METABOLIC RISK-STRATIFIED PRECONCEPTION CARE AND OXIDATIVE-INFLAMMATORY STATUS IN WOMEN WITH RECURRENT PREGNANCY LOSS

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Background. *Recurrent pregnancy loss (RPL) is a multifactorial reproductive disorder. The European Society of Human Reproduction and Embryology defines RPL as the loss of two or more pregnancies and estimates that it affects approximately 1–2% of couples [1]. Its management requires attention to established causes as well as potentially modifiable factors that may influence reproductive health.*

Metabolic abnormalities, oxidative stress, and chronic low-grade inflammation may contribute to impaired implantation and early pregnancy failure. Azizi et al. reported increased inflammatory activity and oxidative stress in women with RPL and metabolic syndrome [2]. Al-Sheikh et al. also identified increased lipid peroxidation, impaired antioxidant defence, and increased expression of inflammatory cytokines in women with recurrent miscarriage [3]. These observations provide a rationale for investigating metabolic and oxidative-inflammatory status before conception.

Preconception assessment offers an opportunity to identify metabolic disturbances before a subsequent pregnancy. However, metabolic risk may vary substantially among women with RPL, making individualized assessment relevant. Evaluating changes in biochemical markers following risk-stratified preparation can help characterize the biological response to preconception care.

Objective. To evaluate oxidative stress and inflammatory biomarkers in women with recurrent pregnancy loss according to metabolic risk and to assess their changes following individualized preconception care.

Materials and methods. A prospective study included 165 women: 115 with recurrent pregnancy loss and 50 apparently healthy women planning pregnancy who served as controls. Women with RPL were stratified into three metabolic-risk groups: group I (n=28), group II (n=64), and group III (n=23).

Clinical and metabolic assessment included body mass index, waist circumference, fasting glucose, triglycerides, high-density lipoprotein cholesterol, insulin, and the homeostasis model assessment of insulin resistance (HOMA-IR).

Oxidative and inflammatory status was evaluated using serum malondialdehyde (MDA), interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and interleukin-10 (IL-10). Women with RPL underwent a 3-month individualized preconception preparation programme according to their metabolic risk profile. Biomarkers were reassessed after completion of the intervention. The analysis focused on the metabolic burden at baseline and the direction and magnitude of biomarker changes following preparation.

Results. Metabolic syndrome was detected in 24.3% of women with RPL compared with 6.0% of controls. At least one component of metabolic syndrome was present in 80.0% and 34.0%, respectively (Table 1). Thus, the difference between groups extended beyond the diagnosis of metabolic syndrome to the presence of individual metabolic abnormalities.

Table 1. Metabolic abnormalities in women with RPL and controls

Indicator	RPL (n=115)	Controls (n=50)
Metabolic syndrome, %	24.3	6.0
At least one component of metabolic syndrome, %	80.0	34.0

RPL: recurrent pregnancy loss.

Increasing metabolic risk was accompanied by a progressive oxidative-inflammatory imbalance. The highest-risk group showed the most pronounced abnormalities: baseline MDA was 4.82±0.21 nmol/mL, IL-6 was 8.9±0.6 pg/mL, TNF-α was 9.6±0.5 pg/mL, and IL-10 was 3.1±0.2 pg/mL.

After 3 months of individualized preconception care, MDA decreased to 3.58±0.17 nmol/mL, IL-6 to 6.1±0.4 pg/mL, and TNF-α to 6.9±0.4 pg/mL. IL-10 increased to 4.2±0.2 pg/mL. All four changes in the high-risk group were statistically significant ($p<0.001$; Table 2).

Table 2. Biomarker changes in the high-risk group after preconception care

Biomarker	Baseline	After 3 months	Change, %	p
MDA, nmol/mL	4.82±0.21	3.58±0.17	−25.7	<0.001
IL-6, pg/mL	8.9±0.6	6.1±0.4	−31.5	<0.001
TNF-α, pg/mL	9.6±0.5	6.9±0.4	−28.1	<0.001
IL-10, pg/mL	3.1±0.2	4.2±0.2	+35.5	<0.001

Change, % = (post-intervention − baseline) / baseline × 100.

The changes were concordant across the measured panel: lipid peroxidation and pro-inflammatory marker concentrations declined, while IL-10 increased. The findings indicate improvement in the measured oxidative-inflammatory profile after the preparation period.

Discussion. The higher frequency of metabolic syndrome and its components among women with RPL supports further investigation of metabolic assessment in preconception care. The observed metabolic risk-dependent biomarker pattern is consistent with the findings of Azizi et al., whose study included 21 women with RPL and metabolic syndrome, 28 with RPL without metabolic syndrome, and 42 healthy controls [2]. Differences in study populations and laboratory methods preclude direct comparison of absolute biomarker values.

The MDA findings are also consistent with the oxidative disturbances described by Al-Sheikh et al. [3]. Their study identified increased lipid peroxidation and reduced antioxidant enzyme activity in recurrent miscarriage, together with increased placental expression of TNF-α and IL-6. The present findings extend this biological rationale to a preconception setting in which serum markers were assessed before and after individualized preparation.

Immune-metabolic relationships are complex. In a study of 34 women with RPL and 30 controls, Ye et al. identified altered amino acid metabolism and differences in circulating cytokines [4]. Both IL-6 and IL-10 were higher in their RPL group. This differs from the low baseline IL-10 concentration described in our highest-risk group and illustrates that cytokine profiles may depend on the population studied and the clinical context. A single cytokine should therefore not be interpreted as a universal diagnostic indicator of RPL.

The concurrent decline in MDA, IL-6, and TNF-α and increase in IL-10 after preconception care suggests a favourable shift in the measured biochemical profile. Nevertheless, biomarker improvement does not itself establish a reduction in miscarriage or an increase in live birth. ESHRE identifies live birth and pregnancy loss as critical outcomes for evaluating RPL interventions [1]. Future studies should relate the biochemical response to these reproductive outcomes and assess the contribution of individual programme components.

Interpretation of the before-and-after changes also requires consideration of potential confounding, natural variation, and regression to the mean. A controlled intervention design and detailed reporting of metabolic-risk thresholds, laboratory assays, and statistical methods would strengthen assessment of the independent effect of risk-stratified preparation.

Conclusions.

1. Metabolic syndrome was identified in 24.3% of women with RPL and 6.0% of controls; at least one metabolic syndrome component was present in 80.0% and 34.0%, respectively.

2. Increasing metabolic risk in women with RPL was associated with a more pronounced oxidative-inflammatory imbalance. The highest-risk group demonstrated elevated MDA, IL-6, and TNF-α concentrations together with a low IL-10 concentration.

3. Three months of individualized preconception care was associated with decreases in MDA, IL-6, and TNF-α and an increase in IL-10 in the high-risk group (all $p<0.001$). These findings support further evaluation of metabolic risk-stratified preconception care with reproductive outcomes as the principal endpoints.

References

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