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Causal Relationship among Sexually Transmitted Infections, Frequency of Ejaculation and Benign Prostatic Hyperplasia: Emerging Facts or Myths?

Vitalis Obisike Ofuru[1]*, Ovunda Jack Omodu[1], Ekechi Stella Amadi[2]

[1]Urology Unit, Department of Surgery, Faculty of Clinical Sciences, Rivers State University, Port Harcourt, Nigeria
[2]Dermatology and Venereology Unit, Department of Internal Medicine, Faculty of Clinical Sciences, Rivers State University, Port Harcourt, Nigeria
Email: *vitalis.ofuru@ust.edu.ng

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Abstract

Background: The prevalence of benign prostatic hyperplasia, BPH is increasing in our environment. Besides androgens and age could there be other risk factors? **Aim:** To investigate the roles of sexually transmitted infections, STI and frequency of ejaculation as risk factors for BPH. **Methods:** It was a prospective observational study carried out among predominantly Christian communities near Port Harcourt, a major cosmopolitan city in the oil rich Rivers State, in the Niger Delta region of Nigeria. Adult males above the age of 40 yrs old with no history of prostate cancer were invited to participate. History of marriage, duration of marriage, number of wives/sexual partners, frequency of sex or ejaculation and present or past history of STI were obtained through an interpreter administered questionnaire. Diagnosis of BPH was based on presence of lower urinary tract symptoms, ultrasound determination of increased prostate size and histopathology report to rule out prostate cancer. Linear logistic regression and odds ration were used to establish strength of association between BPH and frequency of ejaculation and history of various causative organisms for STI. Statistical significance was determined at p value of <0.05. **Results:** 754 respondents participated. Age ranged from 40 to 81 years. 92.6% were in a single relationship. 58.4% had 1 - 5 ejaculations per week. 8.2% has had syphilis, 32.6% has had gonorrhea and 1.1% has had candida infection. There was an observed positive relationship between history of gonorrhoea and increase in prostate size but the association was not statistically significant; syphilis showed no positive relationship with prostate enlargement; incidence of candidiasis was too low to establish causal relationship. Individuals who had sex once a week or less showed a higher prevalence

of moderate/severe enlargement (42.3%) compared to those with more frequent sexual activity (35.7%) a relationship that approached significance (p = 0.071), with an odds ratio of 1.3 and narrow CI (0.9 to 1.7), suggesting a potential association that requires further investigation. **Conclusion:** There is an observed causal relationship between both previous history of gonorrhea infection and reduced frequency of ejaculation and prostate enlargement but these associations do not attain statistical significance and would need further studies.

Keywords

Gonorrhea, Syphilis, Candidiasis, STI, Ejaculation, BPH

1. Introduction

The prostate is found only in natural born males and so its development, growth and disease processes are controlled by the male hormones. The prostate is rudimentary at birth but begins a progressive and sustained growth from puberty when the levels of androgens exponentially rise, attaining an average adult volume of about 18 mls [1]. Prostate volume continues to increase with age [2] with the average percentage increase of total prostate volume and transition zone volume per year of follow-up estimated to be 2.2% and 3.5%, respectively [3].

It is a common knowledge however that all men irrespective of their age do not develop clinical BPH. This may therefore imply that male hormones and age may not be the only aetiological factors implicated in prostate gland enlargement; oestrogens, stromal-epithelial interactions, growth factors, and neurotransmitters [4] and a number of other modifiable risk factors have been thought to play roles [5] [6].

Frequency of ejaculation has also been alleged to affect the development of prostatic diseases [7]. Again, sexually transmitted diseases, STI and consequent intraprostatic inflammation is said to potentially contribute to the development of BPH nodules through secretion of growth factors in excess of that required to replace cells damaged by infection or inflammation [8]-[14].

This study was designed to determine the risk association of sexually transmitted infections and frequency of ejaculation to benign prostatic hyperplasia.

2. Materials and Methods

Study Area: The study was carried out in two communities in Obio-Akpor local government area of Rivers State. Obio-Akpor local government area is close to and forms an integral part of Port Harcourt, the capital city of Rivers State, in the Niger Delta area of Nigeria. Port Harcourt, in addition to being canter of the oil and gas exploration in the Niger Delta of Nigeria, is also a cosmopolitan metropolis with a lot of commercial and social activities.

Study Sites: Mainly large church auditoriums and community town halls

located within the study communities.

Research Design: This was a prospective community based observational study.

Study Population: Apparently healthy males, 40 years and above living in suburbs of Port Harcourt, Nigeria, not previously diagnosed, or being treated for prostate cancer.

Sample Size Determination. Sample size was estimated to be 1050 but every adult male who were 40 years and above and met the criteria were included.

Inclusion criteria: Adult males who were 40 years and above and lived in the Niger Delta area for at least 15 years.

Exclusion criteria: Participants who were on treatment for prostate cancer or whose histology report in the course of the study turned out to be prostate cancer.

Sampling Method Two communities out of 17 communities/wards were selected by simple random sampling method. Every consecutive participant who met inclusion criteria were included.

Study Instrument: Participants were invited by pulpit announcements in churches, radio jingles and community town criers. Using an interpreter administered questionnaire, biodata, anthropometric indices, and medical history including international prostate symptoms score, IPSS which was adopted from the American urological association symptom index, AUASI was obtained from patients by trained medical and para-medical staff. IPSS is a validated questionnaire that determines severity of LUTS by scoring 3 storage and 4 voiding symptoms and has an additional question that estimates the degree of discomfort or bother caused by the symptoms. Past history of sexually transmitted diseases like syphilis, gonorrhea, candidiasis and their duration were obtained. History of number of wives/sex partners of each participant and frequency of sex/ejaculation per week were also obtained. Venous blood was obtained from participants by venipunctures, centrifuged, separated and serum appropriately labeled and stored below 4˚C for determination of prostate specific antigen, PSA was determined using ELISA method (ACUBIND ELISA KIT INCUSA).

All participants had their prostate volume calculated from the equation length × weight × height × 0.52 cm after their prostate parameters were determined with Mindray DP2200 3.5 curvilinear probe. Prostate volume was then classified as normal (≤30 cm^3), mildly-enlarged (31 - 45 cm^3) moderately-enlarged (46 - 75 cm^3) and severely-enlarged (>75 cm^3).

All participants had uroflowmetry as part of routine investigation to make clinical diagnosis of BPH. Digital rectal examination, DRE was carried out for all participants to assess clinical parameters of the prostate. Participants with DRE finding of hard, nodular and asymmetric prostate and all those with serum PSA greater than 4 ng/ml had prostate biopsy and samples sent for histopathology, using a dedicated histopathology laboratory.

All participants with histopathology report suggestive of prostate cancer were excluded from the study.

Data Analysis: The data analysis was done with the Statistical Package for Social

Sciences (SPSS) version 25. The data was summarized using mean and standard deviation for continuous variables, while frequencies and percentages was used for categorical variables.

The chi-square test was used to assess the distribution of prostrate volume in relation to the various organisms causing STI. Linear logistic regression and odds ration were used to establish strength of association between BPH and frequency of ejaculation and presence of various causative organisms for STI. All analysis was done at a 95% confidence level and a p-value less than 0.05 was considered statistically significant

Validity/Reliability of Instrument: The questionnaire used was previously pre-tested in a pilot study with similar population. International prostate symptoms score, IPSS was obtained using a standardized scoring system adopted from the American Urological Association Scoring System [15].

Ethical Considerations**:** ethical approval for the study was obtained from the ethical committee of a tertiary educational institution located in the state where study site was located. Informed consent was obtained from participants and all information about the participants were kept strictly confidential.

3. Results

A total of 754 participants were recruited and age ranged from 40 to 81 years. 93.4% were married and 32.7% had been in a marriage relationship for 20 - 30 years. 92.6% practiced monogamy or had only one sexual partner, 0.8% had 2 - 5 partners; 6.6% were single (**Table 1**). 8.2% have had syphilis in the past, 32.6% have had gonorrhea, and 1.1% have had candidiasis (**Table 2**). 40.1% had less than one ejaculation per week, 58.4% had 1 - 5 ejaculations per week, and 1.6% had 6 - 10 ejaculations per week (**Table 3**). 222 (29.4%) had normal prostate, 232 (30.8%) had mildly enlarged prostate, 300 (39.8%) had moderately or severely enlarged prostate. Of the 222 that had normal prostate, 22 (9.9%) has had syphilis in the past while 200 (90.1%) did not have the infection; of the 232 that had mildly enlarged prostate 16 (6.9%) has had syphilis, 216 (93.1%) have not had the infection and of 300 with moderately or severely enlarged prostate, 22 (7.3%) had syphilis, 278 (92.7%) had not the infection. The prevalence of syphilis is similar across the groups, with 9.9% in the normal prostate group, 7.3% in the moderate/severe group, and 6.9% in the mild group. The Chi-square test indicates no significant association ($X^2 = 2.95$, $p = 0.399$). There is a significant difference in the history of gonorrhea. Among those with mildly enlarge prostate, 27.6% have had gonorrhea, while 72.4% had no history of gonorrhea; 34.0% with moderate/severe enlargement have had gonorrhea against 66% with no history of gonorrhea. This suggests a significant association between gonorrhea and prostate levels ($X^2 = 10.11$, $p = 0.018$). The presence of candidiasis is very low and shows no significant difference across the groups, with none in the moderate/severe group, 1.7% in the mild group, and 1.8% in the normal group. The Chi-square test indicates no significant association ($X^2 = 5.30$, $p = 0.148$) (**Table 4**).

Table 1. Demographic distribution of the study subjects.

	Frequency (n = 754)	Percent (%)
Age Groups (years)		
40 - 49	122	16.2
50 - 59	294	39.0
60 - 69	254	33.7
70 - 79	76	10.1
80 - 89	8	1.1
Marital Status		
Married	704	93.4
Single	50	6.6
Years of Marriage (n = 704)		
1 - 10	88	12.5
11 - 20	182	25.9
21 - 30	230	32.7
31 - 40	128	18.2
41 - 50	74	10.5
51 - 60	2	0.3

Table 2. Distribution of STI.

Type STI	n	Percentage (%)
syphilis		
Yes	62	8.2
No	692	91.8
gonorrhea		
Yes	246	32.6
No	508	67.4
candidiasis		
Yes	8	1.1
No	746	98.9

Multiple logistic regression shows 36.7% of those with syphilis and 40.7% without syphilis had moderately/severely enlarge prostate and 63.3% of those with syphilis and 59.9% of those without syphilis had mildly enlarged or normal prostates. There is no significant difference between those with and without syphilis regarding gland enlargement (p = 0.607, OR 0.8, CI 0.5 - 1.4). Similarly, the proportion of individuals with gonorrhoea who have moderate/severe enlargement (41.5%) is similar to those without gonorrhoea (39.0%). This difference is not significant (p = 0.513, OR 1.1, CI 0.8 - 1.5). The proportion of those that reported positive history of candidiasis was not adequate for a reliable regression study. Individuals who have sex once a week or less show a higher prevalence of moderate/severe

enlargement (42.3%) compared to those with more frequent sexual activity (35.7%). This difference approaches significance (p = 0.071, OS 1.3, CI 0.9 - 1.7) (Table 5).

Table 3. Number of sexual partners and frequency of ejaculation/week.

No. of Sexual Partners	n	%
0	50	6.6
1	698	92.6
2	4	0.5
5	2	0.3
Frequency of ejaculation/Week		
<1	302	40.1
1 - 5	440	58.4
6 - 10	12	1.6

Table 4. Distribution of medical history with prostate size.

Risk factor	Moderately/severely enlarged n = 300 (%)	Mildly enlarged n = 232 (%)	Normal n = 222 (%)	Chi-square (p-value)
Syphilis				
Yes	22 (7.3)	16 (6.9)	22 (9.9)	2.95 (0.399)
No	278 (92.7)	216 (93.1)	200 (90.1)	
Gonorrhoea				
Yes	102 (34.0)	64 (27.6)	80 (36.0)	10.11 (0.018)
No	198 (66.0)	168 (72.4)	142 (64.0)	
Candidiasis				
Yes	0 (0.0)	4 (1.7)	4 (1.8)	5.30 (0.148)
No	300 (100.0)	228 (98.3)	208 (98.2)	

Table 5. Regression analysis of risk factors for prostate enlargement.

Risk factor	Moderately/severely enlarged n (%)	Mildly enlarged/ normal n (%)	Total n (%)	Chi-square (p-value)	Odds ratio (95% Confidence Interval)
Syphilis					
Yes	23 (36.7)	38 (63.3)	60 (100.0)	0.26 (0.609)	0.8 (0.5 - 1.4)
No	278 (40.1)	416 (59.9)	694 (100.0)		
Gonorrhea					
Yes	102 (41.5)	144 (58.5)	246 (100.0)	0.42 (0.513)	1.1 (0.8 - 1.5)
No	198 (39.0)	310 (61.0)	508 (100.0)		
Candidiasis					
Yes	1 (12.5)	7 (87.5)	8 (100.0)	5.34 (0.021)	0.5 (0.1 - 1.1)
No	300 (40.2)	446 (59.8)	746 (100.0)		
Frequency of sex					
<2 per week	198 (42.3)	270 (57.7)	468 (100.0)	3.27 (0.071)	1.3 (0.9 - 1.7)
>2 per week	102 (35.7)	184 (64.3)	286 (100.0)		

4. Discussion

The prevalence of syphilis is similar across the groups in this study, with 9.9% in the normal prostate group, 7.3% in the moderately/severely enlarged prostate group, and 6.9% in the mildly enlarged prostate group. Chi-square test for this finding indicates no significant association (p = 0.399) (**Table 4**). Also, multiple logistic regression showed no significant difference between those with and without syphilis regarding prostate gland enlargement (p = 0.607, OR 0.8, CI 0.5 - 1.4) (**Table 5**). However, Syphilis has been linked to prostate enlargement through the mechanism of inflammation similar to all genitourinary infections [8] [9]. A link between clinical prostatitis resulting from sexually transmitted infections, prostate cancer and prostate enlargement has also been established by Breyer *et al.* and those with self-report of syphilis had increase in the prevalence of nocturia by 1.24 times (95% CI 1.09 - 1.43) and reached near significance for physician diagnosis of enlarged prostate or BPH (PR 1.20, 95% CI 0.97 - 1.47) [9]; however in the study done by Sutcliffe *et al.* there was no association between syphilis and pathologies of the prostate [16].

The study by Chen *et al.* amongst different racial groups showed a lower prevalence of syphilis among patients with prostatitis and prostate cancer [17]. This study focused on histologic BPH and the prevalence of syphilis was not significantly different between those with normal prostate and those with moderately or severely enlarged benign prostate.

In this study gonorrhea was the highest STI reported amongst the participants with almost one-third of the participants having history of previous gonorrhea infection. Different studies have shown various prevalence rates of gonorrhea in those with prostatic symptoms because gonorrhea manifests with different clinical symptoms. Painless milkfish urethral discharge is the usual presentation but it could also present as pustules, purpura or dermatitis which may be missed in dark skinned persons and some authors have reported this as reason for lower prevalence [14] [18]. The study done by Cheng *et al.* in United States of America amongst different ethnic groups showed the most commonly reported STI was gonorrhea with a prevalence of 17.1% in the general population studied and a higher prevalence of 52.4% amongst African-Americans [17]. Breyer *et al.* in their study showed that gonorrhea was the most frequent STI in population with prostatic diseases with a prevalence of 5.5%. Gonorrhea was positively associated with prevalent patient diagnosis of an enlarged prostate (PR 1.18, 95% CI 1.09 - 1.29) and nocturia (PR 1.09, 95% CI 1.02 - 1.16), and inversely associated with PSA elevation (PR 0.94, 95% CI 0.88 - 1.00) [9]. Although there was a statistical significant association in the past history of gonorrhea infection in the population used in our study (X^2 = 10.11, p = 0.018) multiple regression analysis however did not show any significant association between gonorrhea and prostate gland enlargement (p = 0.513, OR 1.1, CI 0.8 - 1.5), implying the significant relationship observed between history of previous gonorrhea infection and prostate gland enlargement in this study may be related to processes of data collection or sample size.

The presence of candidiasis in this population is very low and showed no significant difference across the groups. It is possible that participants did not know or understand the clinical manifestations of candida infection and so could not report it. Candida species cause chronic prostatitis, is difficult to detect and has previously been reported to have low frequency amongst participants in other studies [19]. The prevalence in this study is similar to that reported in another study where different species of candida were isolated in 5.8% of samples [20].

The relationship between BPH and frequency of ejaculation has not been studied. The study done by Sutcliffe *et al.* did not show any association between ejaculation frequency in early adulthood and LUTS [8]. Another study by Jacobson *et al.* concluded that frequency of ejaculation has no effect on lower urinary tract symptoms, peak urinary flow rates, or prostate volume and that any apparent protective association may be due to an artifact caused by the confounding effects of age [7]. Increased ejaculation frequency has been observed by Rider *et al.* in a large cohort study to be protective for prostatic cancer [21].

In our study, individuals who had ejaculation once a week or less showed a higher prevalence of moderate/severe enlargement (42.3%) compared to those with more frequent sexual activity (35.7%). The difference approaches significance ($p = 0.071$, OS 1.3, CI 0.9 - 1.7); an odds ratio of 1.3 and narrow confidence interval of 0.9 to 1.7 also suggest a potential association that requires further investigation

5. Conclusion

This study found no association between previous history of syphilis with prostate enlargement. There was an observed causal relationship between both previous histories of gonorrhea infection and reduced frequency of ejaculation with prostate enlargement but these associations do not attain statistical significance and would need further studies.

6. Recommendation

The authors recommend prevention of sexually transmitted infections through abstinence, use of barriers and adherence to legally approved partners, whichever is appropriate; these will reduce chronic inflammatory processes that have been implicated in prostatic diseases. There is need to investigate the causal relationship of these risk factors and BPH further.

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Conflicts of Interest

The authors declare no conflict of interest.

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