



Miscarriage: A Concise Analysis of a Changing Trend

Dr Anthony Emeka Madu*

UK

Abstract

For a century or more, scientific researchers have, in many ways, demonstrated that miscarriage cannot be prevented, and that there is a pivotal role played by chromosomal aberrations. There has been lowering of the age range of the occurrence of some medical problems as the population of many western societies move to an ageing population. Miscarriage, for decades has been said to be mainly a problem of the older “normal” women without any other underlying relevant medical problem. However, recent observations have shown a lowering of the age of prevalence of miscarriage from the 40s to 30s and more recently, to the 20s.

Over the past decades, it has been said that about 20% of pregnancies end in miscarriage. However, with more recent improved knowledge, understanding and medical technology, in relation to early pregnancy detection and management, this figure has risen dramatically. For women in their early 30s, about 60% of conceptions end in miscarriage, and for women in their early 20s, about 50% of conceptions end in miscarriage, once again demonstrating a rise in the proportion of pregnancy loss in younger women.

This raised other questions on the issues like having a revised fertility window, currently 15 to 35 years, and in matters relating to assisted reproduction management. Here, the author attempts to provide a concise analysis of the current trends in the age of prevalence of miscarriage in women.

Introduction

Miscarriage is defined as the expulsion of a conceptus at any stage of gestation when the conceptus is not capable of surviving independently. Older definition stated that miscarriage is pregnancy loss before 24 weeks gestation [1]. However, current definition states that it is pregnancy loss before 20 weeks gestation [2]. This could be due to the fact that many premature babies born before 24 weeks are currently surviving due to improved neonatal care. Another definition from Tommy’s Organization Research into Miscarriage states that a miscarriage is the loss of a pregnancy during the first 23 weeks of pregnancy [3]. This again indicates a trend in the gestational cut off for miscarriage, or limits of fetal viability.

Miscarriage is one of the early pregnancy complications associated with bleeding and pain in early pregnancy. Miscarriage is also a very common problem and previously thought to occur in 15% to 20% of pregnancies, and some scholars would argue up to 40% of all pregnancies [1]. In comparative analysis, it appears that humans are comparatively less fertile than other mammals in this regard. 85% of human pregnancy losses take place within 12 weeks of pregnancy [1,2]. 25% of all pregnancies terminate through miscarriage within the first 12 weeks of pregnancy, while 15% of miscarriages take place from 13 weeks to 20 weeks of gestation [2].

Fertility window in women is been stated at 15 to 35 years and fertility is said to drop after 35 years of age and drops markedly after 40 years. With the evidence that the author would present in this article regarding the changing trend in miscarriage, the author advocates for a consideration of a review of the fertility window that has been held for some decades.

Menopause in the UK has remained at an average of 52 years with a range of 45 to 55 years [4] but from observations, many women are certainly seeing menopause an earlier age, as low as below 40 years, especially in those with underlying disease(s) that compromises ovarian function. Thus, there appears to be a trend for menopause occurring increasingly in women younger than the average age of 52 years, and in women younger than the lower limit of the age range of menopause.

From ancient times to present times, pregnancy loss has been associated with blame. However, research showed consistently that this is a natural function, and a natural phenomenon [5].. Advances in Fertility Science, has also demonstrated that miscarriage played a pivotal role in the evolution of man.

OPEN ACCESS

*Correspondence:

Dr Anthony Emeka Madu, Specialist Registrar in Obstetrics and Gynaecology/Lecturer in Healthcare (UK) Affiliations: RCOG/FSRH/ILM/NHS/University of Greenwich, UK, E-mail: emymadu@yahoo.co.uk

Received Date: 25 Aug 2020

Accepted Date: 08 Sep 2020

Published Date: 14 Sep 2020

Citation:

Madu AE. Miscarriage: A Concise Analysis of a Changing Trend. *J Gynecol Oncol.* 2020; 3(4): 1040

Copyright © 2020 Anthony Emeka Madu. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Our most recent knowledge

Miscarriage was stated to usually occur in women older than 40 years, as fertility also drops markedly after 40 years. That appeared to be the trend for many years. The syndrome of recurrent miscarriage, though occurring in any age group depending on the cause, still appeared to be more common or severe in women over 40 years old. The author would now discuss the issue of recurrent miscarriage in greater detail, as this could help the reader understand the changing trend.

Recurrent miscarriage is defined as when three or more spontaneous consecutive miscarriages occur in the first trimester of pregnancy from the same biological father. This may not necessarily follow a successful birth. An older definition stated that recurrent miscarriage is when three or more early pregnancies (first trimester) without any intervening successful pregnancy. At that time, many clinicians were reluctant to treat any patient whose history did not fall into this old definition, as technically, this older definition did not meet the criteria for recurrent miscarriage in the policies or protocols of many hospital trusts.

Recurrent miscarriage accounts for 1% to 2% of miscarriages and about 50% of these are stated to be unexplained, because of lack of available scientific evidence to explain the cause. According to Collins et al. [1] there are two main distinct and independent risk factors for recurrent miscarriage, and they are; increasing number of miscarriages and increasing age of the mother.

Other causes of recurrent miscarriage are Antiphospholipid syndrome (anticardiolipin and lupus anticoagulant) antibodies, accounting for 15% of cases, and the most importance cause of recurrent miscarriage that is readily treatable.

Genetic causes account for 3% to 5%. In these cases, one of the couples has a balanced reciprocal or unbalanced reciprocal (Robertsonian) translocation. In the latter, the carrier is normal phenotypically, but 50% to 75% of the gametes are unbalanced. There is no definitive evidence on why chromosomal aberrations are very common in human embryos. Chromosomal aberrations in the human embryos increase with advancing maternal age, thus the latter is considered a risk factor for miscarriage: the rate of miscarriage in women in their early 20s is 50% compared with 80% for women in their early 40s.

In relation to the chromosomal quality in the developing embryo, there is still uncertainty regarding why the pregnant woman's body decide to keeps or expels which embryo in it.

However, as will be explained in some details in this paper, there appears to be an endometrial lining "quality of embryo sensor" that detects a healthy embryo and supports its implantation and growth, and also detects a poorly formed embryo, but does not support the latter's implantation and growth. Understanding how this "embryo quality sensor" works, and how it sometimes does not work well, may lead the scientific community to discover new care and treatments options for women with recurrent miscarriage and infertility.

Dysfunction of the immune system or immune imbalance: There has been hypothesis stating that high levels of uterine lining (endometrium) natural killer cell activity is linked to early pregnancy loss. However, these are yet to be proven [1]. The author will highlight current knowledge of the immunological perspective subsequently in this paper in the section on "the changing trend" below.

Fetal chromosomal malformations cause miscarriages. Some of these chromosomal aberrations are not compatible with human life. The more prevalent and severe they are, the more the risk of miscarriage.

Anatomical malformation: Mullerian duct anomalies accounts for 2% to 8% of women with recurrent pregnancy loss. However, minor variations such as arcuate uterus, occurs in 2% to 3% of women. Fibroids occur in 30% of women, and intramural and submucosal types are thought to cause miscarriage, though there is no much evidence to support this. However, miscarriage is common in women with endometriosis.

Cervical weakness (formerly incorrectly called cervical incompetence). This is not associated with early or first trimester loss but with second trimester miscarriage. It is miscarriage that occurs following painless dilatation of the cervix.

Infection: Recurrent miscarriage has a weak and inconsistent relationship with bacteria vaginosis. However, loss in the second trimester has a stronger association with bacteria vaginosis. Also, miscarriages are more common in women with malaria, HIV, dengue fever and flu, especially in the developing world where tropical infections or diseases are more prevalent.

Endocrine disorders: Thyroid disorders, hypersecretion of luteinizing hormone and diabetes, if well controlled are not significantly associated with early pregnancy losses.

Thrombophilic disorders: While gene mutations in Factor V Leiden and Factor II Mutation (Prothrombin G20210A) are strongly associated with recurrent miscarriage, protein S and C deficiency syndrome are weakly associated with recurrent miscarriage [1].

Majority of pregnancy losses occur very early in pregnancy and in many cases the woman is not even aware of it. Thus, according to Le Page [6], women generally have more pregnancy losses in their lifetime than live births [6], went on to state that previous researches had suggested that early pregnancy losses were the most common outcome of pregnancy and that meta-analysis appeared to have confirmed this.

Hamzelou [7] stated in the News Scientist that miscarriage may occur as a result of excess number of ageing cells and immune response fluctuations, and this discovery support the idea that the timing a conception may prevent early pregnancy loss, and thus raised the chances of the woman having a life birth.

According to Hamzelou [7], 25% of conceptions end in miscarriage in the first 23 weeks of pregnancy, citing some risk factors such as advanced maternal age; overweight and genetic abnormalities, as being responsible for the problem. However, there still remains a puzzle for researchers: why do women actually miscarry, especially 1% of women who suffer recurrent miscarriage? Clearly these women do not suffer from infertility as some who had up to 12 miscarriages in a row, still went on to have a healthy life birth. Also, according to Collins et al. [1], 35% or more of women with recurrent miscarriage will have lost the pregnancy by chance, and are in the unexplained group that was stated earlier in this paper.

The changing trend

About 20% or more of pregnancies end in miscarriages, however, with more recent improved knowledge; understanding and medical technology in relation to early pregnancy detection and management,

this figure is currently higher [5]. For women in their early 30s, about 60% of conceptions end in miscarriage, and for women in their early 20s, about 50% of conceptions end in miscarriage, once again demonstrating a rise in the proportion of pregnancy loss with lowered maternal age [5]. In western countries with lower family size, the average life time estimate for a woman is 2.5 miscarriages.

Around 75% of the miscarriages occur even before early pregnancy symptoms become apparent, that is; symptoms like nausea and missed periods. So essentially, these losses may go without the woman noticing them. Thus, in many cases, early pregnancy loss present like normal menstruation or menstruation that is a bit heavier than normal, or had occurred a bit later than normal.

Over the past years, clinicians have become increasingly aware of this category of pregnancy loss because of clinical assessments and availability of more sensitive urine and blood pregnancy tests, which can detect pregnancy about 6 days, following the last missed menstruation. Miscarriages occurring later on in pregnancy are more symptomatic and thus, more obvious: abdominal pain and cramps, which may be severe; heavy bleeding per vaginum with or without clots; nausea and vomiting, may be more severe.

Klein A. [8] stated that despite some pregnancy losses going unnoticed, any loss is distressing to those affected by it and cited a study in UK which reported the following findings:

- 12% of men and 28% of women had some anxiety following miscarriage.
- 4% of men and 10% of women had some depression following miscarriage.

Also, a cited USA survey stated that 41% felt a sense of guilt. The anxiety and depression relate to uncertainties about any further difficulties getting future pregnancy, and whether such may end up in another loss.

However, of note is the observation that most women who suffered miscarriage go on to have successful pregnancies in the future. By definition, only 1% to 2% of women suffer from 3 or more pregnancy losses in a row (recurrent miscarriage) and 75% of these women would end up having successful pregnancies.

Immunological perspective

According to Hamzelou [7], after every menstruation, stem cells in a healthy uterus enable the lining of the endometrium to build about 10 millimeters of endometrium in about 10 days during the proliferative phase of the uterine cycle. Gynecological and Fertility clinicians already know this phenomenon very well. However, according to the recently reported Brosen's theory, some cells of the endometrial lining stop their divisions (senesce). This leads to inflammatory response and the natural killer cells are recruited to destroy or clear the old cells. This then results in the so called "honeycomb mesh" with holes which allows an embryo of the right size to embed successfully in the endometrium.

Researchers studying samples of endometrium during the uterine cycle reported that the cycle of these natural killer cells occurred in a predictable fashion during the month [7]. In women who suffered miscarriage many times, the numbers of these natural killer cells vary monthly rather than being predictable. They rise continuously for months at a time and then become absent, and then start to build up again. It has been suggested that this pattern of natural killer cell

occur due to fewer stem cells being available for effective endometrial regeneration, and in cited studies, in 40% of women with recurrent miscarriage, stem cells were absent. Thus, more endometrial lining cells go into senescence leading to relatively larger number of natural killer cells to become active and then leading to larger "inappropriate" holes in the honeycomb mesh on the endometrium. It has been suggested that if this was the case, then that could explain why women who frequently miscarry get pregnant easily as the larger holes is more accommodating for the embryo to implant initially but later on the honeycomb mesh collapses leading to miscarriage (Brosen's theory).

According to this recent Brosen's theory, a natural window is then created when the numbers of natural killer cells rise later and subsequently the affected woman has low numbers cells in senescence, thus reducing the effects of the woman having fewer functional stem cells. Currently there is no consensus on Brosen's theory or what is on-going regarding the immunological basis for miscarriage. However, if researchers can properly understand how this immunologically-based endometrial lining quality sensor performs its functions and how it does not, it may lead to us to new treatment in relation to management of infertility and recurrent miscarriage.

There appears to be a consensus that as a woman gets older, the number and quality of egg produced from her ovaries declines. This also have a relationship with natural or early onset menopause. The number of egg peaks at 20 weeks gestation to about 6 million. At birth it drops to 1 million and at puberty to about 300,000 eggs. From puberty to the age of 35, there appears to be an increasing decline on the number and quality of eggs, and a more rapid decline after 40 years. From extensive literature search by the author, it appears there is also no consensus as to the contributions made by these ova decline over time to miscarriage or recurrent miscarriage, and whether the current changing trend in miscarriage may be linked to a changing trend in ova decline over time.

Male contribution

A new dimension of miscarriage is currently increasingly becoming topical: the contributions made by the male factor. For decades fertility has been seen as a woman's problem. However, sperm counts and quality are stated to be lowering and men's fertility window is now becoming apparent. Previously, the age of 55 was considered by some experts as the cut off age beyond which male fertility declines.

We already know that as women get older, the ova quality declines and there is increased risk of chromosomal aberration leading to increased risk of miscarriage. What is the contribution in this regard from the lowering of sperm count and quality with advancing paternal age?

From other "downward" trends seen on many health issues, the author speculates that it is time to put the male contribution into more perspective, in relation to the causes and trends in miscarriage. There appears to be a looming fertility crisis in men [9].

Conclusion

There is now ample scientific evidence showing that the changing trends seen in other health issues have now caught up with miscarriage, the most common complication of pregnancy. We are currently observing miscarriage increasing in high prevalence in women in their early 20s compared with past decades when such was observed more in women in early 30s and 40s.

References

1. Collins S, Arulkumaran A, Hayes K, Jackson S, Impey L. Oxford handbook of obstetrics and gynaecology. 3rd ed. Oxford University Press. 2013;542-5.
2. Dulay AT. Miscarriage. Women health issues. 2019.
3. Tommy's O. Research into Miscarriage. 2020.
4. Hamzelou J. Menopausal woman gives birth after blood plasma injection in ovaries. 2020.
5. Leader. Forget about blame with miscarriage: Its function is entirely natural. Health New Scientist. 2020.
6. Le Page M. Women have more miscarriages than live births over their lifetime. Health. New Scientist. 2018.
7. Hamzelou J. Timing when you get pregnant could prevent a miscarriage. Health. New Scientist. 2017;3113.
8. Klein A. Miscarriage. New Scientist. 2020
9. Sarner M. We're heading for a male fertility crisis and we're not prepared. Health. New Scientist. 2020.