

### Etiological profile of Omani women with recurrent pregnancy loss

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#### ABSTRACT

**Objectives:** To define the different causes of recurrent pregnancy loss (RPL) among Omani women.

**Methods:** This retrospective study included all women with RPL seen between June 2006 and March 2012 in the RPL outpatient clinic in Sultan Qaboos University hospital, Muscat, Oman. The data were collected from the Hospital Information System by screening the electronic records of these patients. The sample size gathered during the study period was 290 women.

**Results:** One hundred and forty (48%) of the examined patients had an identifiable cause for RPL, while in 150 (52%), no cause was identified. The most common causes were immunological factors (35.4%) and the least common were environmental factors (1.7%). Other causes implicated included: chromosomal abnormalities (8%), anatomical factors (9.4%), endocrine disorders (29.8%), infectious causes (3%), and thrombotic causes (12.7%).

**Conclusion:** Recurrent pregnancy loss is prevalent among Omani women. The etiological profile of RPL in Omani women is consistent with that reported elsewhere according to previously published studies, with minor variations.

Miscarriage or pregnancy loss is the most common complication of pregnancy, and a major problem of women's health worldwide.<sup>1</sup> Around one fifth of all women worldwide have suffered at least one abortion, and one in 20 has had 2 or more spontaneous pregnancy losses.<sup>2</sup> Recurrent pregnancy loss (RPL) is defined as occurrence of 3 or more consecutive losses of clinically recognized pregnancies prior to the twentieth week of gestation.<sup>3-7</sup> This affects 3-5% of pregnant women.<sup>3-7</sup> Experts consider 2 consecutive miscarriages to be sufficient for the diagnosis of RPL, which affects around 5% of reproductively active couples.<sup>4</sup> There are several factors that influence the rate of miscarriage including; maternal age, the number of prior spontaneous miscarriages, and parity.<sup>1,4</sup> The risk of miscarriage

increases with maternal age.<sup>8,9</sup> Thirteen percent of primigravidas end up losing their pregnancies,<sup>1</sup> yet the risk of a second consecutive pregnancy loss increases to 17%, and to between 35-40% after 2 consecutive pregnancy losses.<sup>1,4,6</sup> Several studies indicate that in more than 50% of cases of RPL the cause of miscarriage is unknown.<sup>6</sup> The known etiologies of RPL include: parental chromosomal abnormalities, maternal thrombotic tendency, anatomical uterine problems, endocrine factors, infectious causes as well as environmental factors.<sup>5,6</sup> In the Omani population, the prevalence of RPL is estimated to be around 0.8%.<sup>10</sup> This study aimed to identify the etiologies of RPL in Omani women, and to compare them to those reported elsewhere. There is a lack of data in Oman at present outlining the etiological profile of RPL so identifying such etiologies will facilitate management of RPL and improve the outcome of pregnancy.

**Methods. Study sample selection.** This retrospective study was conducted at Sultan Qaboos University Hospital (SQUH), Muscat, Oman, in the RPL clinic of the Obstetrics and Gynecology outpatient department. This is the only clinic specialized in management of RPL in Oman, and caters for patients referred from the various regions of the country. The clinic runs once a week with an average of 4-5 new cases. During the study period between June 2009 and March 2012, 290 cases were recruited as representative of the Omani population.

**Data collection.** The data was collected from the Hospital Information System in SQUH by screening the electronic patient records of the patients who attended the RPL clinic during the study period. Patient personal data (age, gravidity, and parity), details of medical history, family history, social history, and detailed obstetric history including the number of pregnancy losses as well as the results of all the investigations conducted for these patients was obtained. Non Omani women were excluded from the study population.

**Selection of cases.** The study included all women with a history of 2 or more consecutive miscarriages in the first or second trimester based on the definition of RPL. The causative factors for these women with RPL were determined based on the results of investigations

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retrieved from the patient electronic records. These investigations include: peripheral blood karyotyping for both partners, thrombophilia screen for activated protein C resistance, protein C and protein S levels, antithrombin III, anticardiolipin IgM and IgG antibodies, lupus anticoagulant, anti-Beta 2 glycoprotein anticoagulant antibodies, anti-nuclear antibodies, serological test for toxoplasmosis, cytomegalovirus, human immunodeficiency virus, and syphilis infections, as well as thyroid function tests, serum prolactin level, and glycated hemoglobin. Blood was collected on menstrual cycle day 2 to check the level of: follicular stimulating hormone, luteinizing hormone, estradiol, and testosterone when clinically indicated. In addition to these investigations, oral glucose tolerance test was performed for patients with high glycated hemoglobin, a family history of diabetes, history of polycystic ovarian syndrome (PCOS), or clinical suspicion of diabetes mellitus (DM). High vaginal swabs for Chlamydia testing in addition to pelvic ultrasound were performed on all patients. The identified causes of RPL were divided into 8 groups, which were further divided into subtypes according to the findings in the study population. 1) The parental chromosomal abnormalities were sub-divided into: translocation, inversion, insertion, and single gene defect. 2) The anatomical causes were sub-divided into: congenital uterine malformation, intrauterine synechiae, sub mucous fibroids, and cervical incompetence. 3) The endocrine causes were sub-divided into: PCOS, DM, thyroid disease, and hyperprolactinemia. 4) The immunological causes were sub-divided into: antiphospholipid syndrome (APLAs), antithyroid antibodies, and systemic lupus erythematosus (SLE). 5) The thrombotic causes were sub-divided into methylene tetra-hydro-folate

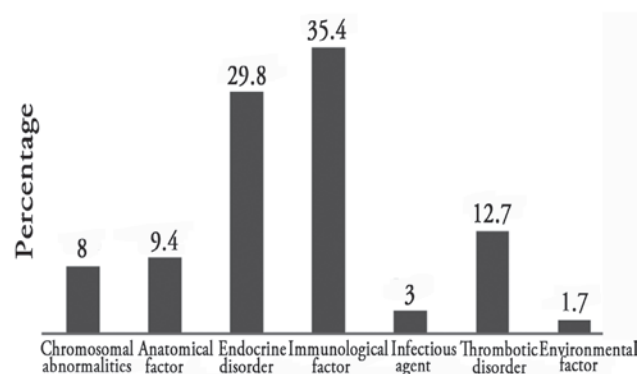
reductase (MTHFR) mutation, protein C and protein S deficiencies, and antithrombin III deficiency.

**Analysis.** The data were processed and analyzed using the Microsoft Excel software version 2007. The information recorded in the transfer sheet was fed to the computer. Data was summarized and presented as numbers and percentages.

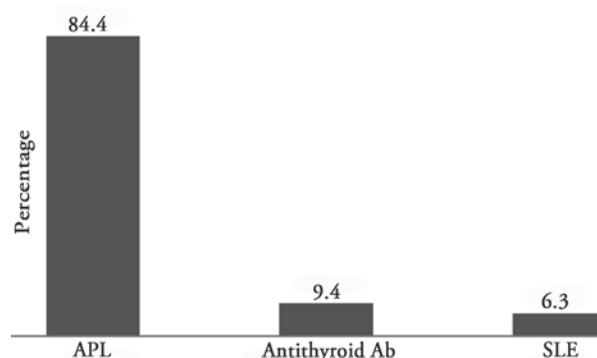
Ethical approval for this study was obtained from the ethical review committee at Sultan Qaboos University before the commencement of the study. All collected information was treated with confidentiality and only used for the purpose of the study.

**Results. Study population demographic data.** The study population consisted of 290 patients. The age of the patients varied from 20-46 years with the average being 32.93 years, their parity ranged from zero to 9; with 47 patients (30%) having no previous deliveries, 60 patients (20.7%) with one previous delivery, 56 patients (19.3%) with 2 previous deliveries, 37 patients (12.8%) with 3 previous deliveries, and 50 patients (17.2%) with more than 3 previous deliveries. The median number of parity was one. The number of miscarriages ranged from 2 to 15, the median was 3 miscarriages.

**Causes of recurrent pregnancy loss.** One hundred and forty patients (48%) had an identifiable cause for RPL, while 150 (52%) had unknown causes. In this study the most common cause of RPL was immunological causes found in 35.4% of the patients, and the least common cause was environmental factors implicated in 1.7% of the patients, as shown in Figure 1. This study showed that the most common cause among the study population is immunological disorders. The most prevalent of these immunological disorders was APLAs



**Figure 1** - Causes of recurrent pregnancy loss in Omani women.



**Figure 2** - Prevalence of immunological disorders among Omani women with recurrent pregnancy loss. APLAs - antiphospholipid syndrome, SLE - systemic lupus erythematosus, Ab - antibody

followed by antithyroid antibodies, and SLE as shown in Figure 2. The frequency of the endocrine abnormalities in patients with RPL caused by endocrine problems was: PCOS 16.7%, DM 38.9%, thyroid disease 37%, and hyperprolactinemia 7.4%. The positive thrombophilia was divided into MTHFR mutation (21.7%), protein C and protein S deficiency (69.6%), and antithrombin III deficiency (8.7%). The anatomical causes were implicated in 9.4% of cases. These were sub-divided into: congenital uterine anomalies 18%, intrauterine adhesions 6%, cervical incompetence 23%, and sub mucous fibroids; which are the most frequently found anatomical abnormalities (53%). The prevalence of the different chromosomal abnormalities in affected couples was; balanced translocation (66%), inversion (20%), insertion (7%), and single gene defects (7%).

**Discussion.** The prevalence of RPL in Oman is 0.8%.<sup>10</sup> The etiological factors of RPL are widely variable according to previous studies. This variability is mostly due to the difference in the definition of RPL, as well as the differences in the study designs, methods of data collection, and sample size. In addition, ethnicity, and characteristics of the study population can lead to differences in the findings. Immunological disorders were the most frequently implicated cause of RPL among our study population (35.4%), with APLAs being the most common disorder encountered (84.4%), and similar to previous study findings.<sup>10</sup> In a study from the USA,<sup>11</sup> the prevalence of immunologic factors among 214 women with recurrent spontaneous abortions was 65%. Cervera et al<sup>12</sup> in 2010 reported the prevalence of RPL in APLAs patients as 15-90%. The prevalence of endocrine disorders among the study population was 29.8%, with DM recorded as 38.9%, and PCOS as 16.7%. Carrell and Peterson,<sup>4</sup> and Rai et al<sup>13</sup> reported that the prevalence of PCOS among women with RPL attributed to endocrine problems was 40%, which is much higher than our findings. Another cause for RPL is thrombotic disorders, which were implicated in 12.7% of our cases. Serrano et al<sup>14</sup> reported an abnormal thrombophilic genotype in 8% of 100 women with RPL, which is slightly lower than in our study population. The frequency of anatomical abnormalities in our study was 9.4%, and this is in line with previous studies, which reported the incidence of anatomical abnormalities ranging from 1.8-37.6%.<sup>15</sup> The prevalence of intrauterine adhesions was 6% compared with 21.8% in a cohort study reported by Ventolini et al.<sup>7</sup>

This study showed that 8% of couples had an abnormal karyotype, which is slightly higher than the 6% that was reported from USA among 214 women with RPL.<sup>12</sup> In our study the prevalence of balanced translocation (66%) was higher than that of inversion (20%) among couples with RPL. This is in agreement with Carrell & Peterson<sup>4</sup> who reported that chromosomal inversions have been linked to RPL, but is less frequently found than balanced translocation.

In conclusion, RPL occurs among Omani women, and in half of them no cause was identified. The etiological profile of Omani women with RPL is similar to the etiological profile reported elsewhere, with immunological disorders the most frequently implicated cause. Further studies are needed with a larger sample size and consideration of the diverse ethnicity of the Omani population.

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