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LETTER TO THE EDITOR

Age considerations in the management of recurring miscarriage

David A. Crosby[1] · Sarah M. Cullen[1] · Cathy M. Allen[1]

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Dear Editor,

We found that in women ≥ 40 years old with recurrent miscarriage (RM), cytogenetic errors are common and antiphospholipid syndrome (APLS) is uncommon.

The incidence of RM is between 1 and 5%, with some heterogeneity among the definitions used [1, 2]. Recent reports suggest that the incidence of RM may have increased over the past decade [3]. Some of this increase may be attributed to improved case recognition, while the sociodemographic shift towards delayed childbearing continues to present clinically in age-related pregnancy losses. Chromosomal errors occur more frequently in the conceptions of older women [2]. Despite this, most RM guidelines adopt a standardised approach to investigation and management for women regardless of age. This non-specific approach exposes RM patients to possible delay and even to potential harm from empiric therapies while inappropriate, expensive investigations are undertaken.

We performed a retrospective study of patients attending the RM service in a large tertiary referral centre between 2014 and 2017. Data on demographics, clinical features, investigations, management, and obstetric outcomes were analysed by female age groups: (i) 25 to 34, (ii) 35 to 39, and (iii) ≥ 40 years. Anti-Müllerian hormone (AMH) testing was offered to women ≥ 35 years.

One hundred seventy cases of RM were analysed. The mean age of women attending the service was 36.3 years (range 22–43). Approximately one third of patients were aged 25–34 years, one third were aged 35–39 years, and almost one third were women over the age of 40 years.

Only 2.4% of cases ($n = 4$) were found to be due to APLS; none of these cases were in women ≥ 40 years. Where karyotype analyses on products of conception (POC) were available (27.1%, $n = 46$), chromosomal abnormality was demonstrated in the majority of cases (76.1%, $n = 35$). In women ≥ 35 years who had AMH testing, the median AMH was 7.5 pmol/L (SD12.7).

Outcome data on the RM patients are generally reassuring. Half of all the patients with RM went on to conceive again and the majority had successful outcomes. 78.8% ($n = 67$) had live born infants and 21.2% ($n = 18$) suffered a subsequent miscarriage. Outcome data on subsequent pregnancies was stratified according to female age (Table 1). In women over 40 years ($n = 49$), 51.0% ($n = 25$) conceived again. Of these, 72.0% ($n = 18$) had a live birth and the subsequent miscarriage rate was 28.0% ($n = 7$).

One of the challenges in managing patients with idiopathic RM is in counselling individuals on how best to optimise their chances of one or more live births. The significant psychological impact of RM on patients must be considered in adopting an expectant management approach. In an attempt to individualise advice, we routinely assess ovarian reserve (OR) (AMH and antral follicle count). We counsel those with low OR about the potential implications of diminishing OR on family size [4] and advise them to attend fertility services if not pregnant within 4–6 months of trying to conceive.

In those women with low AMH result (< 5 pmol/L, $n = 29$), 51.7% ($n = 15$) conceived again. Of these, 80.0% ($n = 12$) had a live birth and the subsequent miscarriage rate was 20.0% ($n = 3$).

In conclusion, in women ≥ 40 years with RM, APLS is rare. Formal testing for APLS can introduce delay, especially in instances where the test needs to be repeated 12 weeks apart [5]. As cytogenetic evaluation of the POC is much more likely to identify the cause of miscarriage, we suggest that women ≥ 40 years presenting with less than three consecutive miscarriages should be offered this test; it is likely to explain the cause and thereby obviate the need for thrombophilia testing or other approaches which are unlikely to benefit the patient. An AMH level < 5 pmol/L in women ≥ 35 years does not appear to increase the rate of miscarriage in subsequent pregnancy.

✉ David A. Crosby
crosbyd@tcd.ie

[1] National Maternity Hospital, Holles Street, Dublin 2, Ireland

Table 1 Pregnancy outcome data on subsequent pregnancies stratified by female age

	N	%
All women ($n = 170$)		
Pregnant again	85	50.0
Miscarriage	18	21.2
Live birth	67	78.8
Aged 25–34 inclusive ($n = 55$)		
Pregnant again	22	40.0
Miscarriage	3	13.6
Live birth	19	86.4
Aged 35–39 inclusive ($n = 66$)		
Pregnant again	38	57.6
Miscarriage	8	21.1
Live birth	30	78.9
Aged ≥ 40 ($n = 49$)		
Pregnant again	25	51.0
Miscarriage	7	28.0
Live birth	18	72.0
Aged ≥ 35 and AMH result < 5 pmol/L ($n = 29$)		
Pregnant again	15	51.7
Miscarriage	3	20.0
Live birth	12	80.0

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participant or animals performed by any of the authors.

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