

Factors Driving Pregnant Women's Participation in Non-therapeutic Clinical Research in Tanzania: Qualitative Findings from Mwananyamala Regional Hospital, Dar-Es-Salaam Region

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ABSTRACT

Background: Pregnant women's participation in non-therapeutic clinical trials has gained global attention. However, the imposition of unnecessary harm to the fetuses because of their participation is questionable. This is proved by the historical tragedies that resulted from the use of diethylstilbestrol and thalidomide, which caused cancer among daughters of the treated women.

Methods: The study was an exploratory qualitative facility-based conducted at Mwananyamala Regional Hospital in Kinondoni District, Dar-es-Salaam Region, Tanzania, among pregnant women who were enrolled in a clinical trial: "Adverse birth outcomes among mothers who received intermittent preventive treatment with Sulphadoxine-Pyrimethamine in the low malaria transmission region". Data were collected through in-depth interviews and analyzed by thematic analysis with the aid of NVivo computer software.

Findings: Several push and pull factors such as saving of the life of the fetus and the mother; delivery complications; the desire to contribute to maternal-fetal science; societal benefits; incentives; advice from medical professionals; free or voluntary participation, and therapeutic misconception influenced pregnant women to voluntarily participate in non-therapeutic clinical researches.

Conclusion: The study findings show that saving of the life of the fetus and the mother, delivery complications, desire to contribute to maternal-fetal science, advice from medical professionals, and incentives were core factors for pregnant women's participation in non-therapeutic clinical researches in Tanzania. Fetal harms and therapeutic misconceptions decelerate pregnant women's rate to participate in non-therapeutic clinical researches hence bioethical education is highly needed in this aspect.

Keywords

Pregnant women, Non-therapeutic clinical researches, Factors influencing participation in clinical trials, Qualitative research, Tanzania.

Introduction

From the 1980s to the early 1990s, pregnant women have generally been barred from participating in the first and the earliest part of the second phase of drug clinical trials [1]. However, this exclusion

came to be wrongly interpreted by sponsors of those trials who often interpreted it more broadly and restricted admission of pregnant women into later stages of drug trials. [1] Hence, this caused the prolonged total exclusion of pregnant women into clinical trials. One among the grounds for their prohibition has been the idea that pregnant women are vulnerable as research subjects [2]. However, this factor was later criticized for the reason that pregnant women should be considered as a special group that contributes to clinical findings from their unique world of experience rather

than a vulnerable population [3]. Therefore, this clinical necessity facilitated an increased call for the inclusion of pregnant women in clinical trials, in order to expand medical knowledge and healthcare for them [4]. The argument is that without sufficient knowledge of medication efficacy during pregnancy, pregnant women and physicians are forced to make decisions because of substandard data, which in turn, places the fetus at risk [5].

Pregnant women express several factors which make them participate in non-therapeutic clinical trials including, but not limited to, the risk of losing the baby whereby most of them participate as a way to save the baby; previous experience of premature delivery; the role of the doctor and other health professionals whose explanations regarding diagnoses and the proposed treatments influence women's decisions to participate in clinical studies. Moreover, numerous women state free participation as the factor that influenced them to participate [6].

However, regardless of their right to participate in non-therapeutic clinical trials as autonomous beings, the imposition of unnecessary fetal harm as a result of their participation is questionable. Hence, their participation presents an ethical dilemma that raises several ethical questions including 1) how can a non-therapeutic clinical trial be regarded harmless enough for pregnant women and fetuses? 2) How long can the exposure in a non-therapeutic clinical trial be considered to remain safe for pregnant women and fetuses? And, 3) Can non-therapeutic clinical trials' safety be established at an adequately acceptable level for pregnant women and fetuses to conclude a positive benefit-risk ratio?

For quite some time, there has been secrecy to the after-effects that are likely to harm the fetuses because of pregnant women's participation in clinical trials. This is further proved by the historical tragedies that resulted from the use of diethylstilbestrol (commonly referred to as DES) and thalidomide, which attracted the filing of lawsuits by pregnant women against the drug manufacturers. DES was used from 1938 to 1971 to prevent miscarriage; however, it was later realized that this drug did not prevent miscarriage; and over time, it was linked to cancer among the daughters of the treated women. Throughout the late 1950s and 1960s, thalidomide was administered to impart drowsiness, and later it was used to treat morning sickness among pregnant women. However, soon after being prescribed to pregnant women, thalidomide was linked to debilitating birth defects in more than 8,000 newborns and another 7,000 died of their deformities before birth [3].

In this paper, we present some factors driving pregnant women's participation in non-therapeutic clinical research in Tanzania using a case study of a clinical trial titled "Adverse birth outcomes among mothers who received intermittent preventive treatment with Sulphadoxine-Pyrimethamine in the low malaria transmission region," conducted at Mwananyamala Regional Hospital, Kinondoni District, Dar-es-Salaam.

Materials and methods

Study design

This study used an exploratory facility-based design to explore factors influencing pregnant women's participation in non-therapeutic clinical research in Tanzania.

Study setting

The study was conducted at Mwananyamala Regional Referral Hospital in Mwananyamala Administrative Ward in Kinondoni District, Dar es Salaam Region.

Study participants

33 study participants with varied characteristics such as age, level of education, economic status as well as experience with trials were preliminary enrolled in this study out of 631 pregnant women who were enrolled in the clinical trial conducted at Mwananyamala Regional Hospital, Kinondoni District, Dar-es-Salaam between April and August 2018. However, only 14 participants were interviewed at least twice each to provide the information needed for this study.

Data collection procedure

Data were collected using in-depth interview (IDI) which involved conducting an intensive interview with each participant in order to explore the factors that influenced her participation in non-therapeutic clinical research at Mwananyamala Hospital in Kinondoni, Dar es Salaam. Interviews were conducted at participants' places of choice. A quiet conducive place was considered to enhance privacy, confidentiality, and quality recording. All interviews were conducted by the researcher in Kiswahili; a national language understood and spoken by the majority of people in the study area.

Data processing and analysis

All IDIs were audio-recorded, transcribed, and then translated into English. The transcripts were analyzed using a qualitative deductive thematic analysis method through the aid of NVivo Computer software, which assisted in the organization of data and the generation of codes. The thematic analysis method included the following steps: familiarization with the data collected; generation of initial codes; searching for themes; reviewing of themes, defining and naming themes [7].

Ethical considerations

The ethical clearance was obtained prior to the commencement of the study from the Muhimbili University of Health and Allied Sciences (MUHAS) Institutional Review Board (IRB) №: MUHAS –REC-09-2020-373. Permission to interview the pregnant women was sought from the Principal Investigator (PI) of the Mwananyamala Clinical Trial and from the Mwananyamala Hospital Medical Officer where that trial was being conducted. After that, the study participants signed the written informed consent forms demonstrating their willingness to participate in this study. This was done after they had been informed of the aim, objectives, and benefits of participation in this study. Mothers were assured participation was voluntary and would cause no harm to them.

Results

Push factors for pregnant women's participation in non-therapeutic clinical research

The study participants gave varying factors that pushed them to participate in non-therapeutic clinical research. Under this theme, there are four sub-themes, which are saving the life of the fetus and its mother; delivery complications; the desire to contribute to maternal-fetal science; and societal benefits.

a) Saving the life of the fetus and the mother

Saving the life of the fetus and its mother was the most articulated push factor by the participants as the main factor that pushed them to participate in non-therapeutic clinical research. One participant, for example, stated; *"The factors which pushed me to participate in a non-therapeutic clinical trial at Mwananyamala Hospital included saving my life and the fetus ... and the need to improve the health of pregnant women and fetus"* (P-09). Another participant narrated, *"What made me participate in that non-therapeutic clinical trial at Mwananyamala Hospital was the need to protect my fetus against diseases that could make me lose it [miscarriage]"* (P-07).

b) Delivery complications

Some participants said that delivery complications such as maternal morbidity and mortality, eclampsia, and fetal demise or loss were some of the factors that pushed or influenced them to participate in non-therapeutic clinical trials to get solutions to those complications. One participant, for example, reported, *"The adverse effects that we pregnant women face during delivery such as giving birth to a dead baby are the ones which pushed us to participate in non-therapeutic clinical research so as to get solutions to them ... The solutions which will, in turn, benefit other future pregnant women as a result of our contribution in the study"* (P - 01). Another interviewed participant added, *"Another thing which pushed us to participate in non-therapeutic clinical research at Mwananyamala Hospital was to help the researchers to determine what causes eclampsia to us, especially when we are in labor pains ... We also wanted to know if there could be medications which could cure us, so as to prohibit it [eclampsia] from happening ... A lot of mothers lose their lives as a result of this problem"* (P -05).

c) Desire to contribute to maternal-fetal science

Some participants were of the view that factors that pushed them to participate in non-therapeutic clinical research were the desire to contribute to maternal-fetal science by fighting against maternal-fetal diseases that affect them and their future children. Therefore, they believe that by participating in non-therapeutic clinical researches, they would go away with maternal-fetal diseases, which face them. The mothers had hope that non-therapeutic clinical studies would help them and their fetuses against maternal-fetal diseases as there will be new scientific discoveries on how to fight against maternal-fetal diseases. One participant, for example, noted, *"The factors that influenced us to participate in non-therapeutic clinical research at Mwananyamala Hospital included the need to fight against maternal-fetal diseases which*

kill us [pregnant women] ... For example, malaria has affected pregnant women a lot in our societies ... Therefore, that influenced us to participate in non-therapeutic clinical research hoping that there will be scientific discoveries stemming from our participation that will help our society to improve maternal-fetal health" (P-08). Another participant firmly added, *"The factors that influenced us to participate in a non-therapeutic clinical trial at Mwananyamala Hospital included fighting against different diseases such as malaria that affect us and our fetuses"* (P-02).

d) Societal benefits

Societal benefits were also articulated by some participants as the main factors that influenced their participation in non-therapeutic clinical research. They hoped the society would benefit from their participation in non-therapeutic clinical researches where, for example, if medications were produced because of those studies in which they participated, the whole society would benefit too. A study participant stated, *"Another factor which pushed us to participate in non-therapeutic clinical research was to benefit the society ... This is because when I am participating in the research it is not for my benefits only but also for the benefits of our children and others in the society"* (P-05). In addition to that, another participant stated that non-therapeutic clinical research benefits society in general when medications are in place. She narrated, *"The second factor which influenced us to participate in non-therapeutic clinical research was helping the society in general if the medications would be produced ... Therefore, the society would benefit as a result of our participation in non-therapeutic clinical researches"* (P-11).

Pull factors for pregnant women's participation in non-therapeutic clinical research

In this theme, also there were four sub-themes, which are incentives; advice from medical professionals; therapeutic misconceptions; and free or voluntary participation.

a) Incentives

Incentives that were being provided to participants who participated in non-therapeutic clinical research pulled some pregnant women to participate in those researches. In their views, incentives provided, in one way or another is the major factor pulling them to participate in such researches. This view was reported by one of the participants who had this to say, *"There are two or three factors which pulled us to participate in non-therapeutic clinical researches ... The first one was the desire to get materials distributed to the research participants such as packets of sugar ... So, we got influenced to participate in order to get those things ... Poverty pushes one to participate in order to benefit from research incentives including money reimbursed for transport and reasonable compensation for the time spent at the facility"* (P-14).

b) Advice from medical professionals

Some participants expressed the pull factors to participate in non-therapeutic clinical researches as being influenced by the strong trust they had in medical professionals. Hence, this made them

participate in non-therapeutic clinical researches. One mother, for instance, expressed, *“We strongly trust our doctors [medical professionals] and we respect their advice regarding medical issues ... Hence, we can’t say no whenever they advise us to participate in any clinical researches”* (P-02). This view was held by another interviewed participant who said that *“There are many factors that influenced pregnant women to participate in non-therapeutic clinical researches... A pregnant woman may be experiencing certain complications and be advised by medical professionals to participate in a clinical trial which might help her and the fetus in fighting against those complications ... Hence, she finds herself participating in non-therapeutic clinical research”* (P-06).

c) Therapeutic misconceptions

Some pregnant women had the fantasy of being treated by participating in non-therapeutic clinical researches (therapeutic misconception) and as such, that was the main factor that pulled them to participate in the trial. One participant reported that, *“I didn’t expect harms to occur due to my participation ... I participated in order to protect my fetus from different diseases that it might contact ... Because there is a day you can take medicine that can cure you or it can add some problems on you ... Another benefit of non-therapeutic clinical research is that they help in curing pregnant women and the fetuses”* (P-11).

d) Free or voluntary participation

Some of the participants observed that their participation in non-therapeutic clinical research was a result of their own voluntary will after they were assured by researchers that those studies were safe. However, some participants opined that if there were more adverse effects emanating from those trials they could not have participated. One participant stated, *“I participated in non-therapeutic clinical research, after knowing that the study was moral and safe ... However, if there could be more adverse effects, I could not have participated for I had to take care of my health and that of my fetus”* (P-01). Another participant added, *“If those researches are safe, it is okay for pregnant women to participate because they will help them in the future”* (P-09).

The need to protect fetus and participation dilemma

Pregnant women’s participation in non-therapeutic clinical researches has evoked major concern regarding their participation. This concern is about the two conflicting interests between their right to participate in non-therapeutic clinical researches; and the obligation to protect fetuses from unnecessary fetal harm. They argued that fetuses should be protected from potentially harmful trials, in which they have no direct benefit. At the same time, they said that they have their own right to participate in those trials. The issue of balancing between these two competing interests was an ethical challenge to them, which made most of them face various psychological effects such as stress, isolation, unfitness of the mind, blame, and separation when unnecessary fetal harms occur to fetuses. This also triggers endless family conflicts. One participant narrated; *“I participated in non-therapeutic clinical research, after knowing that the study was good and safe but if there could be more adverse effects because I was carrying a*

fetus in my womb, I could not have participated for I had to take of care my health and that of my fetus.” (P-01). Therefore, most of the pregnant women were fearful of exercising their right to participate in non-therapeutic clinical researches so that they could not unnecessarily harm the fetuses.

Discussion

This study explored the factors that influenced pregnant women’s participation in non-therapeutic clinical research in a clinical trial: *“Adverse birth outcomes among mothers who received intermittent preventive treatment with Sulphadoxine-Pyrimethamine in the low malaria transmission region,”* conducted at Mwananyamala Regional Hospital, Kinondoni District, Dar-es-Salaam Region. Saving the life of the fetus and its mother, delivery complications, desire to contribute to maternal-fetal science, incentives, advice from medical professionals, and free or voluntary participation positively influenced pregnant women’s participation in a non-therapeutic clinical trial at Mwananyamala. These reasons were attributed to by, among other reasons, but not limited to, the need to deliver safely; a need to fight diseases that affect pregnant mothers and their future children; a need to know their health status so as to protect themselves and the fetuses; and extreme poverty of some participants.

These results relate to the study by Monteiro, et al., [6] where pregnant women revealed the need to reduce the risk of losing the baby the main factor that pushed them to participate in that study. In other words, they aimed at saving the lives of their fetuses or their babies. Results from this study are also consistent with a study by Meshaka, et al., [8] who demonstrated that pregnant women participate in a clinical trial in order to help medical research and improve medical science knowledge. Furthermore, the study findings corroborate with a study by Vellinga, et al., [9], who argued that incentivizing influences participation in trials. This is, however, contrary to Guideline 19 of the Council for International Organizations of Medical Sciences (CIOMS) 2016, which advocates for pregnant mothers’ autonomous decision-making, as incentives compromise autonomous decision-making freedom. In addition, this finding is contrary to the 1947 Nuremberg Code, which puts it clear that persuasion or pressure of any kind should not be put on clinical trial participants [10].

However, these factors should not be taken to justify unwarranted exposure of the fetuses into any harm for it is not ethically acceptable as it goes against the bioethical principle of beneficence and non-maleficence as provided for in the Belmont Report, 1979. In addition, it is also argued by Singer and Bossarte [11] and Singer and Couper [12], that incentives to research participants may exert undue influence on potential research participants’ decisions about whether to take part in research especially when they are extremely poor. Moreover, advice from medical professionals, also affect the capacity of pregnant women in making decision to participate in non-therapeutic clinical trials contrary to the clinical research regulations such as Guideline 19 of the CIOMS, 2016. Guideline 19 mandates that the decision making for clinical trial

participation should be independent from any interference that may affect personal freedom to make decision.

Consequently, this advice may also exert pressure on part of the participants who, in turn, may participate in non-therapeutic clinical trials unwillingly. Issues become more worsened, especially where there is an aspect of telling half-truths by medical professionals/researchers to the study participants concerning the nature of the study itself. As a result, the participants find themselves causing unnecessary fetal harm contrary to the bioethical principle of non-maleficence [13]. Zolkefli [14], emphasizes telling the truth as it is a participants' right. Therefore, the provision of truthful information enables the participant to either decide to participate in non-therapeutic clinical research or not. Telling of half-truths about the study by medical professionals could lead to therapeutic misconceptions; conflicts of interests between pregnant women's participation in non-therapeutic clinical researches and the need to protect fetuses from unnecessary fetal harms resulting in various psychological effects such as stress, isolation, unfitness of the mind, blame and family separation on part of the participants due to unnecessary harms that affect the fetuses. Hence, these forces may trigger endless family conflicts.

Therefore, this being the case, most pregnant women emphasized that they believed fetuses also have their own right to be protected from harm. This is because, when they participate in non-therapeutic clinical researches, they just participate as their trustees and, therefore, it is not ethical to unnecessarily cause serious harm to them. Therefore, if a pregnant woman participates in non-therapeutic clinical research, which ends in causing unnecessary fetal harms while claiming to exercise her right to participate in those researches, she will be condemned for violating the fetal right to protection from all unnecessary harm contrary to the bioethical principle of non-maleficence [13].

Conclusion and Recommendations

The purpose of this study was to explore factors that influence pregnant women's participation in non-therapeutic clinical research at Mwananyamala Regional Hospital in Kinondoni district, Dar es Salaam. The findings of this study show that saving of the life of the fetus and the mother, delivery complications, desire to contribute to maternal-fetal science, advice from medical professionals, and incentives were core factors for pregnant women's participation in non-therapeutic clinical researches in Tanzania. Fetal harms and therapeutic misconceptions decelerate pregnant women's rate to participate in non-therapeutic clinical researches hence bioethical education is highly needed in this aspect. We propose conducting further studies on this issue and on varied clinical/medical trials in the country to generate comprehensive data on why pregnant women in Tanzania participate in these trials.

Abbreviations

DES: Diethylstilbestrol; IRB: Institutional Review Board; MUHAS: the Muhimbili University of Health and Allied Sciences.

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