Live births resulting from advanced abdominal extrauterine pregnancy, a review of cases reported from 2008 to 2013

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Author(s): Masukume G

Abstract

Introduction: Advanced abdominal pregnancy is classically defined as a pregnancy that has progressed beyond 20 weeks of gestation in which the fetus is growing and developing in the mother’s abdominal cavity. Advanced abdominal pregnancies, in particular those with live births can provide a unique and useful opportunity to understand certain reproductive biologic phenomena.

Methods: PubMed, Scopus and Google Scholar were searched for English language articles that reported a live birth resulting from an advanced abdominal pregnancy from 2008 (the year of the last major review on advanced abdominal pregnancy) to 2013.

Results: 38 cases of an advanced abdominal pregnancy resulting in a live birth were identified from 16 countries. 37.5% males at births (normal average 51.5% males at birth) were observed in this study.

Conclusion: Physiologically males are more vulnerable than females from conception; the presumed hostile extraterine environment of advanced abdominal pregnancy may cause excess demise of males compared to females.

Introduction

Advanced abdominal pregnancy (AAP) is classically defined as a pregnancy that has progressed beyond 20 weeks of gestation in which the fetus is growing and developing in the mother’s abdominal cavity, or the fetus shows signs of having been in the mother’s abdominal cavity [1].

Ovarian, broad ligament and tubal pregnancies are excluded from AAPs definition; however this omission has been contested because from a clinical perspective these pregnancies pose similar diagnostic and therapeutic challenges as AAPs [2]. Others are of the opinion that a placenta implanted in the peritoneal cavity is the best way to define an AAP [3]. Furthermore, the greater than 20 weeks of gestation cutoff is arbitrary.

An AAP resulting in a live birth is extremely rare. This is because abdominal pregnancy has an incidence of about 1 in 400 to 50 000 deliveries [4]; the variable incidence depends on the characteristics of a particular geographic region. In addition, because the fetus is outside the uterus, AAP has a high maternal and perinaetal morbidity and mortality. It is estimated that a woman with an abdominal pregnancy is 90 times more likely to die in comparison to a woman with an intrauterine pregnancy [5]. On average, more than half of AAP babies die [1]. About 20% of AAP infants have malformations or deformations [6].

AAP can be primary or secondary (see Illustration 1). Primary AAP where there is direct implantation of the conceptus into the abdominal cavity is the less common type; certain criteria have to be met for an AAP to be classified as being primary [7]. Secondary AAP due to fimbrial abortion, tubal rupture, ruptured uterus or a ruptured uterine rudimentary horn is the more common type.

An over distended uterus (with excessive stretching of the myometrium) for example occurring with twins was in the 1980s considered to be involved in the etiology of pre-eclampsia [8]. Cases of pre-eclampsia occurring with AAP (non-distended uterus) helped to dispel the hypothesis that excessive stretching of the myometrium was involved in pre-eclampsia’s etiology [8].

In other words, the uterus is not needed for pre-eclampsia to occur, a fact which was revealed by cases of pre-eclampsia occurring with abdominal pregnancies. Thus AAPs in particular those with live births provide a unique and useful opportunity to understand certain reproductive biologic phenomena.

In addition AAP serves as a prototype of pregnancy in males, who lack a uterus, however such a pregnancy would be difficult and dangerous.

Methods

PubMed, Scopus and Google Scholar were searched with the term ‘advanced abdominal pregnancy’ from January 1 2008 (the year of the last major review on AAP [1]); the last search date was November 30 2013.
The title and abstract of articles was used to select articles that could have a live birth resulting from an AAP (AAP was classically defined). Articles citing these identified articles were also considered. The full text of identified English language articles were read to identify a live birth resulting from an AAP. Articles which had a viable birth resulting from an AAP were included.

A single investigator extracted from the identified articles the variables of year reported, country, maternal age, gestational age at delivery, etc. The full list of extracted variables (33) is available in the data set (see Additional file).

Statistical analysis was done using Stata version 12IC (StataCorp LP College Station, TX).

Continuous variables were tested for normality using visual methods namely histograms and inverse normal plots and where the variables were deemed to be not normally distributed the median and interquartile range (IQR) were reported. A one-sample test of proportion (prtest) was used to compare the proportion of male live births to the normal proportion of 51.5%; p < 0.05 was considered to be statistically significant.

Results

38 cases of an AAP with a live birth were identified from 16 countries (in Africa, Asia, the Caribbean, North America and South America) see Table 1 and Illustration 3.

The median age of women was 29 years, IQR 24 – 34 years. Approximately 50.0% of women were having their first pregnancy when they had an AAP.

36.5 weeks was the median gestation at delivery, IQR 33 – 39 weeks. The median birth weight was 2.4kg, IQR 1.35 – 2.85kg.

Of the 32 AAP cases with data on sex of the baby, 12 (37.5%) were males.

In 10 (26.3%) cases, the placenta was not removed, in four of these cases a re-laparotomy had to be done because of complications resulting from the retained placenta. In the remaining 28 (73.7%) cases, the placenta was either removed completely or partially.

18 (47.4%) of the women received blood or blood product transfusion, but it is important to note that in some of the other cases it was not mentioned whether blood or blood products were administered.

In 18 (47.4%) cases the diagnosis of AAP was made before delivery, in 15 (39.5%) cases the diagnosis was not made before delivery and in 5 (13.2%) cases it was not mentioned or unclear if the diagnosis was made before delivery.

30 (79.0%) of the women had sonography before delivery, the remainder of the women either did not have sonography or this information was not mentioned in the articles.

19 (50.0%) cases had an abnormal lie; the lie was unknown in 16 (42.1%) cases; 10 (26.3%) of the cases had a breech presentation.

The proportion of live male births of 37.5% had a 95% confidence interval of 20.7% – 54.3%, two-sided p-value = 0.11.

Discussion

As mentioned earlier, live births from AAP are extremely rare; in recent times nearly 130 million babies are born every year [40] yet only 38 live AAP births were identified over a period of about five years in this study. As has been previously noted in the AAP literature, the following features were also present in this study; symptoms and signs of AAP are generally non specific, an abnormal lie or presentation is common, it is difficult to diagnose AAP despite the widespread use of sonography and there is frequent need for transfusion of blood or blood products [1].

On average, the sex ratio at birth is 51.5% males [41]. The 37.5% male births seen in this study can be attributed to the fact that physiologically males are more vulnerable than females from conception [42]; the presumed hostile extraterine environment of AAP may cause excess demise of males compared to females. Although in this study some data on the sex of the newborn baby was missing, the sex ratio at birth would still be in favor of fewer males compared to females even if all the missing cases were males.

A causal relationship between AAP and excess demise of males is possible because important Bradford Hill criteria [43] are satisfied, namely strength (37.5% versus 51.5% males), consistency (in line with the known biologic fact that males are more vulnerable than females from conception) and temporality (AAP exposure precedes the abnormal sex ratio at birth). However, it is important to note that there was no evidence that the 37.5% observed in this sample was significantly different from 51.5% if p < 0.05 is considered to be statistically significant.

To the best of the investigator's knowledge the sex ratio at birth has not been previously evaluated with respect to AAP.
The median gestation and birth weight at delivery were pre-term (< 37 completed weeks) and of low birth weight (< 2.5kg) respectively; this is not unusual for a pregnancy in an unnatural location.

A case of bilateral [20] and unilateral talipes equinovarus [39] were observed in this study, both cases seemed to be non-syndromic.Crudely, this would yield a congenital talipes equinovarus (CTEV) birth prevalence of 52.6 per 1 000 live AAP births, which far exceeds the estimated CTEV prevalence of 1 to 4.5 per 1000 live births [44]. The etiology and mechanism of development of idiopathic CTEV is unknown [44]; one can only speculate about the role of AAP in the development of CTEV. One infant had bronchopulmonary dysplasia [38] which was likely related to pre-maturity among other factors [45]. Another infant [28] had patent ductus arteriosus, inguinal hernia, undescended testes and phimosis which were very likely related to pre-maturity [46].

"The two key components in successful embryo implantation are the competent embryo and the receptive endometrium that together undertake intimate bilateral communication" [47]. Live births from AAP render this preceding statement debatable because the endometrium does not seem to be invariably essential for successful pregnancy. This has important implications.

It is worth noting that live births from AAP have been described in the setting of HIV infection [17,21], described with twins [37] and one case of abdominal pregnancy diagnosed at 14 weeks of gestation was managed expectantly until delivery at 32 weeks gestation [11].

The key controversy in the management of abdominal pregnancy has been whether to remove or not remove the placenta after delivery [17,20,33]. In this study, in the majority of cases, the placenta was removed successfully after delivery. Ultimately, removal of the placenta seems best done on a case by case basis.

Including only English language articles is a limitation, which led to the omission of relevant cases from the non English language literature for example this French [48] and Persian [49] article. The quality of the reported cases differed, for example some articles lacked information on hemoglobin, the APGAR score and other variables which precluded analysis of these variables. Some full texts of articles meeting the inclusion criteria could not be accessed, namely these reports from Ethiopia, Greece and India [50-52]. A report from Italy not located by the search technique was omitted [53]. Publication bias is possible where only well managed cases were reported. None of the cases mention information about the male partner (father of the newborn); the biologic father is increasingly recognized to play a pivotal role in pregnancy related conditions [54]. Almost none of the cases where the placenta was removed comment on its gross and microscopic features; pathologic examination of the placenta in AAP cases can yield valuable insights [55].

Newspapers remain a valuable source of information [56]; some AAPs with live births have been reported exclusively in newspapers, here is a selection of AAP newspaper articles [57-61].

Conclusion(s)

Physiologically males are more vulnerable than females from conception; the presumed hostile extraterine environment of advanced abdominal pregnancy may cause excess demise of males compared to females.

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Non-technical summary

INTRODUCTION
In extremely rare cases it is possible for the fetus to grow and develop outside the womb; this is known as an abdominal pregnancy. It is extremely rare for a baby to be born alive after an abdominal pregnancy. These cases where the fetus is in the woman’s abdomen but outside her womb can be caused by the fertilized egg accidentally implanting directly into the abdomen instead of the womb. These pregnancies can also happen when the fertilized egg wrongly implants into the tube meant to carry it into the womb, but because the tube is small it bursts and releases the fertilized egg which then accidentally implants into the abdomen. The fetus can also find its way into the abdomen if the womb bursts for some reason. To repeat, all these scenarios are extremely rare.

WHY WAS THIS STUDY DONE?
In the past cases of abdominal pregnancy have helped people to understand some aspects of disease. For example, there is a disease that many years ago was thought to require the fetus to be in the womb for it to occur. When people saw the disease occurring even when the fetus was outside the womb in abdominal pregnancies, this proved that the womb was not necessary for this disease to occur. This means abdominal pregnancies are useful in helping to understand certain things. This study was done because abdominal pregnancies allow us to understand things that we may not otherwise understand.

WHAT DID THE RESEARCHER DO AND FIND?
The researcher searched three medically related databases online that store reports of abdominal pregnancies from around the world. Cases of abdominal pregnancy where the baby was born alive were found and from these cases certain information was collected such as the mother’s age, the length of her pregnancy, the sex of her baby, etc.

The researcher found 38 babies born alive after an abdominal pregnancy from 2008 (the last time when researcher’s did a similar study) to 2013.

Of great interest was the finding that substantially fewer boys compared to girls were born alive following an abdominal pregnancy. In normal pregnancies (where the fetus is in the womb) on average slightly more boys are born alive than girls.

WHAT DO THESE FINDINGS MEAN?
The findings suggest that more boys compared to girls are dying before birth in cases of abdominal pregnancy. This finding is consistent with a known biologic fact that boys are more vulnerable than girls from the moment of conception (when the sperm fertilizes the egg).

That more boys compared to girls are dying before birth with abdominal pregnancy is not too surprising because growing and developing outside the womb is harsh and the more vulnerable boys would be expected not to survive as much as girls.
Illustrations

Illustration 1

Mechanism of developing an abdominal pregnancy. A to D (Secondary abdominal pregnancy), E (Primary abdominal pregnancy). A- tubal rupture, B - rupture of uterine horn, C - uterine rupture, D - fimbrial abortion, E - direct implantation into peritoneal cavity. Note that in cases of AAP due to uterine rupture or a ruptured uterine rudimentary horn, the placenta can remain attached inside or on the uterus.
Illustration 2

Table 1: Selected characteristics of live births resulting from advanced abdominal pregnancies from 2008 to 2013

<table>
<thead>
<tr>
<th>Citation</th>
<th>Year reported</th>
<th>Country</th>
<th>Age (years)</th>
<th>Gestation at delivery (weeks)</th>
<th>Pre-operative diagnosis</th>
<th>Presenting part/lie</th>
<th>Birth weight (kg)</th>
<th>Placenta removed</th>
<th>Sex of baby</th>
</tr>
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<td>[9]</td>
<td>2008</td>
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<td>30</td>
<td>40</td>
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<td>-</td>
<td>3.2</td>
<td>yes</td>
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<td>[10]</td>
<td>2008</td>
<td>China</td>
<td>30</td>
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<td>3.2**</td>
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<tr>
<td>[12]</td>
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<td>22</td>
<td>40</td>
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<td>Transverse</td>
<td>3††</td>
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<tr>
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<td>29‡</td>
<td>33~</td>
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<td>-</td>
<td>2.4**</td>
<td>yes</td>
<td>-</td>
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<td>-</td>
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<td>-</td>
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<td>42</td>
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<td>no*</td>
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<td>39‡</td>
<td>33~</td>
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<td>-</td>
<td>2.6</td>
<td>no</td>
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<td>Female</td>
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<tr>
<td>[20]</td>
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<td>Birth weight (kg)</td>
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<td>1.2††</td>
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<td>38~</td>
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<td>-</td>
<td>T1 0.7 T2 0.8</td>
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</table>

Citation: Year reported Country Age (years) Gestation at delivery (weeks) Pre-operative diagnosis Presenting part/lie Birth weight (kg) Placenta removed Sex of baby

WebmedCentral > Research articles
- not mentioned or unclear, ‡ known to be HIV positive, ~ approximately, § had magnetic resonance imaging, ¶ did not or not known to have had sonography, ** due to uterine rupture, †† due to ruptured rudimentary horn, T1 Twin 1, T2 Twin 2, * had re-laparatomy, † early neonatal death, ‡‡ new born had congenital abnormality or complication
Illustration 3

Countries reporting an advanced abdominal pregnancy with a live birth from 2008 to 2013.