

EFFECTS OF FEMALE UNDERNUTRITION ON FERTILITY FACTORS

ABSTRACT

Nutrition has a profound effect on many aspects of human life, including the ability to successfully create it. The primary objective of this review is to discover how undernutrition affects various female fertility factors including ovulation rate, follicle function, conception rates, time between subsequent conceptions, luteinizing hormone pulse rate, and length of reproductive life. Research articles were collected from the PubMed data base and Google Scholar. Results from most of these studies show marked decreases in one or more of the above mentioned fertility factors when human or animal subjects were exposed to calorie restriction. As undernutrition is known to affect fat stores and body weight, articles examining the relationship between body weight or body fat levels and fertility were also included. These articles showed conflicting results and so more research must be done to discover the true relationship between body fat or fat stores and fertility. However, data has shown that fertility is negatively affected by undernutrition and possibly by low body weight and low body fat stores. This has great implications for the long-term effects of food deprivation, such as is the case in anorexia as well as in food insecurity, on fertility.

INTRODUCTION

Female fertility depends on many factors, including fecundability, fecundity, fertility, follicle function, conception rate, length of time between pregnancies, luteinizing hormone (LH) pulse rate, and length of reproductive life, defined as time from first menstruation to the onset of menopause¹. In this case, fecundability refers to ovulation rate, fecundity refers to conception rate, and fertility refers to the ability to carry viable fetuses¹. LH is necessary for the increased secretion of estrogen, progesterone, and testosterone during ovulation as well as the growth of the corpus luteum and the release of an ovum from a follicle, making it a critical component of female fertility.²

It has long been hypothesized that undernutrition, or the under consumption of nutrients leading to a negative nutrient balance, has a profound effect on these factors². It has also been theorized that because fat converts androgens to estrogens, body weight and body fat may affect fertility.¹ Relative fatness may influence the direction of metabolism of estrogen to the most potent or least potent forms.¹ Although there has been much research on this topic, researchers have yet to arrive at a common consensus about which, if any, of these factors causes a significant change in fertility².

This topic is of great interest to potential human mothers who want to deliver healthy offspring and also of great interest to industries that might depend on regular offspring, such as the ranching industry. This is also of particular concern to physicians in areas where mothers do not have access to regular and proper nutrition or who may suffer from anorexia nervosa or other disordered eating behaviors.

The purpose of this review is to discover if there is indeed a consensus on how fertility is affected by undernutrition. The articles collected emphasize that undernutrition does indeed negatively affect fecundability, fecundity, fertility, follicle function, conception rate, time between pregnancies, LH pulse rate.^{1,3-7} The articles collected also show that body weight and body fat have no clear effect on fertility.^{6, 8-11} Although some articles found that body weight and body fat did indeed affect reproductive development^{6,9,10}, others found that these factors were completely unrelated to reproductive development^{8,11}.

METHODS

Articles were found using the Google Scholar and PubMed databases. Terms such as “malnutrition and fertility”, “calorie restriction and fertility”, and “body fat and fertility” were used in the PubMed databases. Although these searches yielded many results, most were review articles. These were helpful because the references led to some original research that was included in this paper. Similar terms were entered into Google Scholar with much more helpful results. Most of the articles used in this paper were found on Google Scholar. Later, specific articles and aspects of fertility were searched for on both PubMed and Google Scholar. “Malnutrition and luteinizing hormone”, for example, was used to find articles specific to the effects of undernutrition of luteinizing hormone levels, one of which will be used in this paper.

Articles were chosen based on primary article status first and then on relevance to the topic. After this, articles that were less relevant were discarded. Nine original research articles were chosen in addition to other helpful review articles used for reference.

RESULTS/DISCUSSION

Ovulation is an important factor that affects fertility and appears to be negatively affected by undernutrition, either by decreasing ovulation or leading to structural defects that could compromise fertility. Alexander et al.¹ conducted a study on rats to test fecundability, fecundity, and fertility. Ovulation, measured by counting corpora lutea at estrus, decreased by 74% in the calorie restricted group as opposed to the ad libitum group.¹ This evidence would suggest that undernutrition decreases ovulation, therefore compromising fertility. However, Sosa et al.⁴ conducted a similar experiment with sheep and found the number of corpora lutea to be relatively similar between the calorie restricted group and the control group.⁴ The conflicting evidence was most likely due to the duration of time animals were malnourished in each study. The rats were exposed to chronic protein-energy undernutrition while the ewes were exposed to short-term undernutrition, thus leading the difference in ovulation.^{3,4} Sosa et al.⁴ did find another detrimental effect of undernutrition on female reproduction: functionality of follicles. This was measured through imaging techniques such as ultrasonography and laparoscopy as well as blood sampling.⁴ It was discovered that undernutrition, even for this short period of time, led to a large presence of follicles in the static growing phase which, despite reaching ovulation, persisted static during the follicular phase.⁴ These large follicles showed evidence of functional alterations which could compromise fertility.⁴

Undernutrition also affects fertility by decreasing conception rates and increasing the time between one conception and the next. In an experiment on Hereford cows, it was discovered that conception rate and time from delivery to next conception is influenced by undernutrition.⁵ Cows were divided into four groups: 1) those that received adequate feed before and after giving birth to the first calf, 2) those that received adequate feed before birthing and inadequate amounts after, 3) those that received inadequate feed before birthing and low, but adequate, levels of feed after, and 4) those that received inadequate feed before and after birthing.⁵ In the second group, a slight reduction was observed in number of cows showing estrus and conception rate, suggesting that undernutrition decreases conception rates between birth of one calf and conception of the next.⁵ Cows in the third group experienced a greater time period between giving birth and next conception but a normal conception rate, suggesting that undernutrition increases time from one conception to the next.⁵ Cows in the fourth group experienced a lower conception rate, a reduction in estrus, and a greater time between birthing and conception.⁵ This article provides evidence that calorie restriction decreases conception rates and increases time between giving birth and next conception. A longitudinal study of human women in a poor, rural community showed a similar effect.⁶ An experimental group that was supplemented with calories and vitamins recovered fertility after 7.5 ± 2.6 months while an un-supplemented control group recovered fertility after 14.0 ± 4.0 months.⁶ Both groups lactated the entire period between pregnancies.⁶ This study strengthens the argument that calorie restriction decreases fertility by increasing the time between deliveries by 40%.⁶ Undernutrition decreases conception rates and increases the time from one conception to the next, therefore decreasing fertility.^{5,6}

Undernutrition also affects fertility by decreasing luteinizing hormone (LH) pulse frequency. Williams et al.⁷ investigated the relationship between calorie restriction, exercise, and LH levels in the blood. Four women were monitored over three menstrual cycles and subjected to three treatments: a control treatment with normal diet and exercise, a calorie restriction treatment coupled with intense exercise, and an intense exercise treatment.⁷ It was found that LH

pulse frequency significantly decreased when the women experienced calorie restriction and intense exercise but not during the control period or the intense exercise period.⁷ However, mean LH levels in the blood and peak amplitude levels were similar between all groups.⁷ Although the small sample size necessitates further research, these results suggest that high-volume training combined with caloric restriction may decrease LH pulse frequency, and therefore possibly prevent the expulsion of an ovum from the follicle, negatively affecting female fertility.⁷

Finally, undernutrition may affect maturation and length of reproductive life but research does not agree if these fertility factors are affected by calorie restriction, body weight, or body fat distribution. Chavez et al.⁶ studied the length of reproductive life in women experiencing calorie restriction and found that the onset of puberty occurred at a very late average of 15.5 years and the onset of menopause occurred at the very early age of 40.4, decreasing total reproductive life to 25 years.⁶ This clearly shows that undernutrition shortens reproductive life. However, a study that controlled weight gain in rats through intense exercise or calorie restriction found that reproductive development was accelerated in the group that was subjected to intense exercise compared with the ad libitum-fed control group and the calorie restriction group, regardless of body weight, and body length.⁸ This would suggest that exercise, not calorie restriction, body weight, or body fat, affects reproductive development.⁸ A conflicting study found that puberty onset was linked with total body weight in mice, not exercise or total body fat levels, supporting the hypothesis that fertility may be decreased by undernutrition if it decreases total body weight.⁹ Another study conducted by Lassek et al. found that girls with female-patterned fat distribution, or increased gluteofemoral fat deposits, experienced early menarche.¹⁰ This study, which took its data from the NHANES III study, supports the hypothesis that undernutrition would delay menarche, and therefore shorten reproductive life, if it led to a lack of female-patterned fat distribution. However, a final study measured the relationship between body fat, total body weight and age at menarche through DEXA scans and found such a wide variety of body shapes and weights at menarche as to dismiss the hypothesis that a certain body weight or fat level has to be achieved to allow menarche to occur.¹¹ Clearly, more research must be done to discover the true relationship between calorie restriction, exercise, body weight, body fat distribution, and reproductive development.

In conclusion, although undernutrition appears to decrease fertility, it is still unclear as to how this occurs. Several factors have been shown to be affected by undernutrition, including ovulation, conception rates, time between subsequent conceptions, and LH pulse frequency. The relationship between undernutrition, total body weight, and body fat composition and fertility is even more unclear. Although some studies support the idea that low body weight or body fat can delay menarche and hence, shorten reproductive life^{6,9,10}, not all studies agree^{8,11}. Although it can be concluded that undernutrition may affect fertility through decreasing ovulation, decreasing conception rates, increasing time between subsequent conceptions, and decreasing LH pulse frequency, no conclusions can be drawn about the effects of calorie restriction, exercise, body weight, and body fat distribution on the length of reproductive life.

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Response to Reviewer

I did not change effect to affect because I believe I used the word correctly. I did follow suggestions 2,4-14, 16-21, 23-25, 27-28, and 30-32. Most of these were simple sentence structure and so would be incredibly tedious and unnecessary to discuss here. I appreciated these comments however as they helped me to realize things about my paper that I had not considered before.

Through suggestions 3 and 22 I actually realized that I had been using a word wrong throughout my paper and changed malnutrition, which could be any number of nutrition related imbalances, to undernutrition, or the under consumption of nutrients that leads to a negative nutrient balance. This is truly what I wanted to research and discuss, not all nutrition problems (such as over consumption or under consumption of specific nutrients).

I changed the order of one article in response to reviewer comments but there were many facets of the articles that fit under two or more factors of fertility so I was unable to arrange them in such a way where reintroduction of some studies for the sake of discussing a different aspect was not necessary.

In response to the comments about the introductions, I included more definitions and tried to tie in all aspects of my paper both in the introduction and throughout the paper.

I changed the methods section quite a bit to only contain relevant information that led to a shortening of the paragraph in general, giving more room for the results sections.

In response to the results/discussion comments, I tried to reorganize my studies but found this too difficult. I also tried to follow the comment about reorganizing the studies to emphasize the most important and conclusive data above the others.

Research Review Paper Submission Checklist

Please use the following checklist to ensure that you addressed the items students commonly miss from the instructions sheet (put an "x" in each box to confirm that you met this requirement):

- Is your paper formatted correctly? (Single-spaced, left-justified with 0.5 to 1-inch margins, 12-point type in *Times New Roman*, and pages numbered and include line numbers)
- Is your research paper 3-pages in length? (excluding the Author/Title page, Abstract, and
- References)
- Is your title less than 200 characters?
- Does your abstract contain these elements: topic and primary objective of the review, methods of data sourcing and extraction, and results/conclusions (with no references cited)?
- Is your abstract 250 words or less?
- Did you clearly state the purpose of your research review paper in the introduction?
- Did you choose primary research articles not review articles in your paper?
- Are 80% of your references from peer-reviewed journals?
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- Are only credible Internet sources listed?
- Are references numbered sequentially upon first appearance in the text?
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- and semicolons?
- Is the reference list formatted according to AMA style?