Pregnancy related complications in women with hypertrophic cardiomyopathy

R Thaman, A Varnava, M S Hamid, S Firoozi, B Sachdev, M Condon, J R Gimeno, R Murphy, P M Elliott, W J McKenna

Objective: To determine whether pregnancy is well tolerated in hypertrophic cardiomyopathy.

Setting: Referral clinic.

Design: The study cohort comprised 127 consecutively referred women with hypertrophic cardiomyopathy. Forty (31.5%) underwent clinical evaluation before pregnancy. The remaining 87 (68.5%) were referred after their first pregnancy. All underwent history, examination, electrocardiography, and echocardiography. Pregnancy related symptoms and complications were determined by questionnaire and review of medical and obstetric records where available.

Results: There were 271 pregnancies in total. Thirty-six (28.3%) women reported cardiac symptoms in pregnancy. Over 90% of these women had been symptomatic before pregnancy. Symptoms deteriorated during pregnancy in fewer than 10%. Of the 36 women with symptoms during pregnancy, 30 had further pregnancies. Symptoms reoccurred in 18 (60%), symptomatic deterioration was not reported. Heart failure occurred postnatally in two women (1.6%). No complications were reported in 19 (15%) women who underwent general anaesthesia and in 22 (17.4%) women who received epidural anaesthesia, three of whom had a significant left ventricular outflow tract gradient at diagnosis after pregnancy. Three unexplained intrauterine deaths occurred in women taking cardiac medication throughout pregnancy. No echocardiographic or clinical feature was a useful indicator of pregnancy related complications.

Conclusions: Most women with hypertrophic cardiomyopathy tolerate pregnancy well. However, rare complications can occur and therefore planned delivery and fetal monitoring are still required for some patients.

Although few studies have examined the clinical implications of pregnancy in patients with hypertrophic cardiomyopathy, anecdotal documentation of major complications or significant worsening of symptoms in some patients has led to a belief that pregnancy may be associated with a poor outcome.7–8 As hypertrophic cardiomyopathy is diagnosed in more patients as a result of increased clinical awareness and familial screening, more women with the disease will be considering pregnancy. It is therefore important to have some estimate of the risk associated with pregnancy.

Methods

St George’s Hospital Medical School is a tertiary referral centre for hypertrophic cardiomyopathy. The effects of pregnancy on hypertrophic cardiomyopathy were studied in women aged 25–65 years with hypertrophic cardiomyopathy who had been reviewed at St George’s Hospital within the previous five years. The diagnosis of hypertrophic cardiomyopathy was based on the echocardiographic evidence of unexplained myocardial hypertrophy with a maximal wall thickness exceeding two standard deviations for age.7 Patients with cardiac or systemic disease that could have produced hypertrophy or primary valvar dysfunction were excluded. Two hundred women fulfilled these criteria.

Clinical evaluation consisted of history, family history, 12 lead ECG, two dimensional and M mode echocardiography, and 24 hour Holter monitoring. An abnormal blood pressure response during exercise was defined as a failure of systolic blood pressure to rise by more than 25 mm Hg from baseline values or a fall of more than 10 mm Hg from baseline blood pressure during exercise.9 Non-sustained ventricular tachycardia was defined as one or more runs of three or more consecutive ventricular extrasystoles at a rate of more than 120 beats/minute lasting for < 30 seconds.7 A family history of sudden death was defined as two or more sudden cardiac deaths before the age of 40 years.9

To determine the effects and outcome of pregnancy, questionnaires were sent to all patients. Patients were asked if they had been pregnant and how often, if they had experienced chest pain, breathlessness, palpitation, or syncope before, during or after their pregnancies, and whether any of their symptoms had altered during this time course. The presence of symptoms or complications during labour and the postnatal period, as well as the gestation, mode of delivery, and types of anaesthesia or analgesia, were determined. Medications taken before and during pregnancy were also recorded. Questionnaires were returned by 165 (82.5%) women, of whom 127 had been pregnant. These 127 women constituted the final study population. Forty (31.5%) of these women were evaluated before their first pregnancy. Eighty seven (68.5%) women had already been pregnant before referral and therefore were clinically evaluated after pregnancy. The results of the questionnaires were corroborated by review of medical and obstetric notes where available.

Results

Patient characteristics

The final study population consisted of 127 women (mean (SD) age 47 (15) years, range 25–65 years) who had been pregnant. The total number of pregnancies recorded was 271; the mean number of pregnancies per patient was 2.1 (range 1–5).

In the total population, hypertrophic cardiomyopathy was diagnosed in 47 (37.0%) women before their first pregnancy,
in 42 (33.1%) either during or between pregnancies, and in 38 (29.9%) after all pregnancies were completed. Most women did not deliver at St George’s Hospital and records from the preceding 10 years or more were unavailable. Obstetric records were available for 55 (43%) women. Table 1 shows the mean ages at diagnosis and reason for diagnosis of all the women in this study.

Table 2 shows the clinical and echocardiographic data and the results of cardiopulmonary exercise testing obtained from the 40 (31.5%) patients referred and evaluated before pregnancy. All of these data were collected within a year of pregnancy.

Table 3 shows the clinical, exercise, and echocardiographic data at first presentation from the 87 (68.5%) women referred after all pregnancies were completed. Hypertrophic cardiomyopathy was diagnosed in seven of these women before pregnancy, in 42 during or between pregnancies, and in 38 after all pregnancies were completed.

### Antenatal period
Thirty five women (27.5%) experienced one or more cardiac symptoms during the antenatal period. The most common symptom was dyspnoea, which occurred in 26 (20.5%) women. Twenty four (92.3%) of these women had complained of breathlessness before pregnancy; nine (34.6%) experienced worsening breathlessness, nine (34.6%) described little or no change, and six (23.1%) reported an improvement during pregnancy. Chest pain occurred in 12 (9.4%) women; 11 (91.7%) had experienced similar chest pain before pregnancy and four (33.3%) reported a significant increase in frequency of chest pains. Palpitation was reported by nine (7.1%) women, all of whom had experienced similar palpitation before pregnancy; seven (77.8%) reported a greater frequency or duration of palpitation during pregnancy. Both of the women (1.6%) who reported syncpe during pregnancy had a history of recurrent syncpe before pregnancy; this was secondary to paroxysmal atrial fibrillation in one patient and was unexplained in the other. Of the 35 women who complained of symptoms during pregnancy, 30 went on to have further pregnancies. Symptoms recurred in 18 (60%); symptomatic deterioration in subsequent pregnancies was not reported.

### Labour
Eleven women (8.7%) experienced cardiac symptoms during labour. All were known to have hypertrophic cardiomyopathy before pregnancy and all (91%) but one patient who described transient dizziness had described similar symptoms before pregnancy. Four (3.1%) women experienced breathlessness, two (1.6%) chest pain, two (1.6%) transient dizziness, and 3 (2.4%) sustained palpitations. Review of the obstetric notes from the two women who complained of chest pain showed that the chest pain was transient and did not require treatment. Notes were available for two of the four patients who complained of breathlessness: mild breathlessness was documented, finger oximetry recorded normal oxygen saturations, and breathlessness improved after delivery without treatment. One patient who complained of palpitation during labour had an abdominally located implantable cardioverter-deﬁbrillator (ICD) for primary prevention of sudden cardiac death. The ICD was switched off during labour and ECG recordings showed frequent ventricular extrasystoles only. Another patient who complained of palpitations had documented atrial fibrillation during labour, which reverted spontaneously after three hours. One of the patients who described transient dizziness had documented hypotension (30 mm Hg systolic) after epidural insertion. Notes were unavailable for the other patient.

### Postnatal complications
Two primigravida, both with hypertrophic cardiomyopathy diagnosed before pregnancy, developed pulmonary oedema in the postpartum period requiring hospital admission and diuretics. The first patient complained of mild breathlessness before and during pregnancy. Delivery was by planned caesarean section under general anaesthesia for obstetric reasons. She presented five days later with pulmonary oedema. Echocardiography eight weeks after delivery showed asymmetric septal hypertrophy with a maximal wall thickness of 18 mm, no outflow tract gradient, normal left ventricular cavity dimensions, and no evidence of valvar or systolic dysfunction. Review of the obstetric records showed no evidence of...
excessive use of intravenous fluids, blood loss, or significant anaemia during labour.

The second patient complained of mild breathlessness before pregnancy, which worsened during pregnancy. During labour she had an epidural for pain relief and was treated for hypotension with fluid replacement. The rest of labour was uneventful and was followed by a spontaneous vaginal delivery of a healthy baby. She presented five days later with pulmonary oedema. This patient had delivered 20 years previously and therefore pregnancy records were unavailable. Prepregnancy echocardiography was also unavailable. The first available echocardiogram had been made nine years after pregnancy and showed asymmetric septal hypertrophy with a maximal wall thickness of 18 mm, no outflow tract gradient, and no left ventricular enlargement or evidence of systolic dysfunction.

Both women remain well and have not deteriorated clinically since pregnancy. Neither patient has undergone further pregnancy.

### Medications during pregnancy

Thirty (23.6%) women were receiving medication for hypertrophic cardiomyopathy before pregnancy. Fifteen (11.8%) women discontinued medications before or very early in pregnancy. These patients did not report significant symptom deterioration, birth weights were all normal, and no fetal anomalies were reported. In the remaining 15 (11.8%) women medication was not altered; this accounted for 18 pregnancies (6.6% of total pregnancies). A β blocker alone was taken in 14, amiodarone alone in two, a β blocker and amiodarone in one, and digoxin with anticoagulation in one pregnancy. Intrauterine death occurred (at 38–40 weeks) in three (16.7%) of these pregnancies (1.1% of total pregnancies). One patient had been on a β blocker for chest pain and presented with abdominal pain and vaginal bleeding. Placental abruption was diagnosed. The other women had uneventful pregnancies: one had taken amiodarone for sudden death prophylaxis and the other a β blocker and amiodarone for breathlessness and paroxysmal atrial fibrillation. Regular growth scans and necropsy in all three cases failed to detect any fetal anomaly. No intrauterine deaths were reported in women who had not taken medication throughout pregnancy.

### Anaesthesia

Nineteen women (15%) received general anaesthesia for caesarean section; 11 (8.7%) were known to have hypertrophic cardiomyopathy before pregnancy. No complications were reported. Epidurals were used in 39 pregnancies by 24 (18.9%) women. Eleven (8.7%) were known to have hypertrophic cardiomyopathy before pregnancy. No significant left ventricular outflow tract gradient (≥ 30 mm Hg) was recorded before pregnancy in these women. Dizziness was reported after epidural insertion in two of these pregnancies. Obstetric records from one of these patients listed hypotension with a drop in systolic blood pressure of 30 mm Hg; there were no associated maternal or fetal sequelae. Thirteen women (10.2%) with hypertrophic cardiomyopathy diagnosed after pregnancy also received epidurals. Three of these had significant outflow tract gradient at first visit and one other has undergone myectomy since pregnancy. These patients did not report any problem during the epidural or pregnancy.

### Echocardiographic evaluation

Forty women (31.5%) underwent echocardiographic assessment before their first pregnancy (table 2). One (2.5%) patient had a maximal wall thickness over 30 mm but she did not report symptoms before or during pregnancy. Two patients (5.0%) had a significant resting (≥ 30 mm Hg) left ventricular outflow tract gradient, two (5.0%) women had been treated for symptomatic left ventricular outflow tract gradient by myectomy, and one (2.5%) was given a pacemaker (DDDR) before pregnancy. These five women did not complain of

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**Table 3 Clinical and echocardiographic characteristics of women for whom data were unavailable before pregnancy but were collected at first presentation to St George’s Hospital**

<table>
<thead>
<tr>
<th>Time of diagnosis</th>
<th>Before pregnancy</th>
<th>During or between pregnancies</th>
<th>After pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>7</td>
<td>42</td>
<td>38</td>
</tr>
<tr>
<td>Mean age of first pregnancy (years)</td>
<td>24 (2) (19–27)</td>
<td>26 (4) (18–33)</td>
<td>24 (4) (16–36)</td>
</tr>
<tr>
<td>Mean age of review (years)</td>
<td>29 (4) (29–44)</td>
<td>33 (7) (31–44)</td>
<td>34 (3) (27–53)</td>
</tr>
<tr>
<td>Anemia</td>
<td>2 (28.6%)</td>
<td>10 (23.8%)</td>
<td>10 (26.3%)</td>
</tr>
<tr>
<td>Dyspnoea (NYHA III)</td>
<td>1 (14.5%)</td>
<td>9 (21.4%)</td>
<td>11 (28.9%)</td>
</tr>
<tr>
<td>Syncope</td>
<td>0 (0%)</td>
<td>4 (9.1%)</td>
<td>5 (13.1%)</td>
</tr>
<tr>
<td>Palpitations</td>
<td>1 (14.3%)</td>
<td>7 (16.2%)</td>
<td>6 (15.8%)</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (2.6%)</td>
</tr>
<tr>
<td>Non-sustained ventricular tachycardia</td>
<td>0 (0%)</td>
<td>6 (14.3%)</td>
<td>4 (10.5%)</td>
</tr>
<tr>
<td>Paroxysmal atrial fibrillation</td>
<td>1 (14.3%)</td>
<td>3 (7.1%)</td>
<td>6 (15.8%)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>0 (0%)</td>
<td>1 (2.4%)</td>
<td>4 (10.5%)</td>
</tr>
<tr>
<td>FHSVD</td>
<td>1 (14.3%)</td>
<td>6 (14.3%)</td>
<td>6 (15.8%)</td>
</tr>
<tr>
<td>ABPR</td>
<td>1 (14.3%)</td>
<td>6 (14.3%)</td>
<td>3 (7.9%)</td>
</tr>
<tr>
<td>Mean %VO₂ max</td>
<td>78 (16) (54–111)</td>
<td>73 (9) (63–105)</td>
<td>77 (12) (59–100)</td>
</tr>
<tr>
<td>Mean LVWT (mm)</td>
<td>23 (4) (18–25)</td>
<td>25 (5) (15–31)</td>
<td>19 (3) (14–20)</td>
</tr>
<tr>
<td>Mean LVES (mm)</td>
<td>42 (3) (35–49)</td>
<td>44 (4) (30–49)</td>
<td>46 (5) (34–54)</td>
</tr>
<tr>
<td>Mean LVOTG (mmHg)</td>
<td>29 (3) (21–34)</td>
<td>28 (5) (16–41)</td>
<td>30 (6) (17–42)</td>
</tr>
<tr>
<td>Mean fractional shortening (%)</td>
<td>32 (7) (29–47)</td>
<td>36 (6) (28–52)</td>
<td>35 (4) (23–54)</td>
</tr>
<tr>
<td>Mean left atrium (mm)</td>
<td>25 (5) (13–39)</td>
<td>21 (4) (13–36)</td>
<td>22 (5) (11–12)</td>
</tr>
<tr>
<td>Myectomy</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Pacemaker</td>
<td>1 (14.3%)</td>
<td>1 (2.4%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD) and range. %VO₂ max, maximal oxygen consumption during upright exercise testing; ABPR, abnormal blood pressure response to exercise; FHSVD, family history of sudden cardiac death; LVWT, left ventricular wall thickness; NYHA, New York Heart Association.
symptoms in pregnancy or labour. Six (15.0%) women had left atrial enlargement (≥ 45 mm), of whom four (10.0%) had symptoms of chest pain, palpitation or breathlessness before pregnancy (two were taking β blockers for paroxysmal atrial fibrillation). None of these patients complained of deterioration in symptoms in pregnancy, although one developed atrial fibrillation in labour. One patient (2.5%) had left ventricular enlargement (left ventricular end diastolic dimension ≥ 55 mm) and she described a modest increase in breathlessness during pregnancy. No patients had significant systolic dysfunction (fractional shortening ≤ 25%).

In the remaining 87 (68.3%) women echocardiographic assessment was after their first pregnancy because they were referred after pregnancy. In these women echocardiography from the first visit was reviewed (table 3). Three women (3.4%) had a wall thickness of 30 mm or more. Hypertrophic cardiomyopathy had been diagnosed in two of these women between pregnancies—one was asymptomatic and one complained of mild breathlessness before and during pregnancy. Hypertrophic cardiomyopathy was diagnosed in the other patient after pregnancy. She complained of mild chest pain and breathlessness before pregnancy and developed more frequent chest pain during pregnancy.

Five (5.7%) women had significant left ventricular outflow tract gradient (≥ 30 mm Hg). Two of these were known to have hypertrophic cardiomyopathy before pregnancy and one had undergone myectomy; none of them reported significant symptoms in pregnancy. Hypertrophic cardiomyopathy was diagnosed in two women during pregnancy and one reported mild breathlessness before and during pregnancy. Hypertrophic cardiomyopathy was diagnosed in one of these women after pregnancy and she complained of breathlessness before and during pregnancy.

Seven (8.0%) patients had left atrial enlargement (≥ 45 mm); hypertrophic cardiomyopathy had been diagnosed in one before pregnancy and in two between pregnancies. These women did not report symptoms in pregnancy. Hypertrophic cardiomyopathy was diagnosed in four women with left atrial enlargement after pregnancy; two complained of palpitation before and during pregnancy, and one complained of breathlessness before and during pregnancy.

Left ventricular enlargement (left ventricular end diastolic dimension ≥ 55 mm) was noted in five (5.7%) women. Hypertrophic cardiomyopathy was diagnosed between pregnancies in three women who were asymptomatic before and during pregnancy and in two women after pregnancy. One complained of mild breathlessness before and during pregnancy. Two (2.3%) patients (with hypertrophic cardiomyopathy diagnosed in one between and in one after pregnancy) had evidence of systolic dysfunction (fractional shortening ≤ 25%); neither had symptoms before or during pregnancy.

**DISCUSSION**

Pregnancy is accompanied by major physiological changes, which place extra demands on the cardiovascular system. These include an increase in plasma volume (up to 40%) and cardiac output (30–50%). The increased cardiac output is mainly attributable to augmented stroke volume and a modest increase in heart rate. The increase in stroke volume is secondary to an increase in blood volume, as well as a reduction in systemic vascular resistance. Additional stresses are placed on the cardiovascular system during labour and delivery. During labour cardiac output increases by a further 20% during each uterine contraction because of the increased venous return from the contracting uterus and the sympathetic response to pain. Delivery can result in significant blood loss.  

Although these changes may be expected to affect the course of pregnancy in women with hypertrophic cardiomyopathy there have been few systematic studies. This analysis of 127 women with hypertrophic cardiomyopathy assessed 271 pregnancies over 40 years. In the total population (the majority (92; 71.5%) of women were asymptomatic during pregnancy; over 90% of women who reported symptoms had experienced similar symptoms before pregnancy. Prepregnancy symptoms worsened in the minority, although palpitations occurred more frequently during pregnancy in women who had previously reported them. Some patients reported an improvement in their symptoms during pregnancy. Symptoms did not necessarily reoccur in subsequent pregnancies and significant symptom deterioration was not reported. Pulmonary oedema was seen in two women postnatally. These two women have not reported any long term deterioration in their condition since pregnancy. The explanation for pulmonary oedema in these two patients is not clear; in one case pulmonary oedema may have been related to excessive use of intravenous fluid to treat hypotension.

Hypertrophic cardiomyopathy was diagnosed in the majority of women in this study (89; 70%) before, during, or in between pregnancies. However, hypertrophic cardiomyopathy was diagnosed after completion of all pregnancies in 30% of women, thus raising the possibility that these patients were unaffected at the time. Ten (26.3%) of these women had reported cardiac symptoms before pregnancy and, as hypertrophy normally develops during or shortly after adolescence, it is a reasonable expectation that the majority of these women were affected at the time of pregnancy. Even when these patients were excluded from the analysis the number of reported and observed complications remained low.

This series of women with hypertrophic cardiomyopathy included patients with and without risk factors for sudden cardiac death, as well as patients who had undergone myectomy, dual chamber pacing, and ICD implantation before and after pregnancy. No clinical or echocardiographic feature was associated with a poor outcome during pregnancy. Indeed, given the low frequency of adverse events seen in pregnancy, correlations between clinical and echocardiographic features and adverse events would be difficult to show.

One of the most important concerns is whether there is an increased risk of death during pregnancy in hypertrophic cardiomyopathy. In this series no maternal deaths occurred. Interrogation of the extended database of 400 women seen at this centre since 1989 found in 45 recorded cases (11.2%) of death; 44 of these women (mean maternal age 47 (19) years, range 7–82 years). The cause of death was sudden unexplained death in 23, heart failure related in 14, and unrelated to hypertrophic cardiomyopathy in eight women. No patient died during pregnancy or soon after—that is, within six months. Data from the Confidential Enquiries into Maternal Deaths, which registers and investigates all maternal deaths in the UK, also confirms a low mortality in pregnancy. Two of 446 maternal deaths between 1991 and 1996 (figures from 1996 onwards are not yet published) were related to hypertrophic cardiomyopathy. One woman known to have hypertrophic cardiomyopathy died of congestive cardiac failure four weeks after delivery. The other had a sudden death five days after delivery and necropsy showed hypertrophic cardiomyopathy.

Epidural anaesthesia has generally not been advised during pregnancy in women with hypertrophic cardiomyopathy because of its potential to cause venous pooling, to reduce filling pressures, and potentially to exacerbate left ventricular outflow tract gradient. In this study, women who received epidural anaesthesia reported few complications; however, some women may have been unaware of complications and not all obstetric records were available. Moreover, few women had documented left ventricular outflow tract obstruction before pregnancy. In those who reported hypotension or dizziness it is unclear whether this was an exaggeration of a normal response to epidural anaesthesia or whether this was
Study limitations

The main limitation of this study lies in its retrospective nature; however, a large prospective analysis is unlikely given the inherent difficulties encountered when studying the effects of pregnancy in an uncommon disease.

Questionnaires may be subject to responder bias but where possible the results were validated by review of the medical and obstetric notes. Only a minority of symptomatic complaints remained unconfirmed.

We acknowledge that only surviving women were targeted with questionnaires. However, as already stated, no patient reviewed at our institution has died during or within six months of pregnancy. Thirty five women (18%) did not return questionnaires; these patients could not be traced because of recent change of address. However, all but one of these patients were aged over 40 when last reviewed at this centre and are therefore unlikely to contribute to pregnancy related mortality data.

Conclusion

These data suggest that patients with hypertrophic cardiomyopathy generally tolerate pregnancy well without significant symptoms or complications. The cohort studied was representative of the general population of patients with hypertrophic cardiomyopathy including patients with typical symptoms (chest pain, breathlessness, and syncope), patients with one or more risk markers for sudden cardiac death, and patients having undergone myectomy or other invasive procedures. There were no deaths, and no particular clinical or echocardiographic feature was associated with a poor outcome. Although the presence of a significant left ventricular outflow tract gradient did not affect maternal outcome, the effect of epidural could not be fully evaluated in these patients. This study did not include patients with previous heart failure or severe restrictive physiology. These phenomena are rare in hypertrophic cardiomyopathy and such patients rarely contemplate pregnancy. However, the physiological demands of pregnancy in these patients would be expected to lead to haemodynamic compromise and therefore we would not recommend pregnancy in these patients.

ACKNOWLEDGEMENTS

Drs Thaman, Hamid, Firoozi, and Sachdev were supported by Junior Fellowship Grants from the British Heart Foundation.

REFERENCES