African Journal of Current Medical Research

CASE REPORT

Reframing Ethics when Unintended Consequences Arise: A Case Report of a Multiple Micronutrient Study During Pregnancy in Ghana

Lisa H. Gren[1] (PhD, MSPH), Rachel Jaggi (MA)[1], Caren J. Frost (PhD, MPH)[2] L. Scott Benson (MD, PhD, MPH)[1]

[1] Department of Family and Preventive Medicine, University of Utah-USA

[2] College of Social Work, University of Utah-USA

ARTICLE INFO

Article history:
Received 3rd May, 2016
Received in revised form
17th January, 2018
Accepted 21st September, 2018
Available online
7-Dec-2018

KEYWORDS

Ethics; Pregnancy

CORRESPONDING AUTHOR CONTACT*

Assistant Professor
University of Utah, Department of Family and Preventive Medicine
375 Chipeta Way, Suite A
Salt Lake City, UT 84108
***Phone:** 801-585-6232*
Email:
Lisa.gren@hsc.utah.edu

Abstract

In a study of dietary supplementation among women in Ghana, a disproportionately high number of pregnant study participants were found to no longer be pregnant, leading researchers to suspect that the very early identification of pregnancy status made possible by study participation may have contributed to an elevated incidence of elective abortion among study participants. While abortion is legal in Ghana under certain circumstances, misinformation regarding its legality and persistent stigmatization result in many Ghanaian women choosing abortion methods that are unsafe and often illegal. While the study of the potential benefits of dietary supplementation during pregnancy initially appeared to pose very little risk to participants, the unintended and unforeseen consequence of unsafe abortions required researchers to reevaluate study protocol. In the following discussion of this case, we explore the ethical considerations researchers must address when unintended consequences emerge in global health research.

Introduction

Despite dramatic improvements in recent decades, malnutrition continues to be a pervasive public health burden in low income countries, particularly among pregnant women.1, 2 Although there are many approaches to alleviating the health burden of malnutrition, dietary supplementation is the most widely practiced intervention, since it is comparatively cost-effective and has the potential for a relatively immediate impact on the health of the receiving population.3 In recent decades, dietary supplementation programs in low and middle income countries have increasingly relied upon a complete micronutrient supplement with studies showing improvements in a number of pregnancy and birth outcomes, including reductions in low birthweight, neonates that are small for gestational age, preeclampsia, neural tube defects, and other congenital malformations.4

While there is evidence to suggest that multiple micronutrient supplementation during pregnancy may play an important role in improving maternal health in low and middle income countries, the World Health Organization currently only recommends iron and folate supplementation during pregnancy, though guidelines containing recommendations regarding micronutrient supplementation are planned for release in 2016. Before new recommendations could be made, more research was needed to assess both the comparative advantage of micronutrient supplementation and the potential adverse effects associated with overuse or interactions between micronutrients.5 In response to the call for more research on the comparative advantages and risks of multiple micronutrient supplementation during pregnancy, a community-intervention study was launched by institutions in Ghana and from a high income country among women of reproductive age in rural Ghana in 2013. During the course of the study, unintended
consequences emerged that necessitated study modification, leading researchers to explore the ethical considerations of study modification during an active study.

Case

Ten communities in the Barekese sub-district of Ghana were randomized to receive either the complete micronutrient or the iron-folate supplement. In order to identify women within one month of conception, the community health workers were also tasked with conducting urine pregnancy tests at each monthly visit. Community health workers began visiting women and distributing the supplements in July 2013. These community health workers were tasked with visiting the women in their communities monthly to educate them on the benefits of supplementation, perform pill counts, and distribute another month's supply of the appropriate supplement. Additionally, because the purpose of the study was to identify the comparative effects of the two supplementation methods across time, blood serum samples were collected at three points associated with the women's pregnancy: in the first month of pregnancy, in the third trimester, and at three months post-delivery. In order to obtain a serum sample in the first month of pregnancy, women also received monthly pregnancy testing, which informed them of their pregnancy status within 1-2 weeks of conception. The three blood samples were then analyzed for six important biomarkers to provide a detailed picture of the comparative impact of the two supplements from conception through lactation. By the end of January 2014, a total of 13 of the 41 women identified as pregnant by blood tests were found to no longer be pregnant. These participants may have terminated the pregnancies.

Discussion

The proportion of women in the study who were found to no longer be pregnant represented a surprising increase over what the Ghana-specific statistics would have predicted. According to a recent study of maternal health in Ghana, 9% of pregnancies in Ghana end in miscarriage and 7% of pregnancies end in induced abortion.[8] In this case study, 32% of pregnancies ended unexpectedly and were suspected by study personnel in Ghana to be primarily from induced abortions.

Although legal, professional abortion services are not offered widely and continue to be highly stigmatized across Ghana, resulting in women often seeking underground, and likely unsafe, abortions.8-12 In this study, women received monthly urine pregnancy testing, informing them of their pregnancy status within weeks of conception, which was much earlier than would have been possible using traditional methods of pregnancy identification. Early detection, as a result of study participation, may have created a longer window in which women could access abortion services before signs of pregnancy became publicly recognizable, thus allowing women to avoid the stigmatization associated with abortion. The high rate of terminated pregnancies suggested that the study procedures had introduced an element into the participating communities that was altering practices related to pregnancy termination in unanticipated ways. Because of the lack of access to safe abortion services, it is likely that many of the suspected induced abortions were conducted in an unsafe manner and put the women at risk for complications. While the termination of pregnancy was not caused by taking the micronutrient supplements, participation in the study likely contributed to unanticipated behavior change among the women that introduced the potential for harm to participants. This unintended consequence of monthly pregnancy testing put participants in the study at greater risk and necessitated redesign of study protocol.

In order to remove the unintended consequence, the decision was made to alter the study design to remove this element of influence by stopping monthly pregnancy testing. Instead, women were enrolled in the study according to self-report of pregnancy status and/or seeking of professional prenatal care. After such unintended consequences arise, researchers must consider the ethical implications of emergent potential harm to participants in an otherwise minimal risk study, some of which are outlined below.

Recommendation on Ethical Issues

Internal monitoring

- What should the standard for internal monitoring be for studies that do not include experimental interventions? (In this case, micronutrient supplementation has been shown to be very safe and does not require the same oversight required for studies of untested pharmaceuticals drugs or devices).
- Who should be included in the process of internal monitoring?
- How often should internal reviews be conducted?

Study design modification

- How can researchers identify whether observed effects outside the scope of the project represent harm or undesirable consequences as a result of study participation?

Ethical justification for altering the study design in this case hinged on the evident abrupt alteration of typical patterns of behavior among study participants. Under what circumstances should researchers alter the study design? How can researchers weigh whether study modification is ethically necessary?

When unintended consequences outside the scope of the research focus emerge, what responsibilities do researchers have to stakeholders (e.g., the funding organization, participating communities)?

Communication of unanticipated findings

When significant changes to research participation are made after participants have been enrolled, how should the study team work with study participants to help them understand the changes to their own participation in the study?

When should research guidelines at the ethics board review level be modified to manage new risk to study participants?

Unanticipated findings outside the scope of the research focus are inherently not the result of rigorous scientific inquiry, yet may represent important discoveries. What is the appropriate medium for dissemination of such findings to the scientific community?

Conclusion

In our case study, we outline three areas for discussion when an intervention is associated with increased risk of, or actual, harm to participants: internal monitoring, study design modification, and communication of unanticipated findings. Unintended events in the research context, as described here, require evaluation of ethical concerns as well as exploration of the cultural and policy differences that led to the behaviors that manifested as unacceptable risk or harm

References

1. Bhutta ZA, Haider BA. Maternal micronutrient deficiencies in developing countries. *Lancet.* 2008; 371(9608):186-187.
2. Walton E, Allen S. Malnutrition in developing countries. *Paediatrics and Child Health.* 2011; *21*(9): 418-424.
3. Bhutta ZA, Salam RA, Das JK. Meeting the challenges of micronutrient malnutrition in the developing world. *British Medical Bulletin.* 2013; 106(1): 7-17.
4. Willardson, S.L., Dickerson, T.T., Stucki Wilson, J., Ansong, D., Bueler, E., Boakye, I., Marfo, J., Arhin, B. and Alder, S.C. Forming a Supplement Intervention Using a Multi-Theoretical Behavior Model. *American Journal of Health Behavior.* 2013; *37*(6): 831-840.
5. Shankar, A. H., et al. Effect of maternal multiple micronutrient supplementation on fetal loss and infant death in Indonesia: a double-blind cluster-randomised trial. *Lancet.* 2008; 371(9608): 215.
6. Resnik, D.B. What is ethics in research & why is it important? National Institute of Environmental Health Sciences. http://www.niehs.nih.gov/research/resources/bioethics/whatis/. Published December 1, 2015. Accessed June 10, 2016.
7. WHO. About ethics and health. http://www.who.int/ethics/en/. Published 2016. Accessed June 10, 2016.
8. 8.Ghana Statistical Service (GSS), Ghana Health Service (GHS), and Macro International. 2009. Ghana Maternal Health Survey 2007. Calverton, Maryland, USA: GSS, GHS, and Macro International.
9. PNDC Law 102. The consolidated criminal code of 1960 (Act 29) Section 58. The abortion law, 1985.
10. Morhe, E.S.K., Morhe, R.A.S. and Danso, K.A. Attitudes of doctors toward establishing safe abortion units in Ghana. *International Journal of Gynecology & Obstetrics.* 2007; *98*(1): 70-74.
11. Schwandt, H. M., Creanga, A. A., Adanu, R. M., Danso, K. A., Agbenyega, T., & Hindin, M. J. Pathways to unsafe abortion in Ghana: the role of male partners, women and health care providers. *Contraception.* 2013; *88*(4): 509-517.
12. Sundaram, A., Juarez, F., Bankole, A., & Singh, S. Factors associated with abortion-seeking and obtaining a safe abortion in Ghana. *Studies in Family Planning.* 2012; *43*(4): 273-286.

DOI: http://dx.doi.org/10.31191/afrijcmr.v2i2.16