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Research article

Effectiveness of an educational module in improving knowledge, awareness and perception among pregnant women regarding the safe use of prenatal ultrasound

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ABSTRACT

Background: Lack of public understanding, perception and awareness of the biological effects of prenatal ultrasound has led to the non-medical use of ultrasound. An educational programme is required to enlighten pregnant women and the public regarding prenatal ultrasound safety.

Objective: To evaluate the effectiveness of educational modules (video and brochure) in improving knowledge, awareness and perception (KAP) among pregnant women regarding prenatal ultrasound safety.

Methods: This is a quasi-experimental study with a pre-and post-test design. This study recruited 51 pregnant women as respondents from the Obstetrics and Gynaecology clinic (O&G) of Hospital Canselor Tuanku Muhriz (HCTM). The first phase of the study was conducted by distributing a set of closed-ended questionnaires with multiple choice and Likert scale answers to assess the KAP of pregnant women regarding the safe use of prenatal ultrasound, followed by educational modules where the respondents were allocated into three groups (17 watched a video, 17 received brochure and 17 received combined media). After the intervention, the respondents' KAP were assessed using the same questionnaire.

Results: The Wilcoxon signed rank test showed that educational modules like video, brochure and combined media had a statistically significant increase in post-test scores over the pre-test scores (video: mean rank = 9.00, $p < 0.05$) (brochure: mean rank = 9.79,$p < 0.05$) and (combined media: mean rank = 10.17, $p > 0.05$). The Kruskal Wallis test indicated that educational video was more effective in improving the KAP of pregnant women than the brochure and combined media (mean rank = 34.62, $p < 0.05$). Among the parameters, the occupation has the strongest positive correlation with the post-test knowledge score in improving the KAP of pregnant women regarding the safe use of prenatal ultrasound.

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Conclusion: The educational video is the most effective approach for enhancing pregnant women's KAP. The educational module on the safety of prenatal ultrasound is thought to dispel myths by providing accurate information to audiences from various backgrounds.

1. Introduction

Prenatal ultrasound has become a standard modality for evaluating the health of pregnant women and foetuses over the last several decades. Ultrasound is considered a safe procedure by the World Health Organization (WHO), with few known side effects. However, ultrasound is energy that induces biological effects (thermal and mechanical indexes) on foetus development. Even though there is no reported clinical evidence regarding the adverse effects of prenatal ultrasound on the developing foetus, regulatory bodies have advised precautionary measures in routine ultrasonography after reports of scientifically proven biological side effects from animal and laboratory studies. For instance, several studies have found that excessive neuron production during the first year of life in autism spectrum disorder (ASD) patients is perhaps due to abnormal prenatal scanning during pregnancy [1]. The exposure has increased the temperature in the tissue, affecting the foetus's brain development. Another study of the thermal effect of prenatal ultrasound on white rabbits found significant haematological variation during the early postnatal stages. Still, it was reversible as the sample grew older [2]. Breaching safety thresholds can result in harmful bio-effects, directly or indirectly.

Further, the rapid advancement of prenatal ultrasound has resulted in developing new methods such as 3-dimensional (3D), 4D, 5D, and 6D, despite 2D being sufficient to detect any pregnancy issues. 4D imaging, for example, enables the operator to capture 3D images in real time, allowing parents to take photos or Digital Video discs (DVDs) of the foetus and share their joy with family members who are not present during the medical examination [3]. The rapid advancement of prenatal ultrasound has increased patients' demand for keepsake prenatal images and videos. Pregnant mothers' enthusiasm for Prenatal Ultrasound Screening (PUS) has grown due to technological advancements. As ultrasound technology improves constantly, many centres, including some private businesses, are promoting using foetal ultrasound machines to create photos or videos of babies in the womb as keepsakes for parents. This phenomenon has caused the majority of pregnant women to undergo scanning to obtain more detailed information about their foetuses. However, a lack of knowledge and poor understanding regarding the fundamentals of diagnostic ultrasound makes pregnant women perceive it to be entirely safe for their foetuses. Pregnant women's perceptions of prenatal ultrasound appear to be misleading due to the high demand for keepsake images, most probably due to a lack of understanding and awareness in this regard [4].

Further, several private companies have exploited the situation and turned prenatal ultrasound into a tool for creating prenatal portraits [5]. Consequently, current trends in ultrasound examinations during pregnancy have resulted in cases of concern. All these demonstrate a need for more public understanding, perception, and awareness of the biological effects of prenatal ultrasound to promote its non-medical use.

Despite efforts by healthcare professionals to increase pregnant women's knowledge, awareness, and perceptions of prenatal ultrasound safety, reported data on this topic appear to be limited in Malaysia. Consequently, the correct concept of prenatal ultrasound safety has yet to be delivered. Therefore, widespread media coverage should raise awareness of prenatal ultrasound safety for pregnant women. Community-based research is critical for disseminating accurate information and raising awareness among pregnant women about the safety of prenatal ultrasound. Any improper use of ultrasound can be reduced if the correct information is provided. Physical effects such as mechanical vibrations and tissue heating can thus be reduced, lowering complications [6].

An educational intervention has been developed to educate pregnant women about prenatal ultrasound safety. Further, knowledge or awareness of prenatal ultrasound safety can be raised through a video or brochure, giving them a better understanding of how to use it safely. Hence, increased awareness and knowledge will reduce various illnesses, including foetal mortality. Consequently, maternal knowledge and awareness of prenatal care are critical to the foetus's development.

As technology advances, video is increasingly recognised as a flexible learning method for educational purposes. Numerous studies have shown that video can improve learning ability and spread power in delivering knowledge or concepts [7]. Respondents can indirectly capture all the information presented in a video through sound and image movement when watching and listening to it. Further, educational videos are often more accessible in terms of language and communication and more cost-effective. According to researchers, educational video is one of the essential technologies for raising public awareness. A brochure, a picture-filled booklet containing educational information for the general public, is also considered an effective educational intervention for highlighting knowledge, with various benefits [8]. A brochure, for example, uses simple words and colourful images to improve learning and raise awareness. Further, it is cost-effective, affordable, and a reliable future reference for respondents [9].

Information can be conveyed clearly and practically through both educational modules (video and brochure), which can be viewed or read anywhere at any time. These two media cover the introduction to prenatal ultrasound, the general procedure, and the prenatal ultrasound guidelines, which include the timing and use of proper indication scanning and the benefit and risk of prenatal ultrasound. Hence, the distribution of videos and brochures is expected to provide optimal prenatal ultrasound safety education to pregnant women. Consequently, the risk of complications from prenatal ultrasound, which can endanger the mother and foetus and even result in death, can be reduced or eliminated.

In our study, we evaluated the effectiveness of educational modules in the form of videos and brochures in improving KAP among pregnant women regarding the safe use of prenatal ultrasound. Valid and reliable educational interventions will provide a basic explanation and are intended to implement the practices of using video or brochures as an educational tool for pregnant women in improving knowledge about prenatal ultrasound safety.

2. Methods

This study was a quasi-experimental study with a three-group pre–test–post–test design to evaluate the effectiveness of developed and validated educational modules. The recruitment of pregnant women and data collection were done physically at the Obstetrics and Gynaecology (O&G) Clinic of Hospital Canselor Tuanku Muhriz (HCTM) from October 2021 to February 2022. An ethics approval (JEP-2019-175) has been obtained from The National University of Malaysia's research ethics committee (UKM) from March 26, 2019 to March 27, 2022. The study sample was selected by using a quota sampling method. Based on G-power for calculating the sample size (F test) and using a power level of 0.80 (alpha = 0.05, 1-beta = 0.80) with a medium effect size, the minimum required sample size was 51 respondents. The respondents were divided into three groups equally: video (V), brochure (B) and combined media (V + B), each with 17 respondents. Pregnant women who could understand Bahasa Malaysia and English were included in the study, and high-risk pregnant women who refused to sign the informed consent were excluded.

2.1. First phase: pre-test of the study

The purpose of the study was explained, and the respondents were assured of voluntary participation, the confidentiality of data, and the ability to withdraw at any time. Informed consent was obtained from the respondents before data collection. A validated closed-ended questionnaire with multiple choice and Likert-scale answers was given to respondents to assess their knowledge, awareness, and perception regarding the safe use of prenatal ultrasound before receiving the educational intervention. The questionnaire consisted of four sections; (i) demographic data of the respondents, (ii) knowledge and perception of pregnant women concerning the prenatal ultrasound scan, (iii) the expectation of pregnant women regarding the prenatal ultrasound scan, and (iv) awareness of pregnant women relating to the prenatal ultrasound examination. The questionnaire was presented in English.

2.2. Second phase: post-test of the study

After completing the pre-test, the respondents were exposed to an educational video or educational brochure or both according to the group to which they were assigned. The post-test evaluation was done after a 10-min gap. The respondents were required to answer the same questionnaire. Strict instruction was given to the respondents to avoid looking up any references on the internet or in books or asking anyone for additional information.

2.3. Data analysis

Data analysis was performed using SPSS version 25.0 statistical software. The study was conducted using univariate descriptive analysis presented in frequency distribution and percentage to describe the respondents' socio-demographic data and knowledge. For the normality test, our data were not normally distributed. Therefore, all the analysis methods will use the non-parametric approach. A paired Wilcoxon signed-rank test was applied to identify the significant differences between the pre-and post-test scores in each group. A Kruskal-Wallis test was used to compare three or more independent samples of ordinal data and determine the significant differences between the means ranks in the three groups. Statistical tests were used to determine the association between the post-test knowledge regarding the safe use of prenatal care among pregnant women and socio-demographic variables—Spearman's Rho. P-values of <0.05 will be considered statistically significant.

3. Results

3.1. Participants' demographic characteristics

Based on the demographic characteristics of the respondents (Part A), almost all the respondents (98%) were between 22 and 39. Malays represented the majority (80.39%), followed by Indians (11.76%), Chinese (5.88%) and others (1.97%). Most respondents were Muslims, while 11.76%, 5.88% and 1.97% were Hindus, Buddhists and Christians, respectively. Most of the respondents had an excellent educational background, ranging from the highest bachelor's degree with 21 respondents (41.18%)), to STPM/STAM/Diploma with 20 respondents (39.22%), SPM/SPMV with 8 respondents (15.69%) and Master and PMR with 1 respondent (1.96%). Of the 51 respondents, 19 were government employees, while 11, 20 and 1 respondents were housewives, private employees, and self-employed, respectively. Then, for household income, two categories of RM 2000 or less and RM 10000 and above were noted with a minimum number of respondents. In this study, there were 28 multigravida respondents and 23 primigravida women. As such, the ratio of multigravida to primigravida respondents was approximately 6:5. The respondents comprised nulliparous, primiparous and multiparous pregnant women. 22 respondents (43.14%) were multiparous, 19 (37.25%) primiparous, and ten (19.61%) nulliparous.

3.2. Knowledge of pregnant women regarding prenatal ultrasound scan

Part B consists of 6 items regarding the knowledge of pregnant women concerning prenatal ultrasound scans, including routine and additional scans, as portrayed in Table 1. Based on Table 1, 98% of the respondents know what prenatal ultrasound means, and 84.31% (n = 43) know the differences between routine and additional prenatal scans, even before the intervention. Out of 51 respondents, 94.12% (n = 43) underwent a routine prenatal scan, and 70.59% (n = 36) underwent an additional prenatal ultrasound. The most

preferred modes of the scan by pregnant women were 2D with 50% (n = 18), followed by 3D with 19.44% (n = 7) and 5D scan with 16.67% (n = 6). 52.78% (n = 19) of the respondents had four to ten scans over their pregnancy, and others had one to three scans. The majority of the respondents- 52.78% (n = 19) underwent additional scans at the government hospital and 47.22% (n = 17) at private hospitals. 94.44% (n = 34) of the respondents underwent additional ultrasound to know the development of the foetus, followed by 77.78% (n = 28) to identify the baby's gender and 61.11% (n = 22) to understand the expected date of delivery (EDD). However, their level of awareness (Part C) seemed poor, as 52.78% (n = 19) of the respondents proceeded with the scan for the imprudent purpose of having keepsake images and videos. While 22.22% (n = 8) of the respondents responded that they were not satisfied with routine ultrasound, another 11.11% (n = 4) underwent the scan because of the trend.

3.3. Pre-test and post-test knowledge scores regarding the safe use of prenatal ultrasound

Table 2 shows the Wilcoxon signed rank test result, used to determine the difference in the pre-test and post-test knowledge scores regarding the safe use of prenatal ultrasound. Relative to the video ranking, all respondents (n = 17) scored higher results after the video intervention (mean rank = 9.00). The majority of the respondents (n = 14) scored higher marks after brochure intervention (mean rank = 9.79), while only three scored higher in the pre-test (mean rank = 5.33). 12 respondents from the combined media group scored higher following the intervention (mean rank = 10.17), whilst only five respondents scored higher in the pre-test (mean rank = 6.20). This analysis showed that educational modules like video, brochures and combined media significantly increased the level of knowledge among the respondents ($p < 0.05$) (Table 3).

3.4. Effectiveness of the module in improving knowledge and creating awareness among pregnant women regarding the safe use of prenatal ultrasound

There was no significant difference in the mean knowledge score among the three groups before the intervention ($p > 0.05$). However, after the intervention, there were statistically significant differences between the three groups ($p < 0.05$). The mean score for the video group was 24.53 during the pre-test and increased to 34.62 in the post-test. The mean score for the brochure group was 22.88 during the pre-test and decreased to 17.65 in the post-test, while the mean score in the combined media group was 30.59 in the pre-test and 25.74 in the post-test. These mean scores indicated that video is the most effective educational module, compared to brochures and combined media, in increasing knowledge, perception, expectation and awareness of pregnant women regarding the safe use of

Table 1
Knowledge of respondents regarding prenatal ultrasound sca.

Items	Pre-test (%)		Post-test (%)	
	Frequency(N)	Percentage (%)	Frequency(N)	Percentage (%)
I know what prenatal ultrasound scan is				
Yes	50	98	51	100
No	1	2	0	0
I know what is meant by routine and additional prenatal scan				
Yes	43	84.31	50	98
No	8	15.69	1	2
I have undergone a routine prenatal scan				
Yes	43	94.12	49	96.1
No	8	5.88	2	3.90
I have undergone an additional prenatal scan				
Yes	36	70.59	36	70.59
No	15	29.41	15	29.41
i) If yes, mode of scan done				
2D	18	50	18	50
3D	7	19.44	4	11.11
4D	5	13.89	7	19.44
5D	6	16.67	7	19.44
6D	0	0	0	0
ii) Frequency of scan throughout pregnancy				
1–3	17	47.22	14	38.89
4–10	19	52.78	21	58.33
More than 10	0	0	1	2.78
I have undergone additional ultrasound at				
Government Hospital/clinic	19	52.78	16	44.44
Private Hospital/Clinic	17	47.22	20	55.56
I have undergone additional ultrasound because				
I want to know the gender of the foetus.	28	77.78	28	77.78
I seek additional ultrasound scan because	34	94.44	34	94.44
I want to know the expected date of delivery (EDD).	22	61.11	21	58.33
I want to keep images videos of the foetus as mementos.	19	52.78	20	55.56
I was not satisfied with the routine prenatal ultrasound scans.	8	22.22	7	19.44
All my friends undergo the additional prenatal ultrasound scans.	4	11.11	4	11.11

Table 2
Result of Wilcoxon signed rank test.

		N	Mean Rank	Sum of Ranks
Video	Negative Ranks	0[a]	.00	.00
	Positive Ranks	17[b]	9.00	153.00
	Ties	0[c]		
	Total	17		
Brochure	Negative Ranks	3[d]	5.33	16.00
	Positive Ranks	14[e]	9.79	137.00
	Ties	0[f]		
	Total	17		
Combined media	Negative Ranks	5[g]	6.20	31.00
	Positive Ranks	12[h]	10.17	122.00
	Ties	0[i]		
	Total	17		

[a] Video_Posttest < Video_Pretest.
[b] Video_Posttest > Video_Pretest.
[c] Video_Posttest = Video_Pretest.
[d] Brochure _Posttest < Brochure _Pretest.
[e] Brochure _Posttest > Brochure _Pretest.
[f] Brochure_Posttest = Brochure_Pretest
[g] Combined media _Posttest < Combined media.
[h] Combined media _Posttest > Combined media _Pretest.
[i] Combined media _Posttest = Combined media_Pretest

Table 3
Test of statistics.

	Video	Brochure	Combined media
Z	−3.622	−2.865	−2.155
Asymp. Sig. (2-tailed)	.000*	.004*	.031*

Note: *represents P-value is significant ($p < 0.05$).

prenatal ultrasound.

3.5. Association of socio-demographic characteristics with post-test knowledge score of participants on the safe use of prenatal ultrasound among pregnant women

Table 4 describes the association of socio-demographic characteristics and post-test knowledge scores regarding the safe use of prenatal ultrasound of the 51 pregnant women who participated in the study, using different statistical analyses. Occupation is the only socio-demographic factor that shows a significant association was the post-test score at $p = 0.022$. The median post-test knowledge

Table 4
Spearman's rho correlation to the post-test knowledge score of participants on the safe use of prenatal ultrasound among pregnant women.

		Post-test knowledge
Level of education	Correlation Coefficient	.019
	P-value	>0.05
Household income	Correlation Coefficient	.197
	P-value	>0.05
Gravidity (Number of pregnancy)	Correlation Coefficient	−.083
	P-value	>0.05
Parity (Number of giving birth either alive or stillborn)	Correlation Coefficient	−.094
	P-value	>0.05
Age	Correlation Coefficient	−0.197
	P-value	>0.05
Marital Status	Correlation Coefficient	−.062
	P-value	>0.05
Race	Correlation Coefficient	.059
	P-value	>0.05
Religion	Correlation Coefficient	−.234
	P-value	>0.05
Occupation	Correlation Coefficient	−.319
	P-value	<0.05*

Note: *represents P-value is significant ($p < 0.05$).

score among pregnant women was significantly different ($p < 0.05$) concerning occupational status. Pregnant women o working in the government or private sector had a considerably higher post-test score than the housewife and self-employed.

4. Discussion

Most of the respondents involved in this study are between 22 and 39, which is the ideal age for women to get pregnant. This statement was supported by Ref. [10], who claimed that teen pregnancies are a risk for both the mother and foetus and should be avoided. Pregnancy complications, premature births, and birth interventions are common in women over 35, as is an increased risk of specific foetal abnormalities, structural and chromosomal. For instance, after 36 years of maternal age, the risk of having a baby with Down syndrome increases exponentially. Apart from that, most of the respondents are multiparous and multigravida women. They were willing to get pregnant again because they had a more positive pregnancy experience in the previous scanning than first-time pregnant women, especially among the Malays. From 2015 to 2020, the fertility rates of the Malays have significantly increased vis-à-vis the other races in Malaysia. Compared to primigravida women, women who have previously had positive pregnancies will not feel the need for an earlier prenatal ultrasound because they feel more confident.

The study showed that knowledge among the respondents before the intervention was 98% and increased to 100% following the educational intervention. This may be due to the educational intervention presenting more detailed information. A study reported that nearly two-thirds of the sample needed a better comprehensive knowledge at the pre-intervention phase. After the intervention, it displayed a good level of knowledge regarding the urinary tract infection (UTI) [11]. Based on the current study's findings, the educational video was the most effective intervention, compared to the brochures and combined media, in improving pregnant women's knowledge, perception, expectation and awareness about the safe use of prenatal ultrasound. The video combines audio, visuals and animation, which can captivate viewers and allow them to indirectly capture all the information presented in the video. In addition, it is possible to watch video content countless times. It is also suitable for low literacy populations [12].

Similarly, Sunthornsup et al. concluded that an educational video about juvenile idiopathic arthritis (JIA) is more efficient than a pictorial brochure in improving knowledge about JIA among patients because the combination of words and animation in the video can quickly educate patients [13]. Ramagiri et al. compared the effectiveness of pamphlets and videos as educational material to promote diabetic retinopathy (DR) screening in the urban slums of Hyderabad and concluded that educational videos led to more remarkable behavioural change than pamphlets in motivating people with diabetes for DR screening because they used a story in their video and involved the public in enacting the role, making the video more realistic and engaging [14]. In addition, Conceição et al., 2017 and Abdullah et al. demonstrated that video is more efficient in improving the knowledge of the population due to its cost-effectiveness, brevity and straightforward content that comprises sound and video that easily captivates the audiences [15,16].

Shilbayeh concluded that a pharmacist-led audio-visual intervention via an educational video and a brochure effectively improved patients' knowledge retention and satisfaction with warfarin therapy benefits [17]. However, these reported data show a trend different from our findings. One of the possible reasons is that the respondents may have stopped.

Halfway through the video or brochure because of the lengthy median engagement time [18]. In this study, the respondents were required to spend almost 20 min finishing, which may lead them to skip a part during the intervention. Besides, information in the video and brochure influences respondents' knowledge, perception, expectations, and awareness. From the outcome, most respondents believed that ultrasound is used to detect foetal anomalies or abnormalities and evaluate any pregnancy complication. According to Yang et al., 2021, a prenatal ultrasound can detect a foetus with a cleft lip with a complete palate and facilitate the planning for surgery [19]. Approximately 90% of the respondents believed that demanding ultrasound solely for identifying gender, to create keepsakes images and for their pregnancy satisfaction is contrary to medical purposes. According to Edwards 2002, even though ultrasound is considered a radiation-free modality, the exposure time should still be kept to the minimum possible and used only for medical purposes [20]. The respondents agreed that more prolonged exposure could cause adverse effects to both mother and foetus and that ultrasound does not use ionizing radiation. After the intervention, the respondents were also aware that prenatal ultrasound scan is done from the 1st to 3rd trimester of pregnancy and done routinely for screening and selectively if indicated by the doctor.

As for the participant's employment status, nearly 78% were working mothers with an education level up to tertiary education (43%). Our study results illustrated a significant association between occupation and post-test knowledge scores among pregnant women regarding the safe use of prenatal ultrasound. More than half the employed pregnant women had better knowledge regarding the safe use of ultrasound than non-employed mothers. Compared to homemakers, employed mothers may have better access to the internet, books, and magazines as a source of information and the opportunity to share their experiences with others in the workplace [21]. Increased ability to absorb information will also improve critical thinking, so knowledge should also be increased. Our findings are in line with those of Wong et al. which show that pregnant women with higher occupational status have better nutritional knowledge [21].

Educational level was an essential predicting factor for pregnant women's post-test knowledge. It explained that pregnant women with a good education tended to have higher post-test knowledge and enhanced their understanding of information disseminated by mass media. Women with higher education status may have better exposure to mass media like television, radio and the internet, through which they can gain health information and knowledge. Another similar study has reported a significant association between the level of education and folic acid intake during pregnancy [22]. However, our present results did not find any association between the education level and post-test knowledge score regarding the safe use of prenatal ultrasound among pregnant women. This highlighted that healthcare providers' ongoing efforts to deliver information on the safe use of prenatal ultrasound to pregnant women, regardless of their education level, significantly improved their post-test knowledge. With such correct information, pregnancy complications will be reduced considerably.

Further, our research found no link between gravidity, parity and post-test knowledge of the safe use of prenatal ultrasound among pregnant women. This could be because they have pregnancy experiences, making them more knowledgeable about the pregnancy's progress. Moreover, household income is one of the predicting variables that may be linked to post-test knowledge of prenatal ultrasound safety. Due to their appointment flexibility, higher-income pregnant women were more likely to have an early prenatal ultrasound scan than lower-income women [16]. On the other hand, our research found no link between household income and post-test knowledge of safe prenatal ultrasound use among pregnant women.

Even though most respondents showed good knowledge regarding prenatal ultrasound, they seemed to need better awareness regarding its safe use. This shows the importance of a continuous educational program to be promoted and conducted in Malaysia to avoid imprudent use of prenatal ultrasound. The findings of this study provide new and valuable insights into the safe use of prenatal ultrasound knowledge among pregnant women. One of the strengths of this study is its usage of three types of educational modules commonly used in the current era to evaluate their efficacy. Moreover, we also recruited respondents with different socio-economic backgrounds, levels of education and occupations, a factor shown to influence pregnant women's knowledge, perception, expectation and awareness.

However, the study also has some weaknesses. The most important limitation is the follow-up period. The post-test occurred almost immediately after the pre-test, raising whether the information was retained or whether the results were attributable to short-term memory. Further, the outcomes cannot be generalised to the entire population of pregnant women because this study focuses on pregnant women from one centre. Accordingly, further researchers could include different hospitals.

5. Conclusion

In conclusion, educational video is considered the most effective educational module in improving knowledge, perception, expectation and awareness of pregnant women regarding the safe use of prenatal ultrasound, compared to brochures and combined media. Additionally, future researchers are recommended to conduct more extended multi-centre studies to determine whether such an educational module could improve retention of knowledge after a longer period.

Declarations

Author's contribution

INCI, NMS and SMSSR conceived and designed the experiments. INCI, TR and GKX performed the experiments and wrote the paper. TR, GKX, FWAZ, UMF, and SMSSR analyzed and interpreted the data. INCI, AS, and NMN contributed reagents, materials, analysis tools or data.

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Declaration of interest's statement

The authors declare no conflict of interest.

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Appendix B. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.heliyon.2022.e12773.

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