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Royal Brompton & Harefield NHS
NHS Foundation Trust

PRESS RELEASE

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New research discovers genetic cause for rare heart condition that develops during pregnancy

An international study led by experts from Royal Brompton Hospital and Penn Cardiovascular Institute, USA, has found for the first time that peripartum cardiomyopathy (PPCM), a condition that can lead to a woman developing heart failure in late pregnancy or shortly after delivery, can often have a genetic cause.

PPCM affects up to 700 women a year in the UK. The condition can be life-threatening and the most common symptoms are breathlessness and palpitations. Treatments include drug therapies, such as ace inhibitors and beta blockers, however, in the most severe cases, a heart transplant can be the only long-term option.

Until now, there has been no clear explanation as to why some women develop PPCM. Whilst there are known risk factors, such as pre-existing hypertension and preeclampsia, these cannot explain most cases.

The new findings, published in the *New England Journal of Medicine*, identified a sequence of gene variants in women with the condition. Researchers had sought to determine whether the genetic mutations responsible for a condition known as dilated cardiomyopathy (DCM) might also play a part in PPCM.

The condition shares clinical features with DCM, including enlargement of the heart, a decline in heart function and the risk of sudden death. There are more than 40 genes in which mutations are known to cause DCM, including the TTN gene, which is responsible for making the largest human protein. It has previously been found that variants in the TTN gene cause up to one in five DCM cases.

Researchers compared the prevalence of variants in 43 genes in 172 women with PPCM, recruited from six centres in the United States, Japan and Germany, to those of 332 people with DCM, recruited at Royal Brompton & Harefield NHS Foundation Trust, and a control population of more than 60,000 people.

Around 15 per cent of PPCM patients were found to carry variants that disrupted important heart genes. This was significantly higher than the controls but similar to the patients with DCM (17 per cent). In particular, 10 per cent of women with PPCM had mutations of the TTN gene, compared with just 1.4 per cent of the controls.

The study findings suggest that PPCM can have very similar genetic characteristics to DCM, with variants of the TTN gene found to be the most prevalent genetic disposition of each disease. The results have implications for the way the condition is managed and treated in future, and may mean that relatives of PPCM patients are offered the same genetic screening as families of patients with DCM.

James Ware, consultant cardiologist at Royal Brompton & Harefield NHS Foundation Trust and clinical senior lecturer in genomic medicine at Imperial College London, was the lead author of the research paper. He said:

> “Our findings explain why a significant number of PPCM cases occur. When we looked at cases without the known risk factors we found a lot of genetic abnormalities. For example, a quarter of patients without hypertension had TTN gene mutations.
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> “This new information tells us more about the condition and discovering that it can be genetic means we can start to think about it in a different way. For example, it raises the question of whether we should be offering gene testing to these patients and screening their relatives, or putting them under close surveillance if they become pregnant, to detect the problem early and begin any necessary treatment as soon as possible.
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> “PPCM has a mortality rate of 5 to 10 per cent, so being able to shed light on why it occurs in some women and not others is an important development and could ultimately save lives. Further research is needed to better understand the value of genetic information in determining the prognosis of PPCM.”

Penny Davis, 34, developed heart palpitations and shortness of breath while pregnant with her three-year-old daughter Poppy in 2011. By the time she was 18-weeks pregnant she was fainting and having blackouts, and a 22-week scan found her heart was beating too fast. Subsequent tests, including an electrocardiogram (ECG) and an echocardiogram, found a heart abnormality and she was later diagnosed with PPCM. Penny, a part-time HR manager from Walton-on-Thames in Surrey, said:

> "Finding out there was something wrong with my heart while I was pregnant felt like the end of the world. Because I was pregnant the treatment was limited and this was very worrying. I was prescribed beta blockers and my palpitations calmed down.
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> "It was a huge relief when Poppy was born in January 2012 with no health problems. I had been told PPCM could get worse after birth and it did straightaway. A few days after the birth I thought I was dying because I had strong palpitations and felt so dizzy. I was prescribed ACE inhibitors and the term "heart failure" was used by the team at my local hospital for the first time – they had avoided saying it before so not to stress me out during pregnancy. It hit home how bad it was and that I may never get better."

Penny was told she could not breastfeed due to her medication and was advised to reduce her fluid intake and adopt a low salt diet to aid her heart function. Doctors also told her it would not be safe for her to have more children.

> "Having to accept I would only have one child was like going through a grieving process. I made the most of everything with Poppy, thinking I'd never be able to do it again."

Penny was referred to experts at Royal Brompton Hospital, in June 2012, who suspected her PPCM was connected to a thyroid problem and that, if this was the case, she may be able to have more children.

> "I had hope for the first time. The care at Royal Brompton was incredible – I had so many tests so the team could really understand my case. My heart totally recovered and I have come off ACE inhibitors, but I'm still monitored carefully.

> “I was overjoyed to find out I was pregnant last year, and I’m due in April. I never thought it would be possible. My heart function dropped slightly during pregnancy but it has stabilised and I’m being scanned every four weeks. Every so often I panic a bit because of what happened last time, but I know I’m in good hands now.”

The new research was jointly led by Dr Zoltan Arany at the University of Pennsylvania, Drs Christine and Jon Seidman at Harvard Medical School, and Dr Dennis McNamara at the University of Pittsburgh Medical Center. It was supported by the NIHR Royal Brompton Cardiovascular Biomedical Research Unit, Imperial College London, the National Institutes of Health, the Foundation Leducq, Howard Hughes Medical Institute and the Medical Research Council.

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