

# Ethnicity and Prostate Cancer in Southern Nigeria: A Preliminary Report

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## ABSTRACT

**Introduction:** The natural history of prostate cancer varies among patients. The aim of this study is to detect any variations in clinical and pathological characteristics of the tumor in patients from different ethnic groups in Southern Nigeria. **Patients and Methods:** Consecutive patients who presented with features of prostatic diseases at the Urology Units of University of Port Harcourt Teaching Hospital, Port Harcourt and Nnamdi Azikiwe University Teaching Hospital, Nnewi, were evaluated prospectively with history, physical examination, and relevant investigations using a proforma. Data obtained were collated and analyzed statistically using the Chi-square test and Microsoft Excel. **Results:** Of 187 patients studied, 169 were analyzed. Eighty-six were Ibos, 31 Ijaws, 25 Ikwerres, and 12 Ogonis. Two were from each Etche, Urhobo, Opobo, and Effik; 4 from Andoni, and 3 Ibibio. Fifty-seven (66.3%) Ibos presented with the disease at higher ages (70–80 years) than 19 (61.3%) Ijaws and 11 (91.7%) Ogonis. These age differences were statistically significant with 95% and 99.9% confidence, respectively. All cases were adenocarcinomas. Clinical features, pattern of serum prostate-specific antigen levels, grades of the tumors, tumor metastases, and complications were similar for all ethnic groups. Although more Ibos had tumors with relatively more aggressive metastatic features, there was no statistical significance. **Conclusion:** Clinical and pathological features of adenocarcinoma of the prostate in Ibos, Ikwerres, Ijaws, and Ogonis were found to be similar. However, Ibos presented with the disease at older ages than Ijaws and Ogonis.

**KEYWORDS:** Ethnicity, prostate cancer, Southern Nigeria

## INTRODUCTION

The black race, compared with other races, has been cited in different studies,<sup>[1-4]</sup> as harboring the most aggressive variants of prostate cancer. However, biological characteristics of the tumor also vary extensively among blacks. Black population are known to vary in ethnicity, environmental, cultural, and economic indices. These factors have been cited in different studies<sup>[6-9]</sup> as affecting the incidence, natural history, and prognosis of prostate cancer. The aim of this study is to compare the clinical and pathological features of prostate cancer in patients from various ethnic groups in Southern Nigeria. This is a preliminary report.

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## PATIENTS AND METHODS

The study was carried out prospectively in two centers in Southern Nigeria - University of Port Harcourt Teaching Hospital Port Harcourt and Nnamdi Azikiwe University Teaching Hospital Nnewi in Eastern Nigeria. Ethical Committee approval of the project was obtained from each institution. Consent was also obtained from individual patients.

New and consecutive patients who presented to the urology units of the hospitals with features of prostatic diseases were evaluated with history, physical examination, and relevant investigations, using a common proforma. Information sought in the proforma included personal data, age, place of origin of both parents and grandparents, ethnic group, place of residence, family history of prostate cancer, lower urinary tract symptom (LUTS), nonurinary tract symptoms of diseases, findings on general and systemic physical examination, digital rectal examination findings, results of

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hematological investigations, serum prostate-specific antigen (PSA) assay, serum electrolyte and creatinine, urinalysis, urine microscopy culture and sensitivity, abdominal ultrasonography, ultrasonography of the prostate, and plain radiological examination of the chest, pelvis, limbs, and axial skeleton. Liver function tests, intravenous urography, and plain radiographic skull examination were done with specific indications. Separate consent was obtained for prostate biopsy. This was done on each patient with Tru-Cut needle® (Cardinal Health) via the rectal route with blind digital guiding of the needles. In six cases, prostatic tissues were obtained from open prostatectomy for supposedly benign prostatic enlargement. The perineal route was used in eight cases in which the rectal route was considered unsuitable.

Anesthesia for prostate biopsy was by the pudendal block.<sup>[10]</sup> The pudendal block was supplemented with 30 mg of intravenous pentazocine in whom the block was not adequate. All patients had oral ciprofloxacin 500 mg q-12 hourly, metronidazole 400 mg q-8 hourly, and paracetamol 1 g q-8 hourly for 5 days postbiopsy. Each specimen was preserved in 10% formaldehyde and sent with the request for histology to the Anatomical Pathologists in the institutions who did the histology. Each tumor was staged based on Whitmore-Jewett staging of prostate cancer.<sup>[11]</sup> Results obtained were subjected to statistical analysis and organized in prose, tables, and bar and pie charts, using the Microsoft Excel2003 Version (Microsoft Corporation, Redmond, WA, USA). Patients who were natives of ethnic groups outside the ones in this study were excluded. The Chi-square test (Karl Pearson) was used to evaluate various groups of data based on patients' ethnic groups of origin.  $P \leq 0.05$  was considered as statistically significant.

## RESULTS

During the period August 2002 to August 2004, 187 patients were recruited but only 169 satisfied the criteria for inclusion in the analysis. Eighty-six patients were Ibos, 31 Ijaws, 25 Ikwerres, and 12 Ogonis. Others were 2 from each Etche, Urhobo, Opobo, and Effik, 4 from Andoni, and 3 Ibibio. These were grouped as "others" because they had insufficient data for analysis.

All cases of prostate cancer seen in this study were adenocarcinomas. Malignant stromal tumors of the prostate were not encountered. The mean age of Ibos at presentation was  $71.1 \pm 3.8$  years. The mean ages of patients from other ethnic groups and standard deviations were as follows: Ijaw  $67.1 \pm 4.2$  years, Ikwerre  $70.5 \pm 4.6$  years, and Ogoni  $66.2 \pm 2$  years. Of Ibo patients, 57 (66.3%) patients presented with the disease at ages of 70–89 years. Nineteen (61.3%) of Ijaws patients presented at ages between 50 and 69 years. Fifteen (60%) Ikwerre patients presented at ages between 70 and 89 years while 11 Ogonis (91.7%) presented at ages between 60 and 69 years [Table 1]. The differences in ages at the presentation of Ibos and Ijaws have statistical significance with 95% confidence ( $P < 0.05$ ) for Chi-square values with or without Yates' correction. There was no statistically significant difference between the ages at the presentation of the Ibos and the

Ikwerres ( $P > 0.05$ ). The Ogonis presented with adenocarcinoma of the prostate at lower ages than the Ibos. This observation has statistical significance with 99.9% confidence,  $P < 0.001$ .

The predominant clinical features in patients from all ethnic groups were LUTS. These included frequent micturition, poor stream of urine, hesitancy, feeling of incomplete voiding, and straining at micturition. The most common non-urinary tract symptoms included: Bone pains, poor penile erection, Inability to walk, constipation, and lethargy [Table 2].

The responses of patients on presence or absence of history of prostate cancer in their respective nuclear and extended families were grouped into three as follows: (1) Those with family history

**Table 1: Distribution of ages of patients with adenocarcinoma of the prostate from the various ethnic groups**

Age (years)	Ethnic group and number of patients				
	Ibo	Ijaw	Ikwerre	Ogoni	Others
40-49	2				
50-59	12	6	2		3
60-69	15	13	8	11	8
70-79	41	10	13		2
80-89	16	2	2	1	
Total	86	31	25	12	13

**Table 2: Distribution of lower urinary tract symptoms and nonurinary tract symptoms in patients from the ethnic groups**

Symptom	Ethnic group and number of patients				
	Ibo	Ijaw	Ikwerre	Ogoni	Others
Frequent micturition	56	21	17	10	4
Poor stream of urine	51	20	17	11	5
Hesitancy	41	15	11	5	4
Urgency	39	17	8	4	3
Feeling of incomplete voiding	30	15	8	1	1
Straining	28	7	5	5	2
Nocturia	27	15	10	6	3
Hematuria	24	6	6	5	1
Intermittency	21	7	7	7	2
Urge incontinence	20	6	8	5	1
Dysuria	19	12	3	2	5
Acute retention of urine	18	10	12	4	1
Chronic retention of urine	8	3		3	
Terminal dribbling of urine	4	7	10	2	5
Incontinence of urine	1	2			
Nonurinary tract symptoms					
Bone pains	23	12	13	2	5
Poor penile erection	19	8	5	1	
Inability to walk	15	5	1	1	2
Constipation	15	3	5	1	
Weight loss	14	6	8		4
Numbness in lower limb	13	1	1		1
Other symptoms	60	31	21		2

Other symptoms: Lethargy, passing blood in stool weakness in lower limbs, leg swelling, tremors, and fecal incontinence

of prostate cancer, (2) those with no family history of prostate cancer (3) patients who did not know whether or not they had family history of the disease. The number of patients in each group is presented with bar charts in Figure 1.

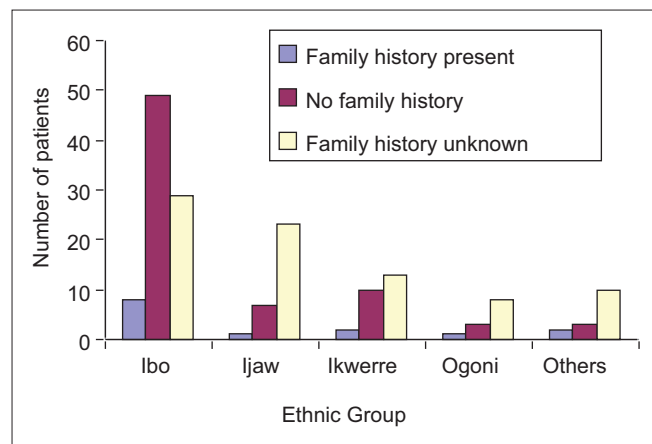
The most frequent finding on physical examination of the patients in each group included pallor, pedal edema, herniae, hemorrhoids, and paraplegia. Enlargement, hardness, and nodularity of the prostate were the most frequent anatomical changes in the gland [Table 3].

The serum PSA values of patients from each group are presented graphically to show the pattern in each group [Figure 2]

**Table 3: Findings on physical examination of patients from the various ethnic groups**

Sign	Ethnic group and number of patients				
	Ibo	Ijaw	Ikwerre	Ogoni	Others
Pallor	42	18	16	10	7
Herniae	20	8	5	3	
Hydrocele	15	6	7	2	
Paraplegia	8	2	2	1	
Pedal edema	7	5	2		
Paraparesis	4	3	1		
Digital rectal examination findings					
Enlarged prostate	78	18	20	7	10
Hard prostate	40	9	9	4	3
Nodular prostate	34	8	7	4	3
Firm prostate	28	4	2	3	1
Lax anal sphincter	17	2	3		
Asymmetrically enlarged prostate	11	1			
Obliterated median sulcus	11	4	7	4	1
Hemorrhoids	10	3	4	1	
Fecal incontinence	9	3	2		
Fixed rectal mucosa	1	1			
Other findings	9	4			

Other findings: Pedal edema, rectal prolapse, rectal bleeding, cachexia, jaundice, and fixed anal mucosa



**Figure 1:** Family history of prostate cancer of patients from Ibo, Ikwerre, Ogoni, and others

irrespective of age of patients; poorly differentiated tumors were the most common variants of adenocarcinoma of the prostate in patients from all ethnic groups. These were seen in 44 Ibos, 16 Ijaws, 9 Ikwerres, and 5 Ogonis [Table 4].

The majority of the patients (67 Ibos, 28 Ijaws, 19 Ikwerres, and 9 Ogonis) presented with advanced disease – stages C and D [Table 5].

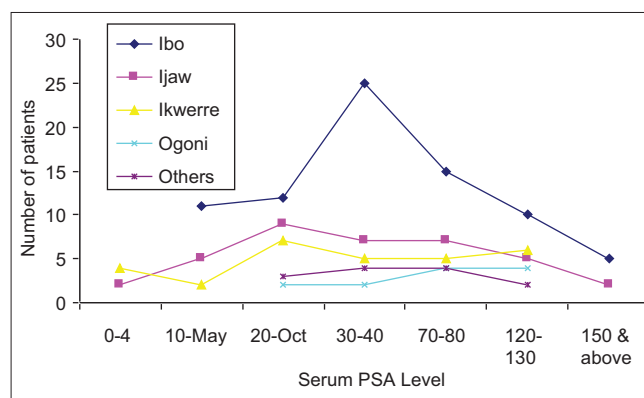
Complications included anemia, urinary tract infection, hypertension, chronic renal failure, and paraplegia. These were collated according to ethnic groups of patients [Table 6].

## DISCUSSION

An ethnic group refers to a race of mankind, tribe, nation (group of tribes or nations) having, or thought to have, and the same original ancestors or descent.<sup>[12]</sup> Citizens of such a group are usually united by language and custom, and usually live as a community (or as communities) under common traditional political systems.<sup>[12]</sup> In indigenous population, people of the same ethnic group seem to share common genetic, environmental, social, economic, cultural, and similar occupational factors. These factors tend to have interethnic variations and have been known to be risk factors in the etiology of malignant diseases.<sup>[7,8]</sup> Adenocarcinoma of the prostate is one of the most common malignant diseases of aging male population in Nigeria and has been linked to environmental risk factors.<sup>[13]</sup>

Southern Nigeria is multiethnic. The ethnic groups include the Yorubas, Ibos, Ibibios, Anang, Effiks, Ijaws, Ogonis, Ikwerres, Urhobos, etc., These seem to vary significantly in origin, environment, culture, and levels of social and economic development. The Ikwerres share geographical contiguity with the Ibos and both seem to have closeness in origin, inter-ethnic activities such as intermarriages, cross border migration and inter-ethnic integration. Patients from Urhobo, Effik, and Ibibio were not sufficient in number for analysis in this preliminary report.

Salient findings from this study include the observation that the Ibos presented with the disease at a higher mean



**Figure 2:** Serum prostate-specific antigen of patients from Ibo, Ikwerre, Ogoni, and other ethnic groups

**Table 4: Distribution of ages of patients, ethnic group, and degree of tumor differentiation**

Age	Ethnic group/degree of tumor differentiation (I II III)/number of patients											
	Ibo			Ijaw			Ikwerre			Ogoni		
	I	II	III	I	II	III	I	II	III	I	II	III
40-49	-	-	2									
50-59	3	2	4	4	-	2	-	-	2			
60-69	-	1	7	1	-	6	-	-	4	3	2	4
70-79	7	3	26	1	1	6	2	-	3			
80-89	1	-	5	-	-	2				-	-	1
90-99	-	-	-									
Total	11	6	44	6	1	16	2		9	3	2	5

I: Well differentiated, II: Moderately differentiated, III: Poorly differentiated

**Table 5: Stages of the tumors at presentation**

Tumor	Ibo	Ijaw	Ikwerre	Ogoni	Others
Stage					
A	5	1	1		2
B	12	2	5	1	1
C	27	13	9	2	3
D	42	15	10	9	9
Total	86	31	25	12	15

**Table 6: Co-morbid conditions and complications of prostate cancer**

Co-morbid condition/ complication	Ethnic group/number/(%)			
	Ibo	Ijaw	Ikwerre	Ogoni
Urinary tract infection	56 (65.1)	15 (48.1)	12 (48.0)	3 (27.3)
Anemia	51 (59.3)	25 (80.6)	17 (68.0)	9 (81.8)
Hypertension	37 (43.0)	15 (48.1)	5 (20.0)	3 (27.3)
Chronic renal failure	34 (40.7)	10 (32.3)	3 (12.0)	4 (36.1)
Hematuria	24 (27.9)	9 (29.0)	10 (40.0)	4 (36.1)
Paraplegia	8 (9.3)	2 (6.4)	2 (8.0)	1 (9.1)

age ( $71.1 \pm 5.5$  years) than the Ijaws ( $67.2 \pm 6.2$  years), and the Ogonis ( $66.2 \pm 5.5$  years). Also noteworthy is that majority of Ibos (66.3%) presented with the disease at older ages than Ijaws (61.3%) and Ogonis (91.7%) [Table 1]. The differences between ages at the presentation of Ibos and Ijaws on one hand, and Ibos and Ogonis on the other respectively have statistical significance and need further investigation.

Age is the most significant of the risk factors in the development of prostate cancer.<sup>[14]</sup> The mean ages at the presentation of Ibos and Ikwerre patients agree with previous reports in Port Harcourt<sup>[15]</sup> and elsewhere in Nigeria.<sup>[16-18]</sup> However, these reports were on mixed population of patients from different ethnic groups. The means ages of Ogonis and Ijaw patients fell to the lower limits of these observations in Nigerians. The low mean and average ages of these patients agree with findings of mean age of prostate cancer patients of 61 years (peak of 66-70 years) observed by Wasike *et al.*<sup>[19]</sup> in Nairobi Kenya. Factors that might have contributed to the lower average ages at the presentation of Ijaws and Ogonis include small sample

sizes of patient population from these ethnic groups. It is also possible that Ibos had more male geriatric population, higher life expectancy, and greater awareness of the problems of prostate cancer than Ogonis and Ijaws at the time of this study. However, observations on such characteristics of Ibo population compared with Ogonis and Ijaws have neither been documented here nor elsewhere in the literature.

From this study, it also appears that Ogonis and Ijaws developed adenocarcinoma of the prostate at younger ages than Ibos or that Ogonis and Ijaws harbored more aggressive variants of the disease than Ibos, since adenocarcinoma of the prostate occurring in younger age groups has been known to have worse prognosis than that seen in the elderly.<sup>[20]</sup> Two theoretical concepts, however, make spurious simple conclusions on times of initiation of adenocarcinoma of the prostate in patients of this population groups. These are the concepts of total preclinical phase (T PCP) and length bias. The total preclinical phase is defined as "the time interval between the biological disease initiation and the time at which symptoms of the disease lead to clinical diagnosis."<sup>[21]</sup> It is difficult to know the times of biological initiation of the cascades of cellular and molecular events that culminated in adenocarcinoma of the prostate in each patient and each patient group. Evidence had since been available that the prostatic glandular epithelium begins neoplastic changes early in a man's adult life, and that these changes do not become clinically apparent or significant until decades later.<sup>[22]</sup> The concept of length bias as enunciated by Feinleib and Zelen<sup>[23]</sup> relates to the rate (per unit time) or velocity of evolution of the cellular and molecular processes that occur from biological initiation of the disease (including premalignant, preinvasive, and invasive periods) to final diagnosis. The rate of progression of these events may vary from patient to patient. In other words, the TPCP period of clinical invasion may vary among patients and patient groups. If, for instance, the initiation of malignant events starts in one patient in adolescence, progresses slowly into old age, and in another, it starts at middle age and progresses rapidly to clinical malignancy within the same period of middle age, and if diagnosis is made in both patients at the same time, it will be erroneous to conclude that the malignant process started in the latter at younger age than the former. Studies are necessary to determine the times of initiation and rate of progression of prostate cancer in Nigerians.

Another salient finding in this study is that clinical and pathological features of adenocarcinoma of the prostate, including its complications are similar, irrespective of ethnic group and ages of the patients. The similar pattern is characterized predominantly by signs and symptoms of lower urinary tract dysfunction (mainly obstruction) and axial skeletal invasion. Features of soft tissue spread were relatively uncommon. In addition, poorly differentiated (Grade 3) disease was the most common variant in each ethnic group, with a similar pattern of serum PSA value, which seems to reflect tumor burden instead of ethnic variation [Figure 2]. This similarity in biological behavior seems to suggest a common initiating molecular origin,

and that the same molecular and cellular mechanisms were involved in the progression of the disease. Adenocarcinoma of the prostate in Caucasians and American blacks has been extensively investigated in these respects. Gene products expressed by the tumor (anti-apoptotic genes) have been used to localize “the most probable initial transforming events to stem or progenitor basal cells of the prostatic glandular epithelium.”<sup>[24,25]</sup> Also gene mutations involving tumor suppressor pathways<sup>[26,27]</sup> and overexpression of oncogenes<sup>[28]</sup> have been known to be involved in tumor proliferation and short patients’ survival. Whether identical gene mutations observed in Caucasians and black Americans are involved in the initiation and progression of prostate cancer in Nigerians living in Nigeria is uncertain. They may not necessarily be so as gene mutations frequently occur in relation to environmental risk or causative factors.<sup>[29,30]</sup>

In spite of enormous problems posed by prostate cancer, this study revealed marked ignorance of the family history of the disease and absence of family records in all patient groups irrespective of ethnicity [Figure 1]. It also shows that in all the ethnic groups most of the cases of adenocarcinoma of the prostate were not familial. Even in those with family history of the disease, familial prostate cancer as defined by Bratt<sup>[31]</sup> could not be reproduced. He defined familial prostate cancer as “prostate cancer occurring in each of three generations in the patient’s paternal or maternal lineage;” hereditary prostate cancer as the disease “affecting a cluster of three or more relatives within any nuclear family.” The findings on family history of prostate cancer in this study would probably have been improved by accurate family records in form of death certificates, medical records, and increased levels of health education. However, even in a study of the accuracy of family history of prostate cancer, where these resources were available, accuracy was only 81.6%, and found to be related to site of the malignancy and not dependent on level of education, age, or income.<sup>[32]</sup> A longitudinal study of the families of patients found with the disease may be more informative in investigating familial prostate cancer in Nigerians.

## CONCLUSION

Ibo patients presented with prostate cancer at older ages than Ogonis and Ijaws. However, theoretically this would not mean that Ibo patients developed the disease at older ages than Ijaws and Ogonis. Irrespective of ethnicity, clinical and pathological features of prostate cancer were similar for Ibo, Ijaw, Ogoni, and Ikwerre patients. This suggests that similar genetic and molecular mechanisms were involved in the initiation, evolution, and progression of the disease in patients studied from these ethnic groups. These molecular mechanisms can be more vigorously studied for a common approach to the cure of this malignancy. Also irrespective of ethnicity, most of the cases of prostate cancer were sporadic. However, it is expected that the presence of accurate family records and improved level of health education could improve the accuracy of family history of prostate cancer and awareness of the patient groups studied.

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## Conflicts of interest

There are no conflicts of interest.

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