



Effect of Age and Parity on Knowledge of Cervical Cancer Screening Among Women of Child Bearing Age in Anambra State

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Abstract

Identification of characteristics of women in terms of age and parity as related to their uptake of existing screening services can give significant data to forming cervical cancer screening administrations. This study was aimed to assess the effect of age and parity on knowledge of cervical cancer screening among women of child bearing age in Anambra State. The study adopted a quasi-experimental research design. The study was conducted at Chukwuemeka Odumegwu Ojukwu University Teaching Hospital Awka and General Hospital Onitsha between June 2019 to September 2019. Using multi-stage (purposive) sampling technique, the sample size for this study consisted of one hundred and eighty four (184) women (134) subjects for experimental group and 50 subjects for control group) attending antenatal in public hospitals in Anambra State. The instrument contained five questions on demographic data of the respondents, questions on knowledge of cervical cancer and practice questions with four point response options. The reliability of the instrument was established by using Cronbach alpha for estimating the internal consistency of the instrument. Data entry and analysis were done using Statistical Package for Social Science (SPSS) and inferential statistics (ANCOVA) was used to test the null hypotheses at 0.05 level of significance. The results showed that all the women of different age groups and women of all parity levels benefitted from the exposure to health education programme. The study therefore concludes that exposing women of child bearing age to health education programme improved the practice of cervical cancer screening practice. The knowledge of cervical cancer, knowledge of cervical cancer screening and knowledge of modes of prevention of cervical cancer are critical in determining cervical cancer screening uptake among the women. It is thus concluded that exposing women of child bearing age to health education programme improved the cervical cancer screening practice than not exposing them to any treatment. With adequate knowledge of cervical cancer and a positive perception of cervical cancer screening, utilization of cervical cancer screening services is uniform among women of all parity level.

Keywords: Age; Parity; Knowledge; Cervical cancer screening; Women of child bearing age.

1. Introduction

Knowledge is a blend of understanding, esteem, relevant information and expert opinion that gives a domain for assessing and joining new data and experiences. Bandura [1] maintained that information on health risks and advantages makes the precondition for change and if child bearing mothers need information about how their way of life propensities influence their health, they have little motivation to get themselves through the travail of changing the unfavorable propensities they appreciate. Child bearing period is the regenerative period in a woman's life from adolescence to menopause. It is the time during which she is physiologically ready to conceive children. Medicinally, the best age for kid bearing stays 20 - 35 years, hence child bearing age is of an age when women are typically ready to bring forth kids. Child bearing women has higher risks of developing dangerous tumors that are can spread into the cervix and attack close by tissues. As these tumors develop, some malignancy cells can sever and venture out to inaccessible spots in the body through the blood or the lymph framework and structure new tumors a long way from the first tumors. Cancers are typically named after the organ or tissues where they structure. For instance brain cancer structures in the cells of the cerebrum, breast cancer forms in the breast while cervical cancer forms in the cervix [2].

Cancer is a gathering of maladies including unusual cell development with the possibility to attack or spread to different parts of the body. Cancer alludes to any of an enormous number of ailments portrayed by the advancement of strange cells that partition wildly and be able to invade and decimate ordinary body tissue. Cancer frequently can spread all through the body [3]. Cancerous tumours can be amiable dangerous. As these tumors develop, some cancer cells can sever and venture out to far off spots in the body through the blood or the lymph framework and

structure the tumors a long way from the first tumors. Cervical Cancer accordingly is an ailment wherein the cells of the Cervix become unusual and begin to develop, wildly, shaping tumors [4]. Cervical cancer is a kind of disease that happens in the cells of the cervix — the lower some portion of the uterus that interfaces with the vagina. Cervical cancer therefore an infection wherein malignant (cancer) cells structure in the tissues of the cervix. There is limited research evidence on how cervical cancer and parity relate. Parity is the total number of pregnancies carried over the threshold of viability. It is the number of times a woman has been pregnant and carried the pregnancies to a viable gestational age.

High parity has long been suspected of being associated with an increased risk of cervical cancer [5], but previous analyses of this association have not taken the strong effect of knowledge of cervical cancer screening into account. The effect of age and parity on knowledge of cervical cancer unclear, although several studies in different populations have examined this question. High parity may be accounted for by some socio-cultural beliefs favouring delivery of many children including the value of children as sources of wealth and security [6]. Similarly, Roy, *et al.* [7] indentified parity as strongly related risk factor of cervical cancer. Castanon, *et al.* [8], examined cervical screening at age 50–64 years and the risk of cervical cancer at age 65 years and older. Authors found that most women could continue child bearing irrespective of their age in a bid to meet certain family and societal demand at the expense of their health. Parity in this part of the country could be attributed to the practice of couples in search of male issues as it is common in Igbo land.

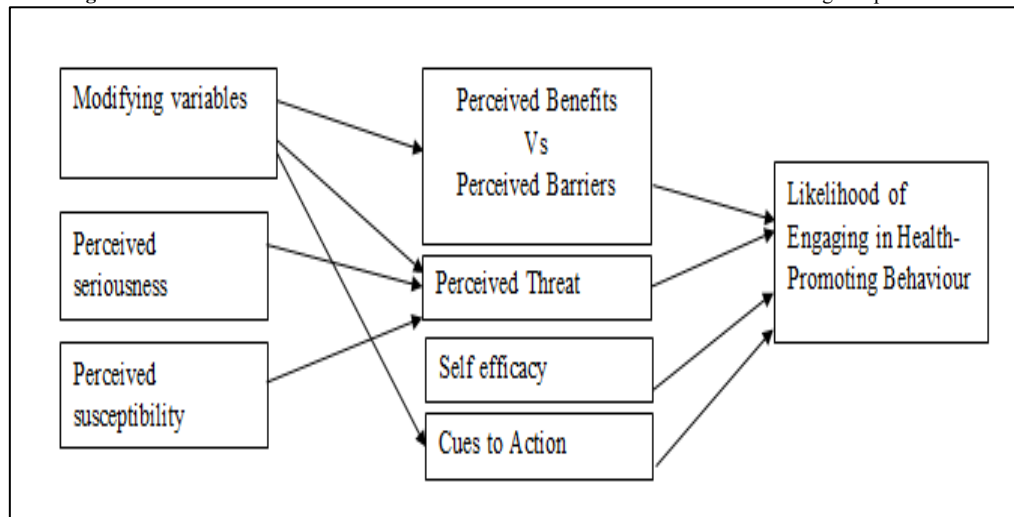
Related studies on cervical cancer bothers on knowledge and practices of cervical cancer screening [9], cervical cancer prevention and the acceptability of HPV Vaccination [10], Awareness and knowledge of cervical cancer [11]. Cervical cancer screening among university students [12]. The findings from these previous studies may have limited generalizability to women in Anambra state who have different cultural beliefs, family and social norms. Obviously, uptake of screening programmes can be accelerated by raising awareness about cervical cancer risk factors including young age at first sexual intercourse [13], high parity [14], infections with the human papillomavirus [15], young age at first full-term pregnancy [16].

Apart from Segni, *et al.* [17] who assessed the level of knowledge and Associated factor toward cervical cancer among women Age (21-64) years in Gulele sub-city Addis Ababa Ethiopia. There is no specific stipulation on the relationship between age and parity on knowledge of cervical cancer screening; public hospitals do not currently practice cervical cancer prevention education in a systematic and systemic manner, instead doctors are encouraged to offer 'opportunistic screening' at the hospitals as one of the strategies to reach more women with cervical cancer prevention programme [18-20]. Women of child bearing age in Anambra State were chosen to participate in the study because they are mostly in the age group (18 – 40 years) in which knowledge can be acquired through formal/informal education and other methods. These will potentially enhance uptake of the screening and hence reduction of morbidities and mortalities resulting from cervical cancer especially in the state. It is in the light of the above that the researcher seeks to examine the effect of health education programme on knowledge and practice of cervical cancer among women of child bearing age attending in Anambra State.

1.1. Theoretical Framework

The Health Belief Model is a comprehensive questionnaire which helps physicians to prevent the diseases. Besides, the basis of this model is encouraging the participants to take part and increasing their awareness which creates acceptable behaviour. Feeling the threatening risk of cervical cancer (perceives susceptibility) is the first step for preventive action. Afterwards, the intensity and life threatening complications of the cancer, receiving positive signs from surroundings and positive symptoms of cancer, believing in accuracy and the benefits of the preventive programmes and the inhibitory factors of accurate behaviour which have less importance than its advantages and finally performing preventive behaviour, which has been summarized in Figure 1.

The HBM was spelled out in terms of four broad areas representing the perceived cervical cancer threat and net benefits, perceived cervical cancer susceptibility, perceived cervical cancer severity, perceived benefits and perceived barriers. These concepts were proposed as accounting for people's readiness to Act' an added concept, 'cues to action' would activate that readiness and stimulate overt behaviour. A recent addition to the HBM is the concept of 'self-efficacy' assumes that the likelihood of taking action is not only a function of beliefs related to outcomes, but also a function of a person's belief that he/she is behaviourally capable of achieving the desired outcome [21].

Figure-1. The Health Belief Model of Women's Likelihood of Cervical Cancer screening and prevention

1.2. Statement of the Problem

Cervical cancer poses a great burden on women's health due to its high incidence and the poor prognosis of most patients. Low screening coverage has been attributed to several factors, including limited access to and availability of screening services, screening cost, lack of trained service providers, inadequate equipment and supplies, inadequate monitoring and evaluation of screening programmes, and a health service system that is overwhelmed by health demands. It seems that they still ignore the occurrence and the likelihood of cervical cancer prevalence among women. Most women of child bearing age seem not to have enough understanding about cervical cancer screening centers and what they entail. Significant number of women, though aware of health risks in cervical cancer, still appears to ignore the preventive actions of cervical cancer screening. Failure of the early detection seems to have caused death in many instances which is more than deaths from other diseases. From all indications, the burden of cervical cancer is rising but with the early detection through screening and structure health education, the disease needs not claim so many lives again. Some Nigerian women seem to present cases of cervical cancer at an advanced stage of the disease at which little or no therapy can be adopted.

1.3. Research Questions

The following were the research questions that guided the study.

1. What is the pretest and posttest mean cervical cancer screening knowledge scores of women of child bearing age of different age groups exposed to health education programme and those not exposed?
2. What is the pretest and posttest mean cervical cancer screening knowledge scores of women of child bearing age of different parity exposed to health education programme and those not exposed?

1.4. Hypotheses

Specifically the following null hypothesis will guide the study.

1. There is no significant difference in the mean cervical cancer screening knowledge scores of women of child bearing age of different age groups exposed to health education programme and those in control group
2. There is no significant difference in the mean cervical cancer screening knowledge scores of women of child bearing of different parity exposed to health education programme and those in control group

2. Material and Method

2.1. Research Design

The study adopted a quasi-experimental research design specifically, it used pre-test post-test with control group. The design seeks to establish the cause and effect relationship between the variables of interest. Quasi experimental design was used because some researchers who conducted similar studies to examine the impact of Health Education programme on knowledge and Attitude at Risk behaviour of students also used quasi-experimental design [22].

2.2. Area of the Study

The study area is Anambra state; Anambra is a state in southeastern Nigeria. The people of Anambra state are predominantly civil servants, business men and women. The area was chosen because cervical cancer was ranked second (8.8%) among the five commonest cancers reported in the state.

2.3. Population of the Study

The population for the study consisted of all women of child bearing who registered for antenatal in public hospitals in Anambra State within the period of the study. There are two (2) tertiary hospitals and thirty three (33) functional general Hospitals in Anambra State as shown in Appendix. This category of women were chosen because

they are within the child bearing age and this vulnerable to cancer of the cervix. It is also assumed that their lifestyle will have great influence on their health.

2.4. Sample and Sampling Techniques

The sample size for this study consisted of one hundred and eighty four (184) women (134) subjects for experimental group and 50 subjects for control group) attending antenatal in public hospitals in Anambra State. Multi stage sampling technique was used for the study. Simple random sampling technique was used to select two senatorial zones out of the three senatorial zones in Anambra State. Purposive sampling technique was used to select all public hospitals because they are homogenous in characteristics. Thereafter, a simple random sampling technique of fish bowl without replacement was used to select two public hospitals in each of the selected zones. Simple random sampling technique was used to place the two hospitals selected in each senatorial zone experimental and control group. Simple random sampling was used to select antenatal days. The pregnant women who registered and attended antenatal clinics regularly in the four selected hospitals during the period of study and who satisfied the inclusion criteria participated in the study. The inclusion criteria were: the subject must be confirmed pregnant, duly registered at antenatal

2.5. Instrument for Data Collection

The instrument used for data collection was cervical cancer knowledge and practice test questionnaire (KNOCERC) the instrument was self developed by the researcher following review of related literature. The instrument is in three sections (A, B and C). Section 'A' contained five questions on demographic data of the respondents (ie Age, level of education ethnicity parity level and occupation) section 'B' contained twenty four questions on knowledge of cervical cancer and section 'C' on the other hand consisted (12) practice questions with four point response options of very often, often, Rarely and Never.

2.6. Reliability of the Instrument

To ensure the consistency of the instruments used for data collection, the reliability co-efficient of the instrument was determined by administering it to 20 pregnant women who will not form part of the study sample. The estimation of the reliability co-efficient of the instrument was obtained from the responses of the women using Kuder Richardson Kr.20 on section B Knowledge of cervical cancer which has the co-efficient of 0.7 practices towards of cervical cancer was analysed using Gonbach's Alpha at 0.8 coefficient. Hence the instrument was considered reliable.

2.7. Method of Data Collection

The researcher held conferences with the six research assistants in the experimental and control hospital on procedure of the programme and time on different days. Pre-test was administered first and collected followed by the Health Education Programme. The post-test was given after the completion of the programme and questionnaires was collected. The illiterate respondents was asked to complete the questionnaire by verbally responding to questions in the presence of the researcher / research assistants.

2.8. Control of Extraneous Variables

The following measures were taken to control extraneous variables that will likely to affect the results of the experiment.

- Training of research assistants was carried out by the researcher. This was so designed to ensure that the trainees had the same training exposure, which would eliminate bias that could arise from trainers' personality
- To avoid experimental bias and to maintain homogeneity of instruction, the training of the research assistants was done by the researcher and the use of a common lesson plan which was provided by the researcher
- Effects of pre-test on post-test was minimized by making sure that the time for post-test was not too long after treatment to avoid forgetting what they had learned
- The pre-test items was reshuffled and renumbered before use for post-test.

2.9. Method of Data Analysis

The data generated were analyzed using mean and standard deviation which was used to answer the research questions and inferential statistics (ANCOVA) was used to test the null hypotheses at 0.05 level of significance in the Statistical Package for Social Science (SPSS). The raw data was entered into the SPSS sheet and the variables well labelled. Analysis was done based on the research objectives.

3. Results and Discussion

3.1. Research Question one

What is the pretest and posttest mean cervical cancer screening knowledge scores of women of child bearing age of different age groups exposed to health education programme and those not exposed?

Table-1. Pretest and Posttest Mean Cervical Cancer Screening Knowledge Scores and Standard Deviation of Women of Child Bearing Age of Different Age Groups Exposed to Health Education Programme and those in Control Group

Age Groups	Pre test			Post test			Mean Gain Score
	N	Mean	SD	N	Mean	SD	
Health Education Programme Group:							
18-28 years	64	13.97	2.89	64	19.72	2.65	5.75
29-39 years	67	13.97	3.44	67	19.79	2.59	5.62
40-50 years	3	12.67	3.51	3	18.33	1.15	5.66
Control Group:							
18-28 years	22	14.77	3.21	22	16.88	3.64	2.11
29-39 years	22	13.41	4.49	22	13.95	3.80	0.54
40-50 years	6	9.00	3.63	6	11.00	5.25	2.00
Total:							
18-28 years	86	14.17	2.98	86	18.94	3.20	4.77
29-39 years	89	13.83	3.71	89	18.35	3.86	4.52
40-50 years	9	10.22	3.83	9	13.44	5.57	3.22

The results in [table 1](#) shows pretest, posttest mean cervical cancer screening knowledge and mean gain scores of child bearing age based on their treatment groups and age groups. In terms of their mean knowledge based on age groups, pretest and posttest mean cervical cancer screening knowledge scores for those within ages of 18 – 28 were 14.17 and 18.94 with a mean gain score of 3.92; those within the age group of 29-39 were 13.83 and 18.35 with a mean gain score of 4.52. Women within the ages of 40 and 50 years had pretest and posttest mean knowledge scores of 10.22 and 13.44 respectively and mean gain score of 3.22. In terms of treatment groups, women of child bearing of different age groups exposed to health education programme had higher mean cervical cancer knowledge than those of similar age groups in control group. This is demonstrated by the mean gain scores of 5.72, 5.62 and 5.66 of women between the ages of 18-28 years, 29-39 years and 40-50 years respectively for those exposed to health education programme compared to the mean gain scores of 2.11, 0.54 and 2.00 for equivalent age groups in control group. This suggests that all the women of different age groups benefitted from the exposure to health education programme.

Research question one examined cervical cancer screening knowledge scores of women of child bearing age of different age groups exposed to health education programme and those not exposed. In terms of treatment groups, women of child bearing of different age groups exposed to health education programme had higher mean cervical cancer knowledge than those of similar age groups in control group. This finding was not surprising because health education programme provided equal learning experiences on cervical cancer screening tailored for all age groups. [Adamu, et al. \[23\]](#), confirmed that health education presents health information to target populations irrespective of age on particular health topics and provides tools to build capacity and support behaviour change in an appropriate setting. This suggests that all the women of different age groups benefitted from the exposure to health education programme.

Table-2. Pre and Post Mean Cervical Cancer Screening Knowledge Scores and Standard Deviation of Women of Child Bearing Age of Different Parity Exposed to Health Education Programme and those in Control Group

Parity Levels	Pre test			Post test			Mean Gain Score
	N	Mean	SD	N	Mean	SD	
Health Education Programme Group:							
No Child	3	16.00	2.65	3	21.33	2.08	5.33
1-3	75	14.19	2.79	75	19.89	2.49	5.70
4-6	22	12.50	3.31	22	18.68	2.95	6.18
7-9	7	15.14	5.34	7	20.57	2.82	5.43
10 & Above	27	13.89	3.26	27	19.70	2.46	5.81
Control Group:							
No Child	7	16.43	2.76	7	15.43	3.74	-1.00
1-3	22	13.27	3.81	22	14.64	4.14	1.37
4-6	14	12.86	5.08	14	14.71	5.36	1.85
7-9	5	11.80	4.38	5	14.60	4.34	2.80
10 & Above	2	14.00	4.24	2	15.50	2.12	1.50
Total:							
No Child	10	16.30	2.58	10	17.20	4.29	0.90
1-3	97	13.98	3.05	97	18.70	3.66	4.72
4-6	36	12.64	4.02	36	17.14	4.44	4.50
7-9	12	13.75	5.05	12	18.08	4.54	4.33
10 & Above	29	13.90	3.24	29	19.41	2.64	5.51

3.2. Research Question Two

What is the pretest and posttest mean cervical cancer screening knowledge scores of women of child bearing age of different parity exposed to health education programme and those not exposed?

Table 2 shows pretest and posttest mean cervical cancer screening knowledge scores and mean gain scores of women of child bearing age based on their treatment groups and parity levels. In terms of their mean knowledge based on parity levels, those with no child had the highest pretest scores of 16.30 but had the least gain score of 0.90 while those with 4-6 children had the lowest pretest score of 12.64 but a higher mean gain score of 4.50. Those with the highest number of children (10 & above) had pretest score of 13.90, the highest post test mean of 19.41 as well as the highest mean gain score of 5.51. This was followed by those with 1 – 3 children who had 4.72 mean gain score. In terms of treatment groups and parity, although there was relatively large mean gain score (ranging from 5.33 to 6.18) across all the parity levels for exposed to health education programme, those with 4 – 6 children had the highest mean gain score (6.18), followed by those who had 10 children and above with mean gain score of 5.81 while the third in this order were those that had 1 – 3 children. These mean gain scores were all greater than those of women of equivalent parity levels in control group which ranged between -1.00 and 2.80. These suggest that women of all parity levels benefitted from the health education programme.

Research question two is concerned with the mean cervical cancer screening knowledge scores of women of child bearing age of different parity exposed to health education programme and those not exposed. The study found that women of all parity levels benefitted from the health education programme. In a related finding, Jensen, *et al.* [5] supports that no significant association exist between parity levels and cervical cancer screening uptake. Authors reported that a general decline in parity might therefore partly explain the reduction in cervical cancer recently seen in most countries. Similarly, Bjørge and Kravdal [24] in a study of risk of uterine cervical cancer in Norwegian registry data found that parity level had no independent impact on cervical cancer incidence.

3.3. Hypothesis One

There is no significant difference in the mean cervical cancer screening knowledge scores of women of child bearing age of different age groups exposed to health education programme and those in control group

Table-3. Summary of Analysis of Covariance of Child Bearing Mothers' Mean Cervical Cancer Knowledge Scores by Treatment Groups and Age Groups

Source of Variation	Type III Sum of Squares	df	Mean Square	F	P-value	Decision
Corrected Model	1306.123	6	217.687	28.135	.000	
Intercept	1483.950	1	1483.950	191.795	.000	
Pretest Knowledge scores	236.925	1	236.925	30.622	.000	S
Groups	360.644	1	360.644	46.612	.000	S
Age	61.203	2	30.601	3.955	.021	S
Group * Age	49.003	2	24.502	3.167	.054	NS
Error	1369.481	177	7.737			
Total	64875.000	184				
Corrected Total	2675.603	183				

*Not Significant

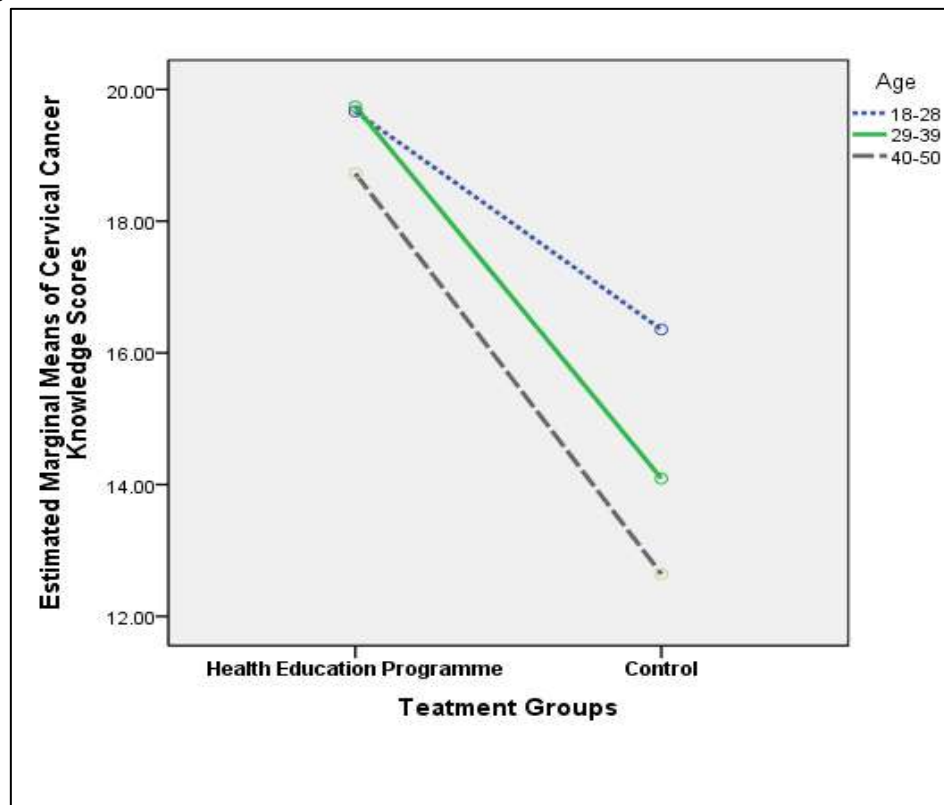
The results presented in table 3 shows that there was a significant difference in mean cervical cancer knowledge scores of women of child bearing age of different ages groups, $F(2,177) = 3.955$, $P < 0.05$. The null hypothesis was therefore rejected. Furthermore, there was no significant interaction between treatment and age on the women's cervical cancer knowledge, $F(2,177) = 3.167$, $P > 0.05$. See figure 2 for the mean plots based on treatment groups and age groups.

Based on the significant main effect of age on mean cervical cancer knowledge, a simple contrast was conducted to ascertain the group that differed from the other. Table 4 presents the result which shows that there was a significant difference in mean cervical cancer knowledge among women between the ages of 18-28 and those within the ages of 29-39 on the one hand, and a significant difference between the ages of 18-28 and those with 40 – 50 years. However, there was no significant difference between women aged between 29-30 years and those between 40 – 50 years in terms of cervical cancer knowledge.

Table-4. Simple Contrast for main effect of Age on Mean Cervical Cancer Knowledge of Women of Child Bearing Age

Age Groups		Contrast Estimate	P-value	Decision
29-39 years vs.18-28years	(16.916-18.011)	-1.095	.026	S
40-50years vs.18-28years	(15.683-18.011)	-2.328	.030	S
29-39years vs.40-50years	(16.916 - 15.683)	1.233	.245	NS

Figure-2. Mean plots of cervical knowledge scores of women of child bearing age by treatment groups and age groups showing no significant interaction effect



3.4. Hypothesis two

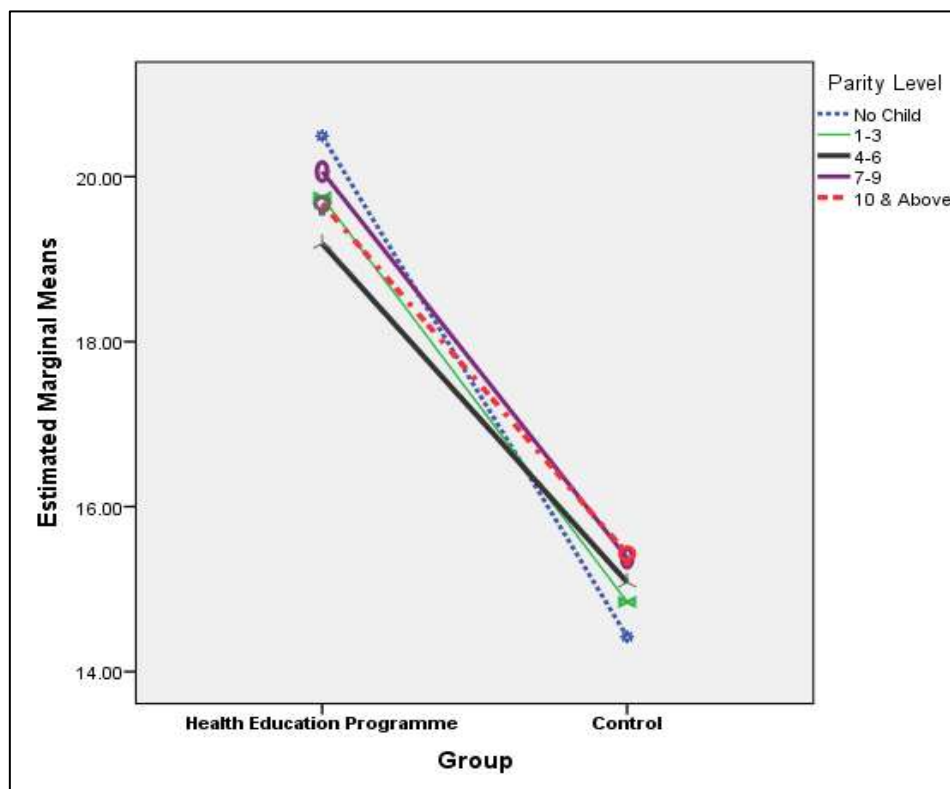
There is no significant difference in the mean cervical cancer screening knowledge scores of women of child bearing of different parity exposed to health education programme and those in control group

Table-5. Summary of Analysis of Covariance of Child Bearing Mothers' Mean Cervical Cancer Knowledge Scores by Treatment Groups and Parity Levels

Source of Variation	Type III Sum of Squares	df	Mean Square	F	P-value	Decision
Corrected Model	1229.237 ^a	10	122.924	14.703	.000	
Intercept	1320.817	1	1320.817	157.983	.000	
Pretest Knowledge Scores	302.926	1	302.926	36.233	.000	S
Groups	375.060	1	375.060	44.861	.000	S
Parity Levels	3.574	4	.894	.107	.980	NS
Groups * Parity Levels	8.060	4	2.015	.241	.915	NS
Error	1446.367	173	8.361			
Total	64875.000	184				
Corrected Total	2675.603	183				

The results presented in [table 5](#) shows that there was no significant difference in mean cervical cancer knowledge scores of women of child bearing age of different parity levels, $F(4,173) = .107$, $P > 0.05$. The null hypothesis was therefore not rejected. Furthermore, there was no significant interaction between treatment and parity on the women's cervical cancer knowledge, $F(4,173) = .241$, $P > 0.05$. See [figure 3](#) for mean plots based on treatment groups and age groups, indicating no significant interaction.

Figure-3. Mean plots of cervical knowledge scores of women of child bearing age by treatment groups and parity levels showing no significant interaction effect. The slope of the line shows that all parity levels exposed to treatment had improved knowledge compared to those in control group



The results presented in table 5 shows that there was no significant difference in mean cervical cancer knowledge scores of women of child bearing age of different parity levels. Ali, *et al.* [25], also found no significant association between parity and adenocarcinoma of the cervix. Furthermore, there was no significant interaction between treatment and parity on the women's cervical cancer knowledge.

4. Conclusion

The study revealed that knowledge of cervical cancer screening among the respondents was high and health education programme significantly increased the cervical cancer screening practice of women of child bearing age. This indicates that most women may have a high level of the general knowledge about the disease but no knowledge of the disease itself or its progression.

The knowledge of cervical cancer, knowledge of cervical cancer screening and knowledge of modes of prevention of cervical cancer are critical in determining cervical cancer screening uptake among the women. It is thus concluded that exposing women of child bearing age to health education programme improved the cervical cancer screening practice than not exposing them to any treatment. With adequate knowledge of cervical cancer and a positive perception of cervical cancer screening, utilisation of cervical cancer screening services is uniform among women of all parity level. Specifically, the study showed that women of all parity levels benefitted from the health education programme except those with 7-9 children whereas those with 4 – 6 children benefitted most from the health education programme.

The findings of this study have a number of implications for education. The results of this study provide facts as regards effect of Health Education programme on knowledge and practice of cervical cancer screening among women.

Cervical cancer screening will contribute to reduce the incidence and mortality of cancer, by diagnosing and treating premalignant lesions, or to promote timely treatment of malignant lesions with reduced morbidity. It is therefore recommended that:

1. Awareness campaigns and education programmes to enlighten the public about cervical cancer screening should be broad to encompass signs and symptoms, risk factors and modes of prevention of the disease.
2. Ministry of Health should work with the schools, churches, institutions of higher learning and the community itself with the aim of increasing the uptake of screening.
3. Future studies can explore new avenues of disseminating information like health talks to young women and men in schools and colleges; outreaches in market places and health briefs at the health facilities when the women are waiting to be seen by a doctor.

Competing Interests

Authors have declared that no competing interests exist.

Authors' Contributions

Author NNS designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. 'Author NNS' and 'Author OAI' managed the analyses of the study. 'Author NNS' managed the literature searches. All authors read and approved the final manuscript."

Ethical Approval

"All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki."

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