Association between Socio-Demographics and Clinical Profile with Therapy Options Received by Cervical Cancer Patients in Two Nigerian Tertiary Hospitals

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ABSTRACT
This study was conducted to determine the associations between the socio-demographics, clinical profile and therapy options received by cervical cancer (CC) patients in Usmanu Danfodiyo University Teaching Hospital (UDUTH), Sokoto and Ahmadu Bello University Teaching Hospital (ABUTH), Zaria. The study used a prospective longitudinal design with retrieved data for 157 eligible CC patients. Pearson's correlation was used to test for association between patients' socio-demographics, clinical characteristics and number of therapy options received while comparisons of proportions were carried out using Pearson's Chi square. Results show that the mean age of the patients was 50.7±9.0 years and 43.3% of patients earned less than ₦50,000.00 per month. The results also reveal most of the 47.1% of patients presented with clinical stage III. Per Vaginal Bleeding (PVB) was the symptoms recorded for 88.5% of the patients while most patients (49.7%) received Chemotherapy (CT) as the major therapy option. There were significant associations between the level of income, (r=0.412, p<0.001), baseline number of symptoms, (r=0.200, p=0.012), number of symptoms after therapy, (r= -0.584, p<0.001) and the number of therapies received by the patients. Clinical disease-stage, baseline number of symptoms and level of income were found to be associated with the therapy options received by the patients.
Keywords: Socio-demographics, Clinical profile, Cervical cancer, Therapy

INTRODUCTION
Cervical cancer (CC) is the most common gynecological malignancy (Daniel *et al*., 2013; Sule and Ochicha, 2017), and the fourth most common cancer among women worldwide. In Africa, CC remain a major cause of morbidity and mortality among women in resource-poor settings (Onyenwenyi and Gugu, 2016). In 2012, Global Cancer Observatory (GLOBOCAN) report showed an estimated 527,624 new cases worldwide, with 27,326 and 14,089 cases from West Africa and Nigeria respectively (Bruni *et al.*, 2017).

The recommended treatment options for CC include surgery, radiation therapy (RT), chemoradiation therapy (CRT) and chemotherapy (CT), administered alone or in combination. The choice of the type and number of therapy option(s) for a patient is stratified mainly by the clinical disease-stage and need for fertility preservation (Katz, 2017; NCCN, 2019; Richard, 2019). Reports indicate that patients in India presenting CC at late stages with poor general conditions received RT alone as valid treatment option in spite of CRT being the standard of care for treating almost all cervical carcinoma patients as recommended by the National Cancer Institute (NCI) alert (Srivastava *et al.*, 2013). Unfortunately, available services for the treatment of premalignant and malignant lesions are grossly inadequate in Nigeria (Richard, 2019), including the tertiary Teaching Hospitals in the North-Western region of Nigeria which are designated as national cancer registries. Furthermore, socio-demographics and clinical profile of patients among others affect the choice between recommended treatment and treatment options for an individual patient. Studies conducted in some parts of Northern Nigeria showed that most CC cases were diagnosed at advanced stages (Aliyu et al., 2015; Musa *et al.*, 2016) and were mostly recommended for induction or neoadjuvant chemotherapy. However, with the limited number of radiotherapy facility and high treatment costs, it become challenging for many CC patients to receive this treatment option (Pasek *et al.*, 2012; Richard, 2019). For the above-mentioned reasons, this study was conducted to determine the associations between the socio-demographics, clinical profile and the therapy options received by CC patients in two tertiary hospitals in Northwest Nigeria.

## MATERIAL AND METHODS
Ethical Considerations
Ethical approvals were obtained from the Health Research Ethics Committees of UDUTH (UDUTH/HREC/2018/No.731) and ABUTH (ABUTH/HREC/CL/05) before commencement of the study. The confidentiality and anonymity of the patients were maintained during and after the study.

Study Design and Eligibility Requirements
Ahmadu Bello University Teaching Hospital (ABUTH) and Usmanu Danfodiyo University Teaching Hospital (UDUTH) were purposively selected for this study being the major cancer registries in North-Western Nigeria. All eligible patients who came to the Radiotherapy and Clinical Oncology clinics of the hospitals between January - June, 2019 were recruited for the study. The study was based on

prospective longitudinal design. A total of 157 patients diagnosed with cervical cancer and treated with chemotherapy, radiotherapy or both, with or without surgery were included in the study. Patients whose socio-demographic and clinical records were adequate were included in the study while patients who declined consent to participate or could not respond to interviews due to severity of the illness were excluded. A summary of selection criteria is presented in Figure 1.
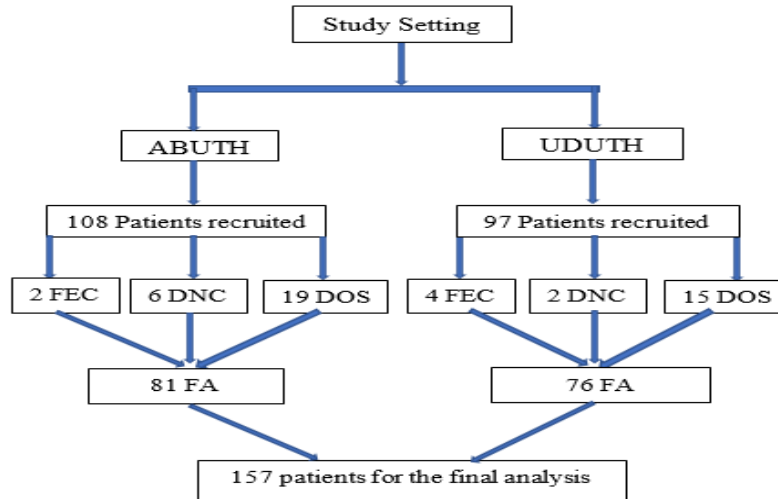
FEC=failed eligibility criteria; DNC=did not consent; DOS=dropped out of the study; FA=final analysis

Figure 1: Selection Criteria for CC patients attending ABUTH and UDUTH for Inclusion in the Study

Study Instruments

A pro forma consisting of three (3) sections (A-C) was used. Section A consist of the patient's socio-demographic information including patient's age, body surface area, marital status, parity, tribe, level of education, and average monthly income in Nigerian naira (₦). Section B collected data on clinical profile of the patient including the diagnosis/clinical staging, presenting symptoms (including per vaginal bleeding, per vaginal discharge, and lower abdominal pain) and laboratory investigation results (including full blood counts and differentials, renal and liver function tests, abdomino-pelvic ultra-sound scan) while Section C was on treatment(s) received by the patient such as the cytotoxic drugs, details of radiation exposure, vehicles and adjuvant drugs as well as surgical operation. Each patient was followed up till her complete or due to have completed her prescribed course/radiation fraction.

Data Analysis

Data obtained was analyzed using SPSS software for windows ver. 20 (SPSS Inc., Chicago, IL, USA). Data was presented as percentages and mean ± SD, geometric means or mean differences with 95% confidence intervals (CI).

Comparisons of proportions were carried out using Pearson's Chi square. Pearson's correlation was used to test for association between the patients' socio-demographics, clinical characteristics and number of therapy options received. A priori significance level of $p < 0.05$ was used throughout.

RESULTS

Socio-Demographic and Clinical Characteristics of the Patients

Table 1 presents socio-demographic and clinical characteristics of patients selected for this study. The results show that the mean age of patients was 50.7±9.0 years 81.5% of the patients were married and 154 or (98.1%) multiparous. A total of 68(43.3%) patients who said they earn an average of ₦50,000.00 or less were 43.3%. Clinically, 74 patients (47.1%) presented with clinical stage III, while stage IVB was the least clinical stage recorded for 3.2% of the patients. Moreover, PVB was the symptoms presented by 139 (88.5%) of the patients. Details of socio-demographic and clinical characteristics of the patients are presented in Table 1.

Table 1: Socio-demographic and clinical profiles of CC patients attending ABUTH and UDUTH

Patient Profile	N = 157	(%)	p-value
Mean Age (Years)	50.7±9.0		
Marital Status			<0.001
Single	1	(0.6)	
Married	128	(81.5)	
Divorced	12	(7.6)	
Widow	16	(10.2)	
Parity			<0.001
Nulliparous	1	(0.6)	
Uniparous	2	(1.3)	
Multiparous	154	(98.1)	
Level of Education			<0.001
Non Formal	61	(38.9)	
Primary	9	(5.7)	
Secondary	54	(34.4)	
Tertiary	33	(21.0)	
Average Monthly Income			<0.001
<₦50,000	68	(43.3)	
₦50,000-100,000	66	(42.0)	
>₦100,000	23	(14.6)	
Clinical Stage			<0.001
I	8	(5.1)	
II	59	(37.6)	
III	74	(47.1)	
IVA	11	(7.0)	
IVB	5	(3.2)	
Presenting Symptoms			
PVB	139	(88.5)	
PVD	113	(72.0)	
LAP	95	(60.5)	
Histological Type			<0.001
Squamous Cell Carcinoma	144	(92.3)	
Adenocarcinoma	12	(7.7)	

PVB = Per vaginal bleeding; PVD=Per vaginal discharge; LAP=Lower abdominal pain

Therapy Options Received by the Patients

A total of six therapy options including chemotherapy (CT), radiation therapy (RT), chemoradiation therapy (CRT), adjuvant chemotherapy (CTS), adjuvant radiation therapy (RTS) and adjuvant chemoradiation therapy (CRTS) were used among the 157 CC patients as shown in Table 2. Results indicate that 78 (49.7%) of the patients were placed on CT out of which 28% of the patients mostly in ABUTH (36 patients) received Cisplatin+Paclitaxel making it the main therapy option received. In addition, 32.5% of patients received chemoradiation while 10.2% had chemoradiation and surgery. External beam radiation therapy (EBRT) was the only form of radiation received by patients treated with radiation therapy.

Table 2: Therapy options for patients attending ABUTH and UDUTH

Therapy Option Received	ABUTH (n =81)	UDUTH (n =76)	Total (N = 157)	*p-value*
Chemotherapy (CT)	63(77.8)	15(19.7)	78(49.7)	<0.001
Cisplatin, n(%)	2(2.5)	0(0.0)	2(1.3)	
Cisplatin+5FU, n(%)	10(12.3)	5(6.6)	15(9.6)	
Cisplatin+Paclitaxel, n(%)	36(44.4)	8(10.5)	44(28.0)	
Carboplatin+Paclitaxel, n(%)	15(18.5)	2(2.6)	17(10.8)	
Radiation therapy (RT)	0(0.0)	1(1.3)	1(0.6)	<0.001
EBRT, n(%)				
Chemoradiation therapy	12(14.8)	39(51.3)	51(32.5)	<0.001
Cisplatin+RT, n(%)	0(0.0)	6(7.9)	6(3.8)	
Cisplatin+5FU+RT, n(%)	2(2.5)	13(17.1)	15(9.6)	
Carboplatin+5FU+RT, n(%)	1(1.2)	0(0.0)	1(0.6)	
Cisplatin+Paclitaxel+RT, n(%)	8(9.9)	19(25.0)	27(17.2)	
Carboplatin+Docetaxel+RT, n(%)	1(1.2)	1(1.3)	2(1.3)	
Chemo and surgery	3(3.7)	4(5.3)	7(4.5)	<0.001
Surgery+Cisplatin+5FU, n(%)	1(1.2)	6(7.9)	6(3.8)	
Surgery+Cisplatin+Paclitaxel, n(%)	2(2.5)	3(3.8)	2(1.3)	
Surgery+Carboplatin+Paclitaxel, n(%)	1(1.2)	5(6.6)	1(0.6)	
Radiation and surgery	1(1.2)	3(3.9)	4(2.5)	<0.001
Chemoradiation and surgery	2(2.5)	14(18.4)	16(10.2)	<0.001
Surgery+Cisplatin+RT, n(%)	0(0.0)	2(2.6)	2(1.3)	
Surgery+Cisplatin+5FU+RT, n(%)	0(0.0)	1(1.3)	1(0.6)	
Surgery+Cisplatin+Paclitaxel+RT, n(%)	0(0.0)	9(11.8)	9(5.7)	
Surgery+Carboplatin+Docetaxel+RT, n(%)	2(2.5)	3(3.9)	2(1.3)	
Type of Radiation Therapy Received				
EBRT, n(%)	15(100.0)	57(100.0)	72(100.0)	-
Radio Intention				
Curative intent, n(%)	12(80.0)	56(98.2)	68(94.4)	<0.001
Palliative intent, n(%)	3(20.0)	1(1.8)	4(5.6)	

FU= Fluorouracil, EBRT= External Beam Radiation Therapy.

Association between Therapy Option Received, Baseline Clinical Stage and Level of Income

Results presented in Table 3 shows that 46.2% of the patients that received CT and CRT presented with baseline clinical stage II and III. There was significant association (p<0.05) between the therapy option received by the patients and their baseline clinical disease-stage. On the level of income, 47 respondents who received CT admitted to earn less than ₦50,000 per month while patients who received CTS, 4(57.1%); RTS, 2(50.0%) and CRTS, 13(81.3%), earned between ₦50,000 - 100,000 per month.

Associations between Number of Therapies Received, Socio-Demographics and Clinical Characteristics of the Patients

As presented in Table 4, results show that baseline number of symptoms significant positive correlation (*p*=0.012) with number of therapies received by the patients. Income levels of patients correlated positively (p<0.001) with number of therapies received but negatively for baseline number of symptoms, (r = - 0.065; p =0.421) and number of symptoms after therapy (r = - 0.295, p = 0.001).

DISCUSSION

This study was conducted to determine the associations between the socio-demographics and clinical profile and with the therapy options received by CC patients in two Nigerian tertiary hospitals. It could be seen that most of the patients in our study were middle aged, married and multiparous. This was similarly reported in previous studies; a rise in CC was seen with increasing age, parity, early and prolonged sexual period (Eze et al., 2013; Aanchal *et al.*, 2017; Neha and Kondakasseril, 2017)

Table 3: Association between therapy option received, baseline clinical stage and level of income

Therapy option received	Clinical stage					p-value <0.001	Level of income			p-value <0.001
	I	II	III	IVA	IVB		<50,000	50,000-100,000	>100,000	
CT (n=78), n(%)	1(1.3)	36(46.2)	36(46.2)	5(6.4)	-		47(60.3)	29(37.2)	2(2.6)	
RT (n=1), n(%)	-	-	-	-	1(100.0)		-	1(100.0)	-	
CRT (n=51), n(%)	3(5.9)	15(29.4)	26(51.0)	5(9.8)	2(3.9)		17(33.3)	17(33.3)	17(33.3)	
CTS (n=7), n(%)	-	6(85.7)	-	1(14.3)	-		3(42.9)	4(57.1)	-	
RTS (n=4), n(%)	4(100.0)	-	-	-	-		1(25.0)	2(50.0)	1(25.0)	
CRTS (n=16), n(%)	-	2(12.5)	12(75.0)	-	2(12.5)		-	13(81.3)	3(18.8)	

CT= Chemotherapy; RT= Radiation Therapy; CRT= Chemoradiation Therapy; CTS = Chemotherapy and Surgery; RTS = Radiation Therapy and Surgery; CRTS = Chemoradiation Therapy and Surgery; n = number of patients

Table 4: Correlation between Socio-Demographics, Treatment and Clinical Profile of CC Patients Attending ABUTH and UDUTH

Variables	No. of therapies received	Clinical stage of the cancer	Baseline no. of symptoms	No. of symptoms after therapy
No of Therapies Received	-	0.11; (0.161)	0.20; (0.012)	0.58[**]; (<0.001)
Parity of patient	0.05; (0.518)	-0.13; (0.095)	-0.02 (0.809)	0.08; (0.336)
Level of education	0.02; (0.813)	-0.19[*] (0.020)	-0.06 (0.466)	-0.05; (0.506)
Level of income	0.41[**] (<0.001)	-0.268[**] (0.001)	-0.065 (0.421)	-0.295[**]; (<0.001)

Data was collected from 157 patients receiving treatment between January - June, 2019. **Correlation is significant at the 0.01 level (2-tailed), *Correlation is significant at the 0.05 level (2-tailed).

Majority of the patients were low-income earners. A study conducted in Abuja revealed that the direct cost of RT for CC is ₦600,000 per course of teletherapy plus approximately ₦150,000 for pre-treatment evaluation in the FCT (Richard, 2019). This showed how affordability would be a greatest challenge to majority of CC patients in Nigeria. Most of the patients presented with advanced-stage disease. This is consistent with previous studies conducted in Nigeria (Aliyu, Jimoh and Yunusa, 2015; Musa *et al.*, 2016).The study showed PVB as the major symptom presented by the patients. A number of studies have reported PVB, PVD and LAP as the most commonly presented symptoms especially in patients with advanced-stage CC disease. However, PVB has shown to be the immediate cause of death in 6% of women with CC (Eze *et al.*, 2013; Neha and Kondakasseril, 2017; Orang'O *et al.*, 2017; Umate *et al.*, 2017).

According to the recommended treatment guidelines, CRT is the most appropriate therapy option for majority of the patients in our study (Katz, 2017; NCCN, 2019), however, CT was found to be the main therapy option received by the patients. Some of the obvious reasons were non-functionality of the radiotherapy machine in ABUTH throughout the period of the study and the breakdown of the machine in UDUTH before the end of the study period. Dr. Richard in 2019 reported that radiotherapy is available in 10 centres all over the country with 2 machines on the average functional at any given time (Richard, 2019). Another possible reason might be the high cost of the CRT as majority of the patients are low-income earners. Our study showed significant association between the socio-demographics, clinical profile and the therapy option received by the patients. It could be seen that majority of the patients who received CT and CRT presented with baseline clinical stage II and III. Most of the low-income patients received CT. In addition, the study showed that, the higher the level of income, the more the number of therapy options received by the patients. This is perhaps due the fact that, for every increase in number of the therapy option, there is a corresponding increase in cost implication. The study also showed that, the higher the baseline number of symptoms, the more the number of therapy options received by the patients and the less the number of symptoms after therapy. This was so because most of the patients who presented with heavy PVB received emergency haemostatic external beam radiation therapy (EBRT) up to 4Gy/fraction. On the other hand, there was a negative association between number of therapy options received and number of symptoms after therapy. This implies that, the more the number of therapy options received the less the number of symptoms after therapy. It was observed that patients who received emergency EBRT had immediate resolution of their PVB.

CONCLUSION

Findings in this study suggest that patients' clinical disease-stage, baseline number of symptoms and level of income were associated with the therapy options received by the patients. Patients presenting with more baseline number of symptoms, had more therapy options received with significant remission after therapy. To achieve optimal treatment of cervical malignances in Nigeria, recommendations of the International Atomic Energy stipulating one radiotherapy machine per 250,000 population should be considered.

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