Recurrent Miscarriage/ Recurrent Implantation failure

Recurrent miscarriage is defined as the recurrent pregnancy loss of 3 consecutive pregnancies but it has also in more recent times defined as recurrent Implantation Failure after 3 consecutive embryo transfers of good quality embryos have failed to achieve a pregnancy.

One may consider starting to investigate after 2 miscarriages as the occurrence of 2 consecutive miscarriages in a young couple would be less than 5%, and in an older couple there is an urgency to investigate even though it is more common, as there is also the background anxiety of reducing ovarian reserve in these patients

The definition is still fairly loose. One may consider a pregnancy as a miscarriage only if visualised on ultrasound or above a certain B-Hcg threshold. Two ultrasound confirming an intrauterine pregnancy that does not show viability should be diagnosed as a definitive miscarriage.

The causes are varied and Aneuploidy remains the biggest cause and responsible for least 90% of miscarriages. An Italian study identified 250 missed miscarriages. Of those, 220 were shown to be chromosomally abnormal, 20 were structurally abnormal abortuses, and only 10 did not have an explanation.

It follows a very similar recent study in which 95% of patients achieved a live birth when chromosomally tested embryos were placed (up to 3 separate transfers if needed).

The other causes include: Anatomical issues such as fibroids, polyps, Uterine septae, and endometriosis. Endocrine issues such as thyroid, high prolactin, PCOS, BMI can also be operative in the aetiology. Autoimmune

factors such as chronic endometritis, natural killer cells, HLA incompatibility, Acquired Thrombophilia, Autoantibody levels and abnormal TSH can also be causative. There is increasing evidence that an overgrowth of the wrong type of microbiomes within the vaginal or uterine environment can lead to recurrent implantation failure, and only a limited panel is tested within Australia.

A shotgun approach is usually taken and 50% of cases may have an underlying cause. Therapies may be limited and the best evidence is for anatomical issues, thyroid dysfunction and only in acquired antiphospholipid syndrome.

The use of antibiotics and probiotics have now come to play a big role, especially where no causative factors are clearly seen.

Progesterone deserves a special mention and although Recent data doesn't support its use empirically in recurrent miscarriage or threatened miscarriage, its use in a small subgroup with >3 miscarriages, appears to be statistically significant in improving outcomes.

Lastly, PGT- A preimplantation genetic testing for aneuploidy (formerly PGS) can identify chromosomally normal embryos, to be transferred following IVF in a bid to avoid miscarriage but it is important to note that there are limitation to the technology for the following reasons.

1. It is simply a selection tool, and would only help those who have high rate of aneuploidy but still makes large numbers of embryos.

2. That no of embryos that can be tested is very dependent on the embryo quality that will allow embryo biopsy.

3. Tests can be inconclusive as there is a degree of false positives and a low-moderate level of mosaicism, although PGT-A has advanced to getting live births even from mosaic embryos.

4. There is a rate of embryo loss due to the biopsy and the subsequent results of the testing that would make them unsuitable for transfer. This then reduces the cumulative LIVE BIRTH RATE when PGT-A is employed. Careful consideration and counselling should take place with a good balanced discussion based on the couples' personal journey and counselling to help them navigate this complicated treatment modality.

DR MAHA RAGUNATH

Fertility Specialist