes of pregnancy in couples with "unexplained" RM. **Methods and Results:** All couples referred to the specialist recurrent miscarriage clinic at St. Mary's Hospital, London, were investigated for an underlying cause. Those with unexplained RM were eligible. Demographic and clinical data were retrieved from a computerised database and medical records. The World Health Organisation (WHO) classification of BMI was used. Univariate analysis demonstrated that BMI, maternal age, number of previous miscarriages and ethnicity were significantly associated with pregnancy outcome. Logistic regression demonstrated that maternal obesity (BMI ≥ 30 kg/m^2) significantly increased the risk of miscarriage in couples with unexplained RM (OR 1.73; 95% CI 1.06 – 2.83). Asian women with a BMI similar to Caucasian women had a higher risk of a further miscarriage (OR 2.87, 95% CI, 1.52 – 5.39). **Conclusions:** Maternal obesity is an independent factor associated with an increased risk of miscarriage in couples with RM. All women with RM should have their BMI recorded at their first clinic visit. The potential effect of weight loss on the outcome of subsequent pregnancies should be assessed in future studies. The increased risk of miscarriage in Asian women needs to be explored further.

Key Words: BMI, miscarriage, obesity, recurrent miscarriage, weight loss

INTRODUCTION

Obesity is associated with menstrual disorders, infertility and sporadic miscarriages.[1-6] A case control study of 4932 women reported that repeated episodes of miscarriages were more common in the obese group compared to those with a normal BMI [Odd ratio of 3.5 (CI = 1.03 – 12.01) *P* – 0.04].[3] At later gestational stages, obesity is associated with an increased incidence of complications affecting both mother and fetus. These complications include gestational diabetes, pregnancy induced hypertension, pre-eclampsia, thromboembolism and antepartum stillbirth.[7-10]

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The Perinatal Mortality report published in 2005 by the Confidential Enquiry into Maternal and Child Health (CEMACH), now known as the Centre for Maternal and Child Health Enquiry (CMACE), indicated that 30% of mothers who had a stillbirth or a neonatal death were obese. Obesity in pregnancy was selected as one of CMACE's two main areas of investigations in maternal health for 2008 – 2011.[11]

Recurrent miscarriage (RM) is defined as three or more consecutive miscarriages. It affects 1% of couples trying to conceive.[12] After comprehensive investigations, more than 50% of these couples were found to have "unexplained" recurrent miscarriage.[13,14] When offered supportive care within the setting of a specialist recurrent miscarriage service, these couples have an excellent prognosis for a future successful outcome.[15-17]

Aim

To determine the relationship between maternal Body Mass Index (BMI) and future outcome of pregnancy in couples with unexplained RM.

MATERIALS AND METHODS

All couples attending our recurrent miscarriage clinic had their demographic and clinical details recorded on a computerised database that prospectively collected patients' data including later pregnancies following the diagnosis, their management and the pregnancy outcome. Demographic details of each couple including BMI, ethnicity, age, outcome of previous pregnancies and medical history such as hypertension, diabetes, kidney disease, thyroid dysfunction and autoimmune disease were recorded. Women were classified into four BMI groups: underweight (<18.5 kg/m2), normal weight (18.5 – 24.99 kg/m2), overweight (25.0 – 29.99 kg/m2) and obese (>30 kg/m2), in accordance with the World Health Organization (WHO) classification of BMI, as cited in.[18] All couples had parental peripheral blood karyotyping performed and the female partner had a pelvic ultrasound scan; screening for anti-phospholipid antibodies (lupus anticoagulant and both IgG and IgM anticardiolipin antibodies); activated protein C resistance and genotyping for the Factor V Leiden mutation. We retrospectively collected the data of the couples where the diagnosis was labelled as unexplained recurrent pregnancy loss and where there was no medical condition. The outcome of the first pregnancy following the diagnosis was examined.

Statistical analyses were performed using SPSS version 15.0. (Window SPSS Inc, Chicago.) Univariate analysis was carried out using chi-square test. Multivariate logistic regression analysis was also carried out with a *P*-value of ≤0.05 considered statistically significant with the magnitude of the effect estimated by odd ratios (OR) based on 95% confidence intervals (CI).

RESULTS

There were 1259 women with a history of RM, 696 of whom had unexplained RM. Their clinical and demographic details are shown [Table 1, Figure 1]. We studied the above mentioned factors to assess their association with future pregnancy outcome. Univariate analysis showed that BMI, maternal age, number of previous miscarriages and ethnicity were significantly associated with pregnancy outcome [Table 2]. A multivariate analysis was performed using a forward stepwise entry method logistic regression as shown [Table 3]. When adjusted for maternal age and number of previous miscarriages, obese women had a significantly increased risk of another miscarriage (53/90; 59%) compared to those with a normal BMI (177/406; 44%) [P = 0.028, OR 1.73 (CI = 1.06 – 2.83)]. There was no statistical significant difference in the miscarriage rate amongst those who were overweight [OR 1.27 (CI = 0.89 – 1.83)] or underweight [OR 0.12 (CI = 0.15 – 1.00)] compared to women of normal weight. Not surprisingly, maternal age ≥35 years significantly doubled the risk of another miscarriage compared to age <35 years [P = <0.0001, OR 1.99 (95% CI = 1.45 – 2.73)]. Furthermore, the number of previous miscarriages had a significant association with further miscarriages. Women with a history of ≥5 miscarriages had a two- fold increased risk of a further miscarriages compared to those with 3 – 4 previous miscarriages [P = <0.0001, OR 2.08 (95% CI = 1.42 – 3.06)]. There was no relationship between history of a previous live birth and future pregnancy outcome.

Interestingly, this study showed that Asian women had a significantly increased risk of a miscarriage (36/53; 68%) compared to Caucasian women (236/542; 44%) [OR 2.87 (CI 1.52 – 5.39)]. This was independent of BMI and of ovarian morphology when analyses between these two groups were performed [Tables 4 and 5].

Table 1: Demographic details of women with unexplained RM (*n* = 696)

		Number (%)
BMI Weight (kg)/ Height (m^2)	Underweight	10 (2%)
	Normal	406 (58%)
	Overweight	190 (27%)
	Obese	90 (13%)
Age (years)		
Median 34 years	<35	369 (53%)
Range (17 – 46 years)	≥35	327 (47%)
Number of previous miscarriages	3-4	542 (78%)
	≥5	154 (22%)
Previous live birth (s)	No previous live births	382 (55%)
	Previous live births	314 (45%)

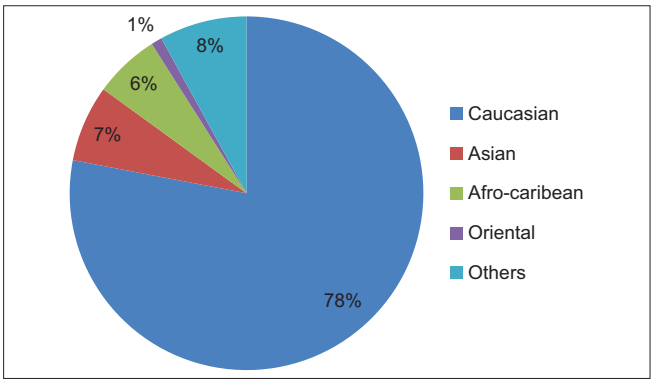

Figure 1: Ethnicity of the study group (*n* = 696)

Table 2: Univariate analysis of the factors associated with pregnancy outcome in women with unexplained RM

Variable	Category	Pregnancy outcome # (%)		*P* value	Odds ratio	95% Confidence interval
		Good	Bad			
Age (years)	<35	222 (60%)	147 (40%)	<0.0001	1.99	(1.45 - 2.73)
	≥35*	146 (45%)	181 (55%)			
Ethnicity	Caucasian	306 (56%)	236 (44%)	0.001	2.87	(1.52 - 5.39)
	Afro-Carribean	17 (41%)	24 (59%)			
	Asian*	17 (32%)	36 (68%)			
	Oriental	3 (43%)	4 (57%)			
	Other	0	1 (100%)			
BMI (Weight kg/Height m^2)	<18.5	9 (90%)	1 (10%)	0.028	1.73	(1.06 - 2.83)
	18.5 - 24.99	229 (56%)	177 (44%)			
	25 - 29.99	93 (49%)	97 (51%)			
	≥30*	37 (41%)	53 (59%)			
Miscarriage (#)	3 - 4	308 (57%)	234 (43%)	<0.0001	2.08	(1.42 - 3.06)
	≥5*	60 (39%)	94 (61%)			

* : The *P*-value Odds Ratio and CI.

Table 3: Logistic regression analysis of the factors associated with pregnancy outcome in women with unexplained RM

Variable	Category	Pregnancy outcome		*P* value	Odd ratio (95% Confidence interval)
		Live birth	Miscarriage		
BMI	Obese (*n* = 90)	41%	59%	0.028	1.73, 1.06 – 2.83
	Overweight (*n* = 190)	49%	51%	NS	1.27, 0.89 – 1.83
	Normal (*n* = 406)	56%	44%		Comparator
	Underweight (*n* = 10)	90%	10%	NS	0.12, 0.15 – 1.00
Ethnicity	Caucasian (*n* = 542)	56%	44%		Comparator
	Asian (*n* = 53)	32%	68%	0.001	2.87, 1.52 - 5.39
	Black, Afro-Carribean (*n* = 41)	41%	59%		1.82, 0.93 – 3.55
	Oriental (*n* = 7)	43%	57%		1.86, 0.39 – 8.79
	Other (*n* = 1)	0%	100%		0
	Not stated (*n* = 52)	48%	52%		1.44, 0.80 – 2.61
Maternal age	<35 (n = 369)	60%	40%		Comparator
	≥35 (*n* = 327)	45%	55%	<0.0001	1.99, 1.45 – 2.73
Number of previous miscarriages	3 – 4 (*n* = 542)	57%	43%		Comparator
	≥5 (*n* = 154)	39%	61%	<0.0001	2.08, 1.42 - 3.06

NS = not significant

Table 4: BMI distributions among Asians and Caucasians

Ethnicity	BMI			
	Underweight	Normal	Overweight	Obese
Asian (53)	2 (4%)	25 (47%)	16 (30%)	10 (19%)
Caucasian (542)	7 (1%)	304 (57%)	158 (29%)	73 (13%)

Chi-square = 3.69 *P* = 0.30 NS

DISCUSSION AND CONCLUSION

Despite comprehensive investigation, a definite underlying cause of the loss of pregnancy has not been identified in more than 50% of couples with RM. This study demonstrates maternal obesity as an independent high risk factor for future miscarriages in couples with unexplained RM. Obese women with a history of unexplained RM have a 73% increased risk of another miscarriage in their subsequent pregnancies compared to those with a normal BMI and should, therefore, be counselled on the potential

Table 5: Distribution of polycystic ovary morphology among Asians and Caucasians

Ethnicity	PCO	Other
Asian (53)	12 (23%)	41 (77%)
Caucasian (536)*	157 (29%)	379 (70%)

*6 no record (1%) Chi-square = 0.74 *P* = 0.39 NS

benefits of weight loss on reproductive outcome. A previous study showed that obese women who achieved weight loss resulting from lifestyle modification programme had a lower miscarriage rate than those who "dropped out".[19]

Although overweight women in this study did not demonstrate an increased risk of miscarriage, they should be advised to avoid further weight gain. Whilst an increased risk of miscarriage in women with a low BMI has been reported, the failure of our study to demonstrate such an association is likely to be due to the small sample size.[20,21]

A recent systematic review demonstrated the difficulties in assessing the true effect of BMI and obesity on reproductive outcomes because of the inconsistencies in BMI classification used in different studies.[5] The use of a single unified categorization of BMI in future studies was recommended in order to assess the true effect of obesity. The strength of our study lies with the use of the WHO classification and the precise inclusion and exclusion criteria. In our study, we only used four categories within the WHO BMI classification for the purpose of statistical analysis without categorizing further the underweight and obese into subgroups.

Studies have shown that certain ethnic groups have a higher cardiovascular and metabolic risks at lower BMI, and this may be because of differences in body shape and fat distribution.[22] The use of a different BMI cut off point in different ethnic groups has been the subject of discussion and an on-going debate.[23] The National Institute of Clinical Excellence (NICE) clinical guideline on obesity CG43 published in 2006, recommended a revised BMI cut off point for overweight and obesity for Asians based on their mortality and morbidity risks i.e. ≥23 kg/m^2 as overweight (increased risk) and ≥27.5 kg/m^2 as obese (high risk).[24]

We saw in our study that Asians had a significantly higher risk of miscarriages than their Caucasian counterparts. The reasons for this remains unclear. In our study group, there was no difference in BMI or polycystic ovary morphology between Asians and Caucasians. Polycystic ovary syndrome has been associated with recurrent miscarriage, though the extent of its contribution remains uncertain.[14,25] A possible explanation may lie with the association between BMI and body fat percentage which differs across ethnic groups.[26] One study examining the body fat percentage/ BMI relationship amongst three ethnic groups (Chinese, Malays and Indians), reported that Indians had the highest body fat percentage and Chinese the lowest for the same BMI. This study also found that for the same amount of body fat as Caucasians who have a BMI of 30 kg/m^2 (cut-off points for obesity as defined by WHO), the BMI cut-off points for obesity would have to be about 27 kg/m^2 for Chinese and Malays and 26 kg/m^2 for Indians and hence, a single universal BMI cut-off point cannot be applied to different ethnic groups.[27] In 2000, the International Association for the Study of Obesity (IASO) and the International Obesity Task Force (IOTF) jointly proposed a revised BMI cut-off points for overweight and obesity for Asians at 23 and 25 kg/m^2 respectively. Indeed, a recent NICE clinical guideline on obesity in 2006, recommended a different cut off point of 27 kg/m^2 for health action for Asians and to use, where possible, waist circumference. This raises the issue of whether clinicians caring for RM women should consider using a lower BMI cut-off point for Asian women in their clinical practice and whether the implications of lowering the BMI would effectively mean an increase in the number of obese amongst Asians. Even if all Asians with BMI ≥ 27.5 kg /m^2 in our study were re-classified as obese, a repeat logistic regression analysis would not change the result of finding obesity an independent risk factor for miscarriage [OR 2.74 (CI 1.45 – 5.19)] compared to BMI ≥30 used in the original analysis [OR 2.87 (CI 1.52 – 5.39)].

In conclusion, we recommend that the BMI of all women with a history of RM should be recorded at their first consultation. Those who are obese should be advised to lose weight through a diet regime and exercise plan. Referral to a dietician and follow up could assist them in weight loss. In addition, BMI should be recorded in subsequent clinic visits to monitor weight loss. The search for more effective methods of assessing risks may help to ease the existing difficulties faced by clinicians who manage RM patients. Further studies need to be conducted to assess the effect of weight loss on the outcome of pregnancies.

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