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Risk factors for prostate cancer in West African Men: The Familial Cohort Study

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ABSTRACT

Prostate cancer (CaP) has been identified as the most common cancer among men globally with higher prevalence, incidence and mortality rates in Black men. This study aims to assess the risk factors for CaP among West African men residing in Nigeria, Cameroon and the United States. A validated Prostate Cancer Transatlantic Consortium (CaPTC) familial cohort study questionnaire was used to collect data on the respondents' characteristics, alcohol consumption pattern, smoking pattern, knowledge of CaP, physical activity level and cancer status. Anthropometric measurements were taken using standard procedures. Data was summarised using descriptive statistics and penalized maximum likelihood logistic regression analysis via Firth method to determine the association between CaP status and independent variables. The results show that 2.21% of the respondents reported to have been diagnosed with CaP. The median age of the respondents was 47 years with 62.21% having poor knowledge of CaP, and 17.11% with central obesity. More than half (62.07%) of the respondents currently drink alcohol, 24.4% are current smokers and 51.5% engage in low physical activity. Number of daughters (OR=1.2435, 95%CI: 1.0045, 1.5393), consistent alcohol drinkers in years (OR=1.0484, 95%CI: 1.0151, 1.0829) and glasses of drink on a typical occasion (OR=1.2145, 95%CI: 1.0560, 1.3968) were associated with CaP status. In the multiple logistic regression, only number of daughters (OR=1.2531, 95%CI: 1.0055, 1.5617) was associated with CaP status. In conclusion, poor knowledge of CaP was observed among the respondents. Alcohol consumption, increased number of glasses of alcohol consumed on typical occasion and increasing number of daughters were associated with CaP status and increased risk of the disease.

KEYWORDS: Prostate cancer, West Africa, obesity, daughters, alcohol consumption

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Introduction

Prostate cancer is the most frequently diagnosed cancer in men. It occurs as a result of genetic mutations or changes of the gene's blueprint of the prostate cell causing the normal prostate cells to divide too quickly or die too slowly (Odedina *et al*, 2016). Black Africans have 70% higher risk of developing Prostate Cancer (CaP) when compared to non-Hispanic whites and 137% higher death rates (American Cancer Society, 2016). Findings have shown that African Americans living in the US have 1.6 times risk of developing CaP when compared to Caucasian men (Al Olama *et al*, 2014; American Cancer Society, 2016).

Prostate cancer has been reported to be the second leading cause of cancer death in men, both in developed and developing countries, with an estimate of 180,890 new cases and 26,120 cancer death in the United States in 2016 (American Cancer Society, 2016). The burden of CaP is projected to rise, with over 75 million prevalent cases, 27 million incident cases and 17 million cancer deaths globally by 2030 (Parkin *et al*, 2003; Ferlay *et al*, 2010).

The higher incidence and prevalence of CaP in Black African and African American compared to other races in the world has increased rate of morbidity and mortality among these populations (Odedina *et al*, 2006; Delongchamps *et al*, 2007; Odedina *et al*, 2009; Akinremi *et al*, 2010; Rebbeck *et al*, 2013).

The known risk factors for developing CaP include: increasing age, African ancestry, family history and certain inherited genetic conditions. Other modifiable risk factors include tobacco use, alcohol consumption, increased body weight, central obesity, poor nutrition, physical inactivity, poor knowledge levels and certain infectious agents. These factors also play major roles in the development of CaP (IHME: 2013; Jacobs *et al*, 2015; World Cancer Research Fund, 2015).

Findings have linked genetic susceptibility of CaP to African heritage and familial disease (IARC, 2014; American Cancer Society, 2016). Also, there are strong evidences that increased body mass index and central obesity increases the risk of CaP incidence and mortality (MacInnis *et al*, 2003; Gong *et al*, 2006; Pischon *et al*, 2008; Martin *et al*, 2009; Stocks *et al*, 2010; Batty *et al*, 2011; Dehal *et al*, 2011; Discacciati *et al*, 2011; Shafique *et al*, 2012).

Alcohol consumption and smoking have also been implicated with the risk of developing CaP (Sawada *et al*, 2014) and reduced smoking have been associated with a decline in CaP mortality rates (Jones *et al*, 2016).

Studies on risk factors for CaP in West African countries are scarce. Since Nigeria is an ancestral home of many Black men living in the diaspora, studies involving Black men from Nigeria and other West African countries may provide information on some of the risk factors predisposing Black men to CaP. This study therefore aims to assess the risk factors for CaP in West African Black men.

Methodology

This study was a cross-sectional study of West African Black men residing in Nigeria, Cameroon and the United States. Data were collected from ten (10) CaPTC sites across the six (6) geo-political zones in Nigeria, one site from Cameroon and one site from the USA. Respondents within the age range of 35 to 75 years, who were willing to participate in the

study and duly signed the informed consent were recruited. A validated CaPTC familial project study questionnaire was used to collect data on the respondents' characteristics, alcohol consumption and smoking patterns, knowledge of CaP (causes, prevention, screening test, signs and symptoms), physical activity level and self-reported cancer status. Anthropometric measurements (height, weight and waist circumference) were taken using the appropriate equipment. Body mass index and central obesity were calculated from the anthropometric measurements. Knowledge of CaP was assessed from twenty (20) questions. Every correct answer was scored as 1 and incorrect answers were scored as 0. Individual total knowledge score was derived by summing all the scores. The individual score was divided by the maximum score (20) and multiplied by 100 to convert it to percentage. The percentage values were then categorized into poor (0 – 40%), moderate (41 – 69%) and adequate (≥70%) knowledge. Data were summarised using frequencies and percentages for categorical variables while median and interquartile range (upper quartile – lower quartile) were used to summarise the continuous variables. We applied penalized maximum likelihood logistic regression analysis via Firth method to determine the association between CaP status and independent variables. In the regression analysis, only 470 out of the 498 respondents were included due to missing observations in some risk factors considered in the model. In addition, several important risk factors could not be included in the model due to missing data which could lead to removal of respondents who reported to have been diagnosed of CaP. Not removing such risk factors could have led to a reduced data pool, especially for those with a positive diagnosis of CaP. To reduce bias in maximum likelihood estimates due to small number of cancer cases in the data, we applied penalized maximum likelihood logistic regression analysis via Firth method (Firth, 1993; Heinze and Schemper, 2002) to examine risk factors for cancer status among the respondents. Firth method is also used to address the problem of separation in logistic regression (Heinze and Schemper, 2002).

Results

Characteristics of the respondents

A total of 498 men participated in the study out of which 11 (2.21%) respondents reported to have been diagnosed with CaP. Among those who reported to have been diagnosed of CaP, 10 (90.91%) reside in Nigeria and only 1 (9.09%) resides in Cameroon. The median age of participants is 47 years with an interquartile range (IQR) of 15 years. The median age at first drink of alcohol was 20 years with an interquartile range of 7 years. The median number of years respondents consistently drank alcohol was 20 years (IQR = 23) and the glasses of drink consumed on a typical occasion among respondents was 3 (IQR = 2). A total of 443 respondents (92.48%) of the respondent were married while 408 (85.18%) of the respondents reside in Nigeria (Table 1).

Table 1: Respondents' characteristics.		
Characteristics	Median	(LQ-UQ)
Age (n = 478)	47	(40-55)
Number of brothers (n = 479)	3	(2-5)
Number of sisters (n = 460)	3	(2-5)
Number of daughters (n = 474)	2	(1-3)
Number of sons (n = 478)	2	(1-3)
Age at first drink of alcohol in years (n = 480)	20	(17-24)
Consistent alcohol drinkers in years (n = 480)	15	(5-28)
Glasses of drink on typical occasion (n = 480)	3	(2-4)
Self-reported Cancer status(n=498)		
Yes	n=11	2.21%
No	n=487	97.79%
Marital status (n= 479)		
Married	n = 443	92.48%
Not married	n = 36	7.52%
Country (479)		
Cameroon	n=27	5.64%
Nigeria	n=408	85.18%
USA	n=44	9.18%

LQ: Lower quartile. UQ: Upper quartile. n: number of observations

Consistent alcohol drinkers: drank alcohol at least once a week for at least 6 months in years

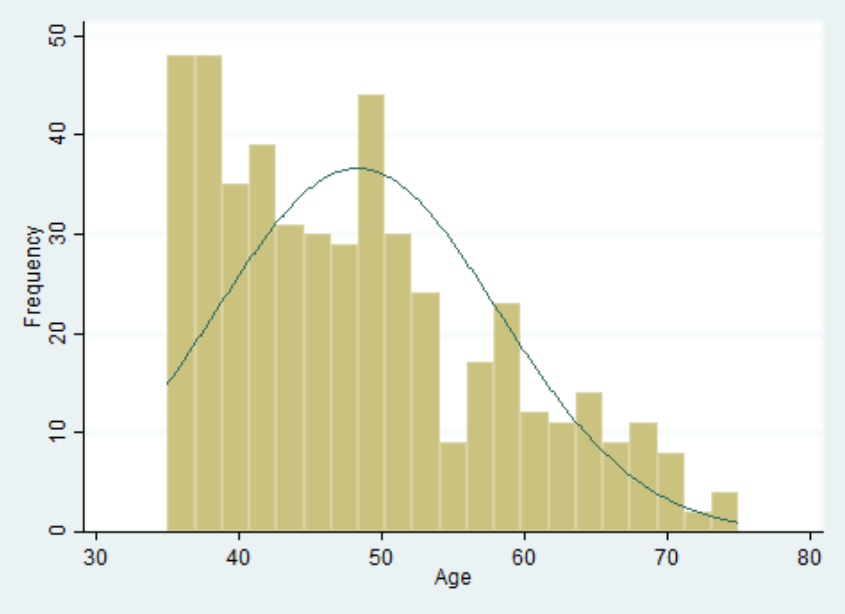

Figure 1 Histogram showing the age distribution of respondents.

Modifiable risk factors for prostate cancer among respondents

Table 2 shows the description of the modifiable risk factors for prostate cancer among the respondents. More than half (62.21%) of the respondents had poor knowledge, 27.81% had moderate knowledge and 9.98% had good knowledge of CaP.

A quarter of the respondents were overweight, 20.9% were obese and 17.1% had central obesity. About 20.4% of the respondents smoke and 79.6% have never smoked. Among the smokers, 24.44% are current smokers while 75.56% had smoked at one time or the other in their lifetime. About 55.65% respondents drink alcohol while 44.35% never drank. Among the alcohol drinkers, 62.07% currently drink alcohol while 37.93% had drank alcohol at one time or the other in their lifetime. About half (51.59%) of the respondents engage in low physical activity.

Table 2: Modifiable risk factors for prostate cancer among respondents.

Modifiable risk factors	Frequency	Percentage
Knowledge of CaP (n=471)		
Poor	293	62.21
Moderate	131	27.81
Adequate	47	9.98
Body mass index (n=345)		
Underweight	69	20.0
Normal weight	112	32.46
Overweight	92	26.67
Obesity	72	20.87
Central Obesity (n=480)		
Yes	82	17.08
No	398	82.92
Physical activity (n=471)		
Low	243	51.59
Moderate	77	16.35
High	151	32.06
Smoking status (n=442)		
smokers	90	20.36
Non-smokers	352	79.64
Smokers (n=99)		
Current smokers	22	24.44
Smoked in a lifetime	68	75.56
Breathe in smoke in the past seven days (n= 480)		
None	306	63.75
One day	18	3.75
Two or more days	26	5.42
Don't know / Refused to answer	130	27.08
Number of days/week tobacco smoke was inhaled (n=480)		
None	332	69.17
One day	5	1.04

Two or more days	13	2.71
Don't know / Refused to answer	130	27.08
Alcohol drinking Status (n=469)		
drinkers	261	55.65
Non-drinkers	208	44.35
Alcohol drinkers (n=261)		
Current drinkers	162	62.07
Drank in a lifetime	99	37.93

CaP- prostate cancer

Smoking in this context is defined as tobacco smoking

Factors associated with prostate cancer status and risk

Presented in Table 3 are the results from the penalized maximum likelihood logistic regression analysis. In the univariate logistic model, the variables, number of daughters (OR=1.2435, 95%CI: 1.0045, 1.5393), consistent alcohol drinkers in years (OR=1.0484, 95%CI: 1.0151, 1.0829) and glasses of drink on a typical occasion (OR=1.2145, 95%CI: 1.0560, 1.3968) were associated with CaP status. Increase in number of daughters, consistent alcohol drinkers in years, and glasses of drink on a typical occasion were associated with increased risk of CaP in men. Age, marital status, number of brothers and sisters, number of sons, age at first drink were not associated with CaP status. In the multiple logistic regression, only number of daughters (OR=1.2531, 95%CI: 1.0055, 1.5617) was associated with CaP status. Likelihood of developing CaP increases with increasing number of daughters.

Table 3: Factors associated with Prostate cancer status among men (n=470).

	Univariate logistic model		Multiple logistic model	
Characteristics	UOR	95% CI	AOR	95% CI
Socio-demographic factors				
Age	0.9987	(0.9412, 1.0597)	0.9997	(0.9401, 1.063)
Marital status				
Married	Ref			
Not married	1.7364	(0.3034, 9.9395)		
Number of brothers	1.1126	(0.9258, 1.337)		
Number of sisters	1.0755	(0.8692, 1.3308)		
Number of daughters	1.2435*	(1.0045, 1.5393)	1.2531*	(1.0055, 1.5617)
Number of sons	1.1888	(0.9486, 1.4898)		
Drinking Habits				
Age at first drink	0.9815	(0.9283, 1.0377)		
Consistent alcohol drinkers (years)	1.0484**	(1.0151, 1.0829)	1.0394	(0.9983, 1.0823)
Glasses of drink on typical occasion	1.2145**	(1.056, 1.3968)	1.0715	(0.8841, 1.2986)

*UOR: unadjusted odds ratio. AOR: adjusted odds ratio. CI: confidence interval. *: p<0.05, ref: reference category*

Discussion

This study assessed the risk factors for prostate cancer in West African men in the CaPTC familial cohort study.

Previous findings revealed a high prevalence of CaP in Black African men (Odedina *et al*, 2006; Delongchamps *et al*, 2007; Odedina *et al*, 2009; Akinremi *et al*, 2010; Rebbeck *et al*, 2013). In this study, the number of respondents who reported to have been diagnosed with CaP out of the 498 was 2.21%, relatively lower. Other respondents who reported not to have been diagnosed with CaP may not have undergone any CaP screening test. Studies have revealed poor screening behaviour among West African men, particularly Nigerian men (Agbugui*et al*, 2013; Ogundele and Ikuerowo, 2015). This might have contributed to the under-reporting of CaP cases. Poor screening behaviour of respondents towards CaP may lead to high prevalence of advanced stage of CaP which is prevalent in CaP management in Nigeria and hence reduce the rate of surviving the disease.

Most of the respondents had poor knowledge on CaP and only one-tenth had adequate knowledge. Few studies conducted in some Nigerian states revealed a low level of awareness and knowledge of CaP risk factors and symptoms (Ukoli *et al*, 2003; Oladimeji *et al*, 2010; Ajape *et al*, 2010; Ogundele and Ikuerowo, 2015). Adequate knowledge on CaP may promote early detection, prevent CaP progression into the advanced stage as well as the rate of morbidity and mortality associated with CaP (Ogunbiyi, 2011; Akinremi *et al*, 2014). Poor knowledge among respondents in this study may put them at risk of developing CaP or having an advanced stage of CaP.

The prevalence of overweight, obesity and central obesity was high among the respondents. Overweight and obesity have been reported to be associated with increased risk of CaP (Stocks *et al*, 2010; Batty *et al*, 2011; Dehal *et al*, 2011; Discacciati *et al*, 2011;; Basset *et al*, 2012; Shafique *et al*, 2012). Obesity has been reported to influence the levels of some hormones and growth factors including insulin and leptin and thereby stimulates the growth of cancer cells (Platz *et al*, 2005). Obesity, particularly central obesity has been reported to increase the risk of advanced CaP (MacInnis *et al*, 2003; Gong *et al*, 2006; Pischon *et al*, 2008; Martin *et al*, 2009). This is due to its lowering effect on serum testosterone levels. Testosterone plays an important role in determining the differentiation status of the prostate epithelium. Therefore, low levels of testosterone may increase the growth of a less differentiated, destructive CaP phenotype (De Pergola and Silvestris, 2013).

This study revealed that about one in five of the respondents smoke and more than half consume alcohol. Studies have revealed that smoking, number of packs smoked, years of smoking and alcohol consumption increase the risk of developing CaP, as well as advanced CaP and death from CaP (Huncharek *et al*, 2010; Rolison *et al*, 2012; ; Sawada *et al*, 2014; Nunzio *et al*, 2015). Also, a study conducted in the US revealed that smokers are less likely to undergo CaP screening and less likely to screen frequently (Rolison *et al*, 2012).

This study showed that increasing number of daughters was associated with increased odds of developing CaP. An earlier study carried out

among the Jerusalem perinatal cohort study by Harlap *et al.*, (2007), found that Israeli men who developed CaP have an impaired ability to reproduce male children. The Y-chromosome has been implicated in the onset of prostate cancer in men (Krausz *et al.*, 2004) and has been suggested to harbour CaP risk (Harlap *et al.*, 2007). However, another study in the US reported that men who were unable to give birth to male children had a lower risk of CaP (Spatz, *et al.*, 2004; Eisenberg *et al.*, 2011) submitting that prostate carcinogenesis may be linked to the X chromosomes. Given these mixed findings, more studies are needed to clearly understand the role of fatherhood and CaP status.

Also, consistent alcohol consumption was found to increase the risk of CaP. Previous studies have established that consistency in alcohol consumption is associated with CaP(Rota *et al.*, 2012; Fowke et al., 2014; Demoury et al., 2016). This might be due to the metabolism of alcohol which releases acetaldehyde which has been suggested to be carcinogenic because it interferes with DNA replication (Seitz and Becker, 2007; Lachenmeier *et al.*, 2012; Zhao et *al.*, 2016).

The current study also shows that CaP risk increases with the number of glasses of alcoholic drink consumed. Earlier studies have consistently shown that a higher volume of alcohol intake on a typical occasion is indeed associated with increased risk of CaP (Fowke *et al.*, 2014; Demoury *et al.*, 2016; Zhao *et al.*, 2016).

In conclusion, poor knowledge of the causes, screening test, signs and symptoms of CaP was observed among the respondents. Alcohol consumption, increased number of glasses of alcohol consumed on typical occasion and an increasing number of daughters were found to be associated with CaP status and increased risk of the disease.

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Conflict of interest

The authors declare that no competing or conflict of interests exist. The funders had no role in study design, writing of the manuscript, or decision to publish.

Authors' contributions

All authors contributed to the study. From data collection, data entry and analysis, manuscript writing and editing.

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