

Removal of fibroids that distort the womb cavity may prevent recurrent miscarriages

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Researchers have found the first, firm evidence that fibroids are associated with recurrent miscarriages. They have also discovered that if they removed the fibroids that distorted the inside of the womb, the risk of miscarriage in the second trimester of pregnancy was reduced dramatically – to zero.

The study, which is published online in Europe's leading reproductive medicine journal *Human Reproduction* today (Wednesday), is the culmination of 20 years of investigation into recurrent miscarriage by Professor Tin-Chiu Li and his team at the recurrent miscarriage clinic at the University of Sheffield and Sheffield Teaching Hospitals (Sheffield, UK). In addition, for the first time it has given a reliable estimate of the prevalence of fibroids in women who have recurrent miscarriages.

Fibroids in or around the womb (uterus) are benign tumours composed of muscle and fibrous tissue. Although they have been associated with spontaneous miscarriage, until now there has been no evidence of their role in recurrent miscarriages (RM). The prevalence of fibroids has been estimated to be between 3-10% in women of reproductive age, but the prevalence is unknown in women who experience RM, which is defined as three or more consecutive miscarriages.

The researchers analysed data from 966 women who attended the Sheffield RM clinic. The women were scanned for uterine anomalies, including fibroids, via transvaginal ultrasound and radiology, and 79 were found to have fibroids. "This enabled us to calculate that the



prevalence of fibroids was 8.2% among women with recurrent miscarriages; this has never been accurately reported before," said one of the researchers, Dr Sotirios Saravelos, who is a clinical research Fellow at the University of Sheffield.

Fibroids were diagnosed and grouped into three classifications:

- Submucosal these grow in the muscle beneath the inner lining of the womb wall and grow into the middle of the womb, distorting the cavity
- Intramural these develop in the muscle wall of the womb and are the most common type of fibroid. They do not distort the cavity and have less than 50% protrusion into the serosal surface – the outer membrane lining the womb
- Subserosal these grow outside the wall of the womb into the pelvis, do not distort the <u>womb</u> cavity, and have a greater than 50% protrusion out of the serosal surface.

Prof Li used minimally invasive surgery (hysteroscopy) to remove cavitydistorting (submucosal) fibroids from 25 women; 54 women with fibroids that did not distort the cavity had no surgery and they were matched with a control group of 285 women whose recurrent miscarriages were still unexplained after all investigations found nothing abnormal; these women also had no intervention.

In the 25 women who had undergone surgery, miscarriage rates in subsequent pregnancies during the second trimester fell from 21.7% to 0%. This translated to an increase in the live birth rate from 23.3% to 52%.

Dr Saravelos said: "This is the first time that it has been shown that removing fibroids that distort the uterine cavity may increase the



chances of a subsequent live birth in women with recurrent miscarriages."

The 54 women with fibroids not distorting the uterine cavity and who had had no surgery also did better after referral to the RM clinic. Pre-referral, the miscarriage rate during the second trimester was 17.6% and this fell to 0% after referral. Live birth rates went up from 20.6% to 70.4% in subsequent pregnancies. This was similar to results from the 285 women with unexplained RM; the second trimester miscarriage rate was 8% pre-referral to the clinic, falling to 1.8% post-referral, while live birth rates increased from 20.6% to 71.9% after referral.

Dr Saravelos said: "These results are interesting because they suggest that the finding of fibroids in women with recurrent miscarriage does not necessarily imply that the fibroids are the only cause of the miscarriage. In addition, they suggest that surgical intervention is not the only means whereby patients with recurrent miscarriage benefit from attending a specialised, dedicated clinic. However, for women with fibroids that distort the uterine cavity, our work shows that removing the fibroids can eliminate miscarriage during the second trimester and double the live birth rate in subsequent pregnancies.

"It has been recognised since the 1980s that women with unexplained recurrent miscarriage have very good pregnancy outcomes following referral to a dedicated clinic without the need for any intervention, and with psychological supportive care, i.e. tender loving care, alone. This usually takes the form of regular visits to a dedicated recurrent miscarriage clinic, regular antenatal scans to check the condition of the baby, reassurance to the mother from the specialist that everything is progressing well and specialist antenatal counselling throughout the pregnancy.

"Interestingly, although women may increase their live birth rate by up to



50% after psychological supportive care, the exact underlying mechanisms involved in this process are not entirely understood. In the present study, the fact that women with fibroids not distorting the uterine cavity do so well, suggests that they also do not have an underlying cause for recurrent miscarriage. As a result, they can also be considered as having 'unexplained recurrent miscarriage', and should be counselled that they have very good chances of a successful pregnancy without the need for any intervention or surgery and with the psychological supportive care offered by a dedicated recurrent miscarriage clinic."

The main limitation of the study is that there was no control group for the women who had their <u>fibroids</u> removed and so it is not possible to tell whether they would have done better without surgery, after referral to the RM clinic. The researchers say that their work highlights the need to perform a randomised controlled trial to investigate this.

"The definitive study requires the recruitment of a rather large number of patients to be randomised between intervention and no intervention. This would require the input of several clinics in a multi-centre randomised controlled trial and its success would depend on the support of all clinics along with that of Sheffield," said Dr Saravelos.

More information: "The prevalence and impact of fibroids and their treatment on the outcome of pregnancy in women with recurrent miscarriage", by Sotirios H. Saravelos, Junhao Yan, Hassan Rehmani, and Tin-Chiu Li. *Human Reproduction* doi:10.1093/humrep/der293

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