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CJOG CLINICAL JOURNAL OF OBSTETRICS AND GYNECOLOGY
ISSN 2640-2890

Review Article

An Appraisal of Recurrent Miscarriage in Sub-Saharan Africa: Occurrence and Possible Solution

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Abstract

A recurrent miscarriage may be defined in the African context as the foetal demise of two or more successive pregnancies before the attainment of the age of viability. A literature review was done to assess the trend of recurrent miscarriage in sub-Saharan Africa. Identifying the main causes, considering the population at risk, and the availability of accurate diagnostic utilities to effectively ensure good management of recurrent miscarriage is an important gynaecologic issue. Over the years, studies have identified several etiologies and yet there's been no tangible implementation of therapeutic strategies. Routine modifications should also be employed to develop new approaches to reproductive prognosis. There is notably scanty information on the cases of spontaneous abortion due to chromosomal abnormalities. Genetic and immunological factors should be considered in the work-up plan for women with RM. About 70% of the cases of RM are considered unexplained, and this may be due to limited resources. We concluded that there is relatively poor management of miscarriage and cases of missed and inaccurate diagnosis of the causes of spontaneous abortion in sub-Saharan Africa. More studies are needed in order to assess the extent of genetic induced miscarriage, where resources are limited, folic acid supplements should be provided for pregnant women.

More Information

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Submitted: September 27, 2024
Approved: October 08, 2024
Published: October 09, 2024

How to cite this article: Emiade S, Musa BOP, Oguntayo AO, Hassan AA, Balogun Y. An Appraisal of Recurrent Miscarriage in Sub-Saharan Africa: Occurrence and Possible Solution. Clin J Obstet Gynecol. 2024; 7(4): 103-106. Available from: https://dx.doi.org/10.29328/journal.cjog.1001173

Keywords: Miscarriage; Abnormalities; Genetics; Etiology; Gynaecology

Introduction

Pregnancy is an extraordinary phenomenon, conversely, about 15% - 25% of pregnancies result in spontaneous abortions. Studies have shown that about 5% of women who have experienced two consecutive abortions will likely lose a third pregnancy [1]. The American Society of Reproductive Medicine states that Recurrent Miscarriage is a distinctive condition characterized by not less than two known clinical abortions excluding biochemical losses (not essentially sequential) [2], while the European Society for Human Reproduction and Embryology states that it is the loss of two or more pregnancy [3] and the Royal College of Obstetricians and Gynaecologists defined it as more than two consecutive pregnancy losses, including non-visualised ones [4]. The expected probability of having three serial spontaneous abortions is about 0.3% - 0.4% however, epidemiological studies have shown a higher incidence [5]. For cases of RM in Africa, we propose that RM may be defined as a consecutive pregnancy loss occurring in a foetus over 500g or less than 24 weeks since it is considered a resource-limited setting where facilities are inadequate. There is a variation in the prevalence of RM among international societies, as the description differs, it affects about 5% of couples. The national guideline of some countries considers two miscarriages for diagnosis of RPL. Many more studies of RM therefore include women with only two previous miscarriages, which from an epidemiological point of view is very difficult [6]. In clinical terms, miscarriage is a loss of a clinical pregnancy before 20 weeks or the loss of a foetus of < 400 grams [5]. The latter definition is the one that fits the African context since there are no true parameters to determine the trend of occurrence of abortion.

Epidemiologic studies have revealed that about 2% of women are likely to experience recurrent pregnancy loss [7]. Existing data suggest that the likelihood of a pregnancy loss of successive pregnancies is 21% after 2 losses, compared with 36% after a third pregnancy loss amongst patients that do not have a history of a live birth [5].

Recurrent pregnancy loss is a condition with several probable causes; multiple predisposing factors may bring about pregnancy. These may include chromosomal, genetic, hormonal, anatomic, systemic, immunologic, infections, and endocrine losses [8], in resource-limited settings more factors

that are considered idiopathic may be involved. Certain infections including *Listeria monocytogenes, Toxoplasma gondii, Rubella, herpes simplex virus (HSV), measles, cytomegalovirus,* and *Coxsackie virus*, have been suspected to be involved in consecutive pregnancy losses [9]. Nevertheless, the role of these pathogenic organisms in recurrent pregnancy loss is vague. Certain studies indicated higher prevalence while others presented similar and even less prevalence of antibodies to certain infectious agents when comparing women with recurrent pregnancy loss with those who carry their pregnancy to term.

Occurrence of miscarriage

It is noteworthy that incomplete miscarriage is the most common type of miscarriage in Sub-Saharan Africa, and this is a source of worry because of the possibility of missed diagnosis as a result of the generally limited resources in the region which may lead to death and even undetected cause of miscarriage. This is the more reason why most miscarriages occurring in this region are usually considered 'unexplained', and this is a source of worry to the local gynaecologists, therefore patients become helpless and may resort to seeking a non-medical and sometimes untoward solution to the problem of recurrent miscarriage.

Major studies showing the trend of recurrent pregnancy loss

An observational study conducted in Sudan, reveals that recurrent miscarriage is more prevalent among women who are over 30 years of age. In this study, most cases of RM were considered unexplained. Inherited thrombophilia accounted for most of the diagnosed cases, followed by endocrine aetiology. There were no recorded cases of RM due to chromosomal/genetic abnormalities, which usually account for most cases of RM, and this may be due to limited resources [5].

Most of the cases reported in Nigeria are a result of cervical incompetence. With a prevalence of 0.85% for cervical incompetence, there were eighty-five elective and ten emergency cerclages with a mean gestational age at the end of pregnancy of 36.06 ± 3.96 *vs.* 25.10 ± 3.99 and mean duration of prolongation of pregnancy of 20.98 ± 4.71 *vs.* 4.00 ± 3.37 weeks in an observational study conducted in the North central region of Nigeria [10]. The immunogenetic approach was employed by Ibrahim, et al. (2017) in a study conducted in Zaria where 100 consecutive women presenting with one or more spontaneous abortions were analysed with about 4% showing positive results for Lupus anticoagulant. Patients who tested positive were more likely to have a history of preeclampsia. Also, Aliyu and Abdullahi, (2012), found in women with an age range of 18-42 years, the prevalence of Antiphospholipid antibodies, Lupus antibodies, and Anticardiolipin antibodies was 14.1%, 4.7%, and 8.2% respectively. While there was 1.2% for a combined APA and ACA. They concluded that the prevalence of APA among women with recurrent miscarriage was at least 3 times higher than that of normal antenatal patients. Reduction in pregnancy losses, preterm deliveries, prolonged-term deliveries, and viable pregnancies were reported after the insertion of cerclage [11]. The child take-home rate was 89.4% after elective and 20% after emergency cervical cerclage [12].

Ajayi et al., in an observational study, examined 1118 infertile women in Nigeria, 26 (2.3%) had Congenital Uterine Anomalies, which were mostly cases of the sub-septate uterus (73.1%), others were bicornuate (11.5%), arcuate (7.7%), unicornuate (3.8%) and inter-cervical septum (3.8%). The average age, BMI, and duration of subfertility in years among infertile women with congenital uterine anomaly were 38.7 (6.6), 27.4 (5.9), and 7.5 (6.9) respectively [13]. The prevalence of Congenital Uterine Anomaly was higher among infertile women between the ages of 35-39 years of age (34.6%), 57.7% among those who were overweight, about 92.3% had secondary infertility, and 34.6% who had previous pregnancy loss. The mean uterine cavity depth of the infertile women with Congenital Uterine Anomaly (CUA) is significantly smaller than that of the infertile women without Congenital Uterine Anomaly. Among infertile women with CUA, 3.8% had an obliterated right ostium while 7.7% had an obliterated left ostium. They concluded that their findings were in agreement with other studies. Sub-septate uterus had the highest of the CUA cases. The infertile women with CUA were mostly cases of secondary infertility and considerably reduced depth of the uterine cavity.

In South Africa, van Niekerk, et al. (2013), reported that the possibility of recurrent miscarriage is highest among women who have had spontaneous abortion at a gestational age of less than 6 weeks, and those with maternal age of over 45 years of age had the highest rate of RM, while those with more than three miscarriages had the highest risk of miscarriage, while in Kenya it was reported that, about 2% of the general population have major uterine anomalies [14].

Endocrine factors

Diabetes mellitus: High glycosylated haemoglobin (HbA1C) values (> 8%) in the first trimester of pregnancy have been found to be associated with an increase in early miscarriage and congenital deformities. Women with well-controlled diabetes mellitus have low or no risk of miscarriage [15].

Polycystic Ovarian Syndrome (PCOS)

Studies have revealed that there is no significant difference in reproductive outcomes between patients diagnosed with PCOS and healthy controls. The rate of live births and miscarriages were similar among the two groups [16].

Thyroid antibodies and disease

There are inconsistent reports, and there is not enough

evidence with regard to the role of thyroid disease in RM. Certain studies posited that elevated thyroid peroxidase in sera appears to be related to recurrent miscarriages, and also in euthyroid patients [17], however, the mechanism is still unclear. Hyperthyroidism has been found to be associated with RM, premature labour, low birth weight, and perinatal mortality [18]. Hypothyroidism is associated with infertility and first-trimester miscarriages, as well as perinatal morbidity and mortality [19].

The proper functioning of the thyroid could be considered in women with a history of thyroid disease or with the clinical indicators thereof. The American Thyroid Association recommends measuring serum thyroid-stimulating hormone in pregnant women [20]: who are over thirty years of age and show symptoms of thyroid disease. Screening of asymptomatic women for subclinical thyroid disease is contentious. Currently screening for thyroid disease of all women who wish to fall pregnant is not recommended, since there are no data to confirm that such a screening mandate has any meaningful outcome. However, certain authors recommend the measurement of thyroid peroxidase antibodies in patients with RPL or preterm birth, where no other cause could be identified [21].

In studies regarding luteal phase defect and progesterone deficiency, a viable corpus luteum is essential for active implantation and maintenance of early pregnancy, primarily through progesterone production [22]. A failing of the luteal phase by way of inadequacy in the secretion of progesterone leads to endometrial development which is not suitable for embryonic implantation and is associated with RM. Luteal phase defect is controversial, as is whether it is related to RM, as a result of the discrepancies in the process of diagnosing and managing it.

In the case of a luteal phase defect, there is no existing effective diagnosis to evaluate the correct occurrence and outcome of luteal phase defect. Studies have shown that endometrial biopsy does not predict fertility status, it may, therefore, not be suitable for detecting this defect [22].

There is a dearth of availability of reported cases of the occurrence of a balanced translocation in Sub-Saharan Africa since both immunogenetic and hereditary studies are inadequate and relatively lacking as is customary in resource-limited settings.

A case of RM associated with balanced translocation of chromosomes was reported in Rwanda, a case of four spontaneous abortions, all foetal demise occurred before the twelfth week of gestation, it was reported as idiopathic and there was no record of medications taken during pregnancy. The karyotype was 46.XX, t(13p,21p) and there was no abnormal karyotype in any other chromosomes. The cytogenetic analysis of the husband also revealed a normal karyotype 46.XY [23].

We suggest that couples with RM should be referred to the geneticist for chromosomal analysis in order to reveal probable genetic aetiology and chromosomal abnormalities responsible for miscarriages to plan prenatal diagnostics and genetic counselling for subsequent pregnancies.

Women with clinical manifestations or a history suggestive of a medical disorder should be subjected to laboratory analysis. For effective management of RM, the basis can be traced to its underlying cause.

Couples with RM issues should be addressed by a specialist and given thoughtfully, compassionately, and with proper passionate support when taken through the treatment process. We also suggest that immunogenetics should be employed in the diagnosis and monitoring of cases with multiple abortions.

Conclusion

There is relatively poor management of miscarriage and cases of missed and inaccurate diagnosis of the causes of spontaneous abortion in sub-Saharan Africa. More studies are needed in order to assess the extent of genetically induced pregnancy loss, and this poses an important reproductive health issue. Over the years, there has been recognition of various etiologies and the putting into practice of effective therapeutic approaches. A total check-up can be initiated following two successive pregnancy losses for the detection of treatable causes that may involve anatomical defects, anti-phospholipid syndrome, endocrine abnormalities, and balanced translocations. Lifestyle modifications should also be implemented to improve reproductive predictions. Though more than half of the cases of RM are considered idiopathic, various treatment protocols are continuously being developed. Notwithstanding the underlying cause of an RPL case, an in-depth follow-up with necessary emotional care can be beneficial to most couples in accomplishing a positive live birth.

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