OBJN
ONLINE BRAZILIAN JOURNAL OF NURSING
ISSN: 1676-4285

ORIGINAL

Understanding of informed consent in clinical research for a vaccine against Zika virus: a cross-sectional study*

Compreensão do consentimento informado em pesquisa clínica de vacina contra o Zika vírus: estudo transversal

Comprensión del consentimiento informado en la investigación clínica de una vacuna contra el virus del Zika: un estudio transversal

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Submission: 07/19/2021
Approved: 06/22/2021

ABSTRACT

Objective: to assess the understanding of the information contained in the Informed Consent Form by the participants of a clinical trial of a vaccine against the Zika virus. **Method**: cross-sectional study using intentional sampling, including a total of 101 volunteers in clinical research in Belo Horizonte, Minas Gerais. A structured questionnaire was used. Data analysis was performed using R software, according to descriptive and inferential statistics. **Results**: the mean of correct answers of the participants regarding the information in the consent form was 66.9%. Most participants signed the document without sufficient knowledge of the research information. The comprehension index was higher among participants who had volunteered in previous research (p=0.039). **Conclusion:** there were important limitations in the participants' understanding of information in the consent form, which compromised the autonomous decision. Adaptations and improvements are necessary in the processes of informed consent for its validity.
Descriptors: Controlled Clinical Trial; Research Ethics; Informed Consent Form.

RESUMO

Objetivo: avaliar a compreensão das informações do Termo de Consentimento Livre e Esclarecido pelos participantes de uma pesquisa clínica de vacina contra o Zika vírus. **Método**: estudo transversal com amostra por conveniência e participação de 101 voluntários de uma pesquisa clínica em Belo Horizonte, Minas Gerais. Utilizou-se um questionário estruturado. A análise dos dados foi realizada no programa R, segundo a estatística descritiva e inferencial. **Resultados**: a média de acertos dos participantes sobre as informações do documento de consentimento foi de 66,9%. A maioria dos participantes assinou o documento sem o conhecimento suficiente das informações da pesquisa. O Índice de compreensão foi maior entre os participantes que tinham se voluntariado em pesquisas prévias (p=0,039). **Conclusão:** verificaram-se limitações importantes na compreensão dos participantes sobre informações do termo de consentimento, o que comprometeu a decisão autônoma. São necessárias adaptações e melhorias nos processos de consentimento informado em prol da sua validade. **Descritores:** Ensaio Clínico Controlado; Ética em Pesquisa; Consentimento Livre e Esclarecido.

RESUMEN

Objetivo: evaluar la comprensión de las informaciones contenidas en el Término de Consentimiento Libre e Informado por los participantes de un ensayo clínico de una vacuna contra el virus del Zika. **Método**: estudio transversal con muestra de conveniencia y participación de 101 voluntarios en una investigación clínica en Belo Horizonte, Minas Gerais. Se utilizó un cuestionario estructurado. El análisis de datos se realizó mediante el programa R, según estadística descriptiva e inferencial. **Resultados**: el promedio de aciertos de los participantes con respecto a las informaciones del documento de consentimiento fue de 66,9%. La mayoría de los participantes firmó el documento sin conocimiento suficiente de las informaciones de la investigación. El índice de comprensión fue mayor entre los participantes que se habían ofrecido como voluntarios en investigaciones anteriores (p=0,039). **Conclusión:** hubo limitaciones importantes en la comprensión de las informaciones del formulario de consentimiento por parte de los participantes, lo que comprometió la decisión autónoma. Son necesarias adecuaciones y mejoras en los procesos de consentimiento informado para su validez. **Descriptores:** Ensayo Clínico Controlado; Ética en Investigación; Consentimiento libre e informado.

INTRODUCTION

Over the years, there has been a global expansion of clinical trials to assess the safety and efficacy of new treatments through research in which the pharmaceutical industry has been exercising leadership[1]. Brazil has been considered a country with high potential for the development of these studies, considering its population diversity, prevalence of pathologies similar to rich countries, as well as lower operating costs[2]. With regard to clinical research with vaccines, in the national context, the Association of Pharmaceutical Research Industry (INTERFARMA) describes an increase from 1.2% to 2.8% between 2014 and 2019, respectively[3].

As an example, the emergence of the Zika virus in 2015 is cited, which inspired a movement in several countries, as well as in Brazil, for the development of an effective vaccine. The Zika virus is transmitted mainly by infected Aedes aegypti mosquitoes, which can cause serious problems in children and adults[4]. Despite outbreaks of virus infection peaking in 2016 and decreasing substantially throughout 2017 and 2018 in the American region, a vaccine is still urgently needed to limit the emergence of another epidemic[4, 5]. In response to this challenge, researchers and pharmaceutical companies globally have implemented clinical trials to assess the efficacy and safety of Zika virus vaccine candidates[4,5]. In Brazil, a research center in Belo Horizonte, Minas Gerais, was the field of the "Phase 2/2B multicenter randomized study to evaluate the safety, immunogenicity and efficacy of a Deoxyribonucleic acid (DNA) vaccine against Zika virus in healthy adults and adolescents". The respective clinical trial was developed by the National Institute of Allergy and Infectious Diseases (NIAID) - and the Vaccine Research Center (VRC) -, by a consortium of researchers from George University Washington (Washington, USA), in partnership with the René Rachou Research Center, Oswaldo Cruz Foundation (Fiocruz).

In order to carry out the study involving human beings, an essential ethical requirement was informed consent, usually formalized through the Informed Consent Form (ICF). The signature of the term records the voluntary and autonomous consent of the participant, in order to guarantee respect for human dignity based on the information about the research previously elucidated[6]. However, consent should not be seen simply as a document for the legal and figurative fulfillment of the participant's agreement to be part of a clinical trial, but must authentically express the autonomy of the decision to participate[7,8].

The quality of the informed consent process in vaccine clinical research can be determined by the participants' degree of understanding[9]. Adequate understanding requires the participant's ability to understand the action and nature of the study, the basic elements of a research protocol, among which are the possible risks and benefits, in addition to predicting its future consequences[10].

There are indications of gaps in terms of participants' understanding of information from clinical vaccine research[11-15], attested both in developed and developing countries[16]. Violations in the informed consent process are frequently described in clinical trials carried out in developing countries. Low levels of formal education, lack of familiarity with research and limited access to health services in these countries have been associated with inadequate informed consent[8, 12, 19, 20].

The understanding of the informed consent is closely linked to the subject's attitude to participate or not in clinical research[17]. In this process of understanding, voluntarism is also discussed, recognized as the possibility of a person to make free choices, without constraint or coercion. Volunteering is a fundamental requirement for consent to be considered valid[15].

Aware of this problem, the researchers involved in the clinical research of the vaccine against the Zika virus recognized the importance of analyzing the factors associated with the understanding of the information in the consent document by the participants in the Brazilian context, as a way of expanding academic and scientific mobilization on this theme in exponential growth in society[1,9].

In this scenario, this study aims to assess the understanding of the information in the Informed Consent Form by the participants of a clinical trial of a vaccine against Zika virus in the Brazilian context.

METHOD

This is an observational cross-sectional study carried out in a research center located in the city of Belo Horizonte, Minas Gerais, Brazil. This study was developed along with a clinical investigation of a vaccine against the Zika virus. The sample of this study consisted of participants in the clinical vaccine investigation, which was the established inclusion criterion. As the participants' experience in signing the informed consent form of the

vaccine clinical trial is essential, this study used the criterion of intentional sampling. Thus, in order for the data to be representative, all 101 vaccine research participants were sought, a target successfully achieved. It is noteworthy that, inevitably, the inclusion criteria of the clinical investigation ended up being juxtaposed to the inclusion criteria of this research, such as age between 18 and 35 years old.

Potential participants were approached immediately after signing the vaccine clinical trial informed consent. At that moment, they received explanations about the purpose of the study, were able to clarify doubts, and the information about the voluntary participation was also reinforced. After reading the ICF, in case of agreement, they registered their participation by signing the term.

Data were collected through the application of a structured questionnaire, composed of two sections, described below: (1) Characterization of the participants - a) in terms of sociodemographic variables: gender, age, education, occupation, previous participation in other researches and access to television and internet; - b) regarding attitude and willingness: it consists of 10 items that assess the attitudes of the participants and the willingness of their decision to participate in the clinical vaccine research, with the answers given in three categories ("no", "yes", "do not know"); (2) Understanding of research information - consisted of 36 items that addressed objectives, benefits, study procedures, risks/ adverse effects and participants' rights, in addition to information about Zika, with responses given in three categories ("no", "yes", "do not know"). Participants who marked the option "do not know" were considered to have answered the question incorrectly in order to be able to compare knowledge about the item with not knowing (indicated by the option "do not know" or error in the question). Response options were presented on a five-point Likert scale and responses were grouped so as not to differentiate "strongly agree" from "agree" and "strongly disagree" from "disagree". Participants who marked the option "I neither agree nor disagree" were considered to have answered the question incorrectly.

It is noteworthy that the researcher approached the target group personally and data collection was carried out in a private place, ensuring privacy and preserving the identity of the participants. Data were collected from May to July 2018. The interviews lasted, on mean, 20 minutes.

The questionnaires were checked, being typed by two people independently, in order to guarantee the reliability of the data collection. To avoid biases in the categorization process of open responses, this step was also developed independently by two professionals. Results were compared, discussed and categorized by consensus.

For data analysis and interpretation, an Information Comprehension Index (IC) was created, defined as the percentage of correct answers in 36 closed questions about the information presented in the ICF, ranging from 0% to 100%. The creation of the CI aimed to express the participant's global understanding of the information contained in the ICF. The participants' level of understanding was categorized as follows: low (<25% of correct answers), moderate-low (≥25% and <50% of correct answers), moderate-superior (≥50% and <75% of correct answers) and high (≥75% accuracy). A percentage of correct answers equal to or greater than 75% was considered satisfactory/adequate, demonstrating a satisfactory understanding of the information for an autonomous decision by the participant[7].

Categorical variables were presented as absolute and relative frequencies and numerical variables as mean ± standard deviation and median (1st quartile – 3rd quartile). To assess normality, numerical variables were submitted to the Shapiro-Wilk normality test and inspection of the histogram. To compare the Comprehension Index between binary variables, the Mann-Whitney test was used. Among variables with three or more levels, the Kruskal-Wallis test was adopted. The correlation between age and the Comprehension Index was evaluated using Spearman's Correlation Coefficient. The analyzes were performed using the R software version 4.0.3, adopting a statistical significance level of 5% ($p \leq 0.05$).

The study followed the steps recommended by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guide[18]. All norms and guidelines for conducting research involving humans were followed. This research was submitted to and approved by the Research Ethics Committee of the Federal University of Minas Gerais, in accordance with opinion substantiated No. 66360017.0.1001.0068.

RESULTS

Most participants were female (57.4%), with incomplete or ongoing higher education (52.5%). The mean age of the participants was 25.9 years old (SD: ±4.3). 16.8% were married and 47.5% reported working. All reported having access to

the internet, more than half (58.4%) reported having the habit of watching television and approximately a quarter (24.8%) had already volunteered in other clinical trials before (Table 1). Table 2 presents the results related to the willingness and attitude of the subjects to participate in the clinical research of a vaccine against the Zika virus.

Table 3 shows the percentage of correct answers for questions about clinical research on a vaccine against the Zika virus and knowledge about the disease, objectives, benefits and study procedures, risks/adverse effects, and participants' rights. Table 4 presents the Information Comprehension Index, which consists of the percentage of correct answers of the participants of the clinical research of vaccine against the Zika virus in the questions related to the information presented in the ICF. It is observed that the participants had mean 66.9 ± 9.6 of correct answers and only 23 (22.8%) had a "satisfactory/adequate" level of understanding of the information (≥ 75.0%). Comparing the Comprehension Index across sociodemographic variables, the index was statistically significant among married participants who had volunteered in previous surveys. Although they did not reach statistical significance, male participants with postgraduate studies and who work outside the home also tended to obtain higher means of understanding. There was no significant correlation between age and the Comprehension Index (ρ=0.100; p=0.320). The detailed results can be seen in Table 5.

DISCUSSION

The results of this study showed that most participants in the clinical research of a vaccine against Zika virus signed the informed consent form without sufficient knowledge of the research information. This conclusion is supported by the fact that less than a quarter of the participants obtained a "satisfactory/adequate" level of global understanding of the information available in the informed consent, that is, a percentage of correct answers [≥ 75%]. Based on the literature, the authors of this study emphasize that the adequate understanding of the information by the participants of clinical research is crucial, in order to provide a voluntary and autonomous decision-making[7, 16].

Table 1 – Distribution by categories of sociodemographic variables in absolute and relative frequencies. Belo Horizonte, MG, Brazil, 2018

Variables	Statistics n (%)
Gender	
Female	58 (57.4)
Male	43 (42.6)
Education	
High school	8 (7.9)
Incomplete/in progress Higher Education	53 (52.5)
Complete Higher Education	30 (29.7)
Postgraduate course in progress	10 (9.9)
Age	25.9 ± 4.3*
Marital status – married	17 (16.8)
Working	48 (47.5)
Watch TV	59 (58.4)
Internet use	101 (100.0)
Internet – Days/week	6.9 ± 0.5*
Participated in another research	25 (24.8)

Source: Prepared by the authors, 2021.
***Mean** ± standard deviation

Table 2 – Distribution of responses to questions that assessed willingness and attitude to participate in clinical research on a vaccine against the Zika virus. Belo Horizonte, MG, Brazil, 2018

Question	Yes n (%)	No n (%)	Do not know n (%)
Volunteering			
Did you feel pressured to participate in the research?	0 (0.0)	101 (100.0)	0 (0.0)
Did you decide on your own to participate in the investigation?	99 (98.0)	2 (2.0)	0 (0.0)
Can anyone decide for you in relation to participating in the investigation?	0 (0.0)	100 (99.0)	1 (1.0)
If you leave the survey, will you lose any benefits?	21 (20.8)	75 (74.3)	5 (5.0)
Do you have any problems if you decide to quit the survey?	1 (1.0)	100 (99.0)	0 (0.0)
Did you feel anxious about the decision to participate?	13 (12.9)	88 (87.1)	0 (0.0)
Did you regret your decision?	1 (1.0)	99 (98.0)	1 (1.0)
Attitude			
Were you afraid to participate in the research?	10 (9.9)	91 (90.1)	0 (0.0)
Can participating in this study help improve your health?	57 (56.4)	35 (34.7)	9 (8.9)
Are all researchers also doctors?	19 (18.8)	60 (59.4)	22 (21.8)
Can participating in the survey help others in the future?	101 (100.0)	0 (0.0)	0 (0.0)
Do you feel special about being a research volunteer?	65 (64.4)	35 (34.7)	1 (1.0)
Do you trust the researchers?	100 (99.0)	0 (0.0)	1 (1.0)

Source: Prepared by the authors, 2021.

A similar phenomenon was observed in studies from other countries[12,13]. A study carried out in India[19], which aimed to assess the quality of informed consent among participants in cancer clinical trials, showed that the mean of correct responses was 60.46%. This result is similar to that found in a systematic review, which identified that the proportion of participants in clinical trials who understood different components of informed consent ranged from 52.1% to 75.8%[10]. These findings indicate that, despite advances in the area, the problem of misunderstanding remains constant in different scenarios[4,14].

On the other hand, most investigations on the subject carried out in Brazil have indicated a lower percentage of correct answers than that found in this study. A possible explanation for this is that this study included people who had, for the most part, a higher education level. Similarly, there was an mean of correct answers very close to that found in this research in another vaccine clinical trial[7], carried out in Brazil, whose sample consisted mainly of people with higher education. The level of education of the participants has been pointed out as one of the main individual sociodemographic characteristics that can influence understanding[6].

It is interesting to think that, despite all the information suggested by national and international norms and guidelines having been included in the vaccine clinical research consent document of this research, many participants had limited understanding of crucial elements present in the informed consent, such as potential risks/effects adverse effects and benefits. It is noteworthy that the term informed that there would be no therapeutic benefit for the participant and that there were health risks, still unknown by the researchers, including the participant's life and

Table 3 – Percentage of correct answers on questions about the information on the clinical research of a vaccine against Zika virus available in the Informed Consent Form. Belo Horizonte, MG, Brazil, 2018

Questions	Right answers n (%)
1. Can you be infected with Zika and not know it? (Y)	43 (42.6)
2. Is Zika transmitted by infected mosquitoes? (Y)	98 (99.0)
3. Is it unlikely that a person who has already been infected with the virus will be infected again? (Y)	31 (30.7)
4. Can Zika be transmitted through unprotected sex? (Y)	42 (41.6)
5. Is there a chance of catching the Zika virus in the region where you live? (Y)	78 (77.2)
6. Does every person with Zika need to go to the hospital for treatment? (N)	30 (29.7)
7. Can a person rarely die from the disease? (Y)	82 (81.2)
8. Can Zika cause complications, such as muscle weakness (Guilain Barré syndrome)? (Y)	92 (91.1)
9. Is there a cure for Zika infection? (N)	55 (54.5)
10. Is the purpose of the research to cure people infected with Zika? (N)	98 (97.0)
11. Is the purpose of the research to test a vaccine to prevent Zika? (Y)	99 (98.0)
12. Is the safety and efficacy of the vaccine being evaluated in this study? (Y)	98 (97.0)
13. The purpose of the Zika research is to improve participants' health (SD/D)	87 (86.1)
14. Will you only receive one dose of the vaccine? (N)	97 (97.0)
15. During product (vaccine) administration visits, will everyone receive the same vaccine? (N)	92 (91.1)
16. Can you get sick from Zika when you get the vaccine? (N)	70 (69.3)
17. The vaccine you will receive will be according to your health status (SD/D)	72 (71.3)
18. The research participant will be able to know which vaccine he is receiving during the clinical trial (SD/D)	95 (94.1)
19. When receiving the vaccine, do you become immune to Zika? (N)	64 (64.0)
20. Are there any risks in participating in the investigation? (Y)	66 (65.3)
21. Can you experience adverse effects from receiving the vaccine? (Y)	90 (89.1)
22. The researcher would not include a participant in the research if there was any risk (SD/D)	6 (5.9)
23. Are researchers aware of all vaccine side effects? (N)	58 (57.4)
24. The researcher may decrease the chance that the research participant will experience side effects (SD/D)	68 (67.3)
25. The researcher may tell you that participation in this research may have less risk than it actually does (SA/A)	7 (6.9)
26. Is there any chance that your health condition will get worse when participating in the Zika research (SA/A)	34 (33.7)
27. Are there any benefits to participating in the investigation? (N)	10 (9.9)
28. The main reason people were invited to participate in the Zika research is so they can benefit from special treatment (SD/D)	88 (87.1)
29. Participating in clinical research can improve your quality of life (SD/D)	30 (29.7)
30. Participating in Zika research can bring you subjective benefits (SD/D)	21 (20.8)
31. Participating in the Zika survey can improve your day-to-day activities (SD/D)	60 (59.4)
32. Researcher may increase the chance that you will benefit from participating in Zika research (SD/D)	86 (85.1)
33. The researcher may say that participation in research offers more benefits than it actually could (SD/D)	87 (86.1)
34. Can you tell the researcher if you get sick? (Y)	101 (100.0)
35. Can you leave from the survey at any time? (Y)	96 (95.0)
36. The participant's well-being is an important aspect to be considered during the research (SA/A)	100 (99.0)

Source: Prepared by the authors, 2021.
Note: Correct answers: (Y) – Yes, (N) – No, (SD/D) – Strongly disagree or disagree, (SA/A) – Strongly agree or agree; domains related to clinical vaccine research assessed: knowledge about Zika – items 1 to 9; objectives – items 10 to 13; study procedures – items 14 to 19; risks/adverse effects – items 20 to 26; benefits – items 27 to 33; participant rights - items 34 to 36.

Table 4 – Analysis of the Comprehensiveness Index of Information from the Informed Consent Form by the participants of the clinical research of vaccine against the Zika virus. Belo Horizonte, MG, Brazil, 2018

Statistic	Comprehension Index
Mean ± standard deviation	66.9 ± 9.6
Median (1st quartile – 3rd quartile)	66.7 (61.1 – 72.2)
Minimum – maximum	41.7 – 88.9
Classification	
Low	0 (0.0%)
Moderate-low	4 (4.0%)
moderate-higher	74 (73.3%)
High	23 (22.8%)

Source: Prepared by the authors, 2021.
Note: the participants' level of understanding was categorized into "Low", "Moderate-Lower", "Moderate-Higher" and "High", according to the percentage of correct answers in the questions. The intervals were defined as [<25%], [≥ 25% and <50%], [≥ 50% and <75%] and [≥ 75%] correct, respectively.

Table 5 – Comparison of sociodemographic variables with the Information Comprehension Index of the Informed Consent Form. Belo Horizonte, MG, Brazil, 2018

Variables	Comprehension Index		p-value
	Mean ± standard deviation	Median (1º Q – 3º Q)*	
Gender			0.469 †
Female	66.4 ± 10.2	66.7 (58.3 – 72.2)	
Male	67.6 ± 8.9	69.4 (61.1 – 72.2)	
Education			0.355 ‡
High School	66.2 ± 13.0	66.2 (58.3 – 73.6)	
Incomplete Higher Education	66.3 ± 7.8	66.7 (61.1 – 72.2)	
Complete Higher Education	66.4 ± 10.3	66.7 (59.0 – 72.2)	
Postgraduate course in progress	72.2 ± 13.2	72.2 (67.4 – 80.6)	
Marital Status			0.028 †
Single	65.9 ± 9.5	66.7 (58.3 – 72.2)	
Married	72.0 ± 9.0	72.2 (63.9 – 75.0)	
Working			0.740 †
Yes	67.4 ± 10.7	69.0 (58.3 – 72.9)	
No	66.5 ± 8.6	66.7 (61.1 – 72.2)	
Watches TV			0.753 †
Yes	67.0 ± 8.7	63.9 (61.1 – 72.2)	
No	66.9 ± 11.0	69.4 (58.3 – 74.3)	
Participated in another research			0.039 †
Yes	69.9 ± 9.5	72.2 (63.9 – 77.8)	
No	66.0 ± 9.5	66.7 (58.3 – 72.2)	

Source: Prepared by the authors, 2021.
Note: *Median (1st quartile – 3rd quartile); †Mann-Whitney Test; ‡ Kruskal-Wallis test.

physical integrity[17,20].

In addition, in this study, the contradictions incurred by the participants when challenged to express essential research concepts such as risks, adverse effects and benefits in different contexts, point to a possible reproduction and memorization of information instead of its real understanding.

Although most researchers believe it is important to test study participants' understanding of informed consent[9], there are questions about how difficult it can be to distinguish between understanding and recall (memory) of trial information. Furthermore, as in previous studies, the signing of the consent document also did not guarantee the expression of autonomous decision-making by the participants[7,17,20].

Thus, these findings, as in other investigations[13,14,17], are worrying, since the lack of understanding undermines one of the ethical pillars of the contemporary practice of clinical research involving human beings. In addition, it opens space for questioning, such as the question of whether there really is a genuinely voluntary involvement of participants in decision-making in a consent process.

This study reveals that the level of understanding was significantly associated with the following factors: being married and having previous experience in another research. It reflects on the fact that participation in previous research can promote contact with specific concepts of this field of knowledge and make the understanding of the information easier. No previous evidence was found that there would be differences between marital status. However, when analyzing the profile of the participants, marital status was probably significant due to the fact that the married participants were older and had a higher level of education. Based on the data, although age and education were not significant in isolation, together they may indicate a different profile of participants with a higher level of understanding. Therefore, it is possible that the result presented here is reflecting the high level of education of a small group, and not a difference due to marital status. The results of this study demonstrate that there was no correlation between understanding and age, as well as no significant differences were found when the groups were separated by gender, findings consistent with the literature[11].

Regarding attitude and willingness, it was observed that most of them chose to participate in the study to benefit people and science. This pattern may be associated with the fact that a large portion of the participants had volunteered in previous research, which expresses prestige in relation to the bonds of solidarity due to their high level of education, factors that may have contributed to the understanding of the meaning of progress and science experimentation and the choice to participate.

On the other hand, these results differ from national and international studies. A Brazilian study, for example, indicated the search for medical treatment as the main factor that influenced participation[8]. In the United States, high percentages mentioned the possibility of helping others and receiving monetary compensation[16]. Commonly, participants in socioeconomic disadvantage confuse the scientific objective of the research with the provision of health care services[8,14,16].

Although practically all the participants responded positively to the question of being satisfied with the information provided in the ICF, some claimed to have signed the document having doubts, a factor consistent with other studies[12]. However, the expression of doubt is an important aspect related to the participants' attitudes, which can influence the quality of informed consent[16]. The literature has suggested that the participants' implicit feeling of trust in relation to the researchers and institutions responsible for the research may be a factor that explains this finding[16,20]. Furthermore, in this study, the high level of education of the participants may be associated with their hesitancy in asking questions or with a tendency to overestimate their own level of understanding.

The mistaken thought that participation in a clinical trial can contribute to improving health status is an aspect that can influence voluntarism. These findings are consistent with previous results[7,11,16] on the quality of the informed consent process in clinical trials. This belief can make participants less critical of aspects of the research. Thus, informed consent should also be seen as an educational process and not only as a normative and legal process[11].

Limitations of the study are the cross-sectional design, which makes it impossible to identify causal relationships between the variables analyzed, the small sample size and the fact that data collection was carried out only in one research center, since the clinical trial was multicenter, with participants from two Brazilian states (Minas Gerais and Sao Paulo) and from eight other countries, which limits the external validity of

the results. These factors made it impossible to generalize the data obtained.

On the other hand, the results of this research have the potential to contribute to the area of research ethics and provide an expanded view of the main gaps in understanding the information available in the consent document in vaccine clinical research in the Brazilian context.

In terms of research, it is suggested that further research in the context of vaccine clinical trials be carried out, especially with participants with a lower level of education, since the limitation of their understanding can be exponentially higher. In addition, according to what has been observed[7,11-17], better ways to communicate the information in the consent document or additional measures to promote understanding need to be found to protect the rights of clinical research participants, especially in vulnerable populations.

CONCLUSION

The study revealed important limitations in the understanding of the participants of the clinical research of vaccine against the Zika virus about essential elements presented in the Informed Consent Form, which did not guarantee the expression of the autonomy of all the participants. Thus, adaptations and improvements in the processes of informed consent are necessary for its validity.

*Paper extracted from the doctoral dissertation "Understanding of informed consent in clinical research: a concept proposition", presented to the Federal University of Minas Gerais, Belo Horizonte, MG, Brazil.

CONFLICT OF INTEREST

The authors have declared that there is no conflict of interest.

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