Linea Nigra and Gynaecomastia as Risk Factors for Prostate Cancer

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Abstract *Background:* Linea nigra and gynaecomastia are presumably markers of estrogen function and impaired androgen receptor activity in certain disease conditions. Since prostate cancer (PCa) is androgen-dependent, Linea nigra (LN) and gynaecomastia could be potentially non-invasive modalities used in the risk assessment of patients during screening and diagnosis for prostate cancer. *Objectives:* This study aims to determine the relationship between prostate cancer with Linea nigra and gynaecomastia. *Methods*: This is a comparative descriptive cross-sectional study on forty patients, twenty with benign prostatic enlargement (BPE) and twenty with PCa, who presented to the urology outpatient department or were admitted to the urology ward of the hospital. A proforma data collection sheet collated demographic information, clinical presentation, prostate-specific antigen (PSA) levels, and Linea nigra and gynecomastia presence. The data obtained were analyzed using the SPSS Version 25 software. Chi-square and Spearman's Rank analysis was used to test for association and relationship at a 95% confidence interval, with a $p < 0.05$ was considered significant. *Results:* The mean age was 71.0250 ± 11.01years, ranging from 39 to 96years. Linea nigra was seen in two (5%) and absent in thirty-eight (95%) of all the patients. The modal age range was the 70-79-year group, and none had linea nigra. Gynaecomastia was seen in four (10%) and absent in thirty-six (90%) of the patients. One patient in the age range of 50-59years, two in the 60-69years range and one in the 80-89 age range had gynaecomastia. A patient with BPE and three with PCa had gynaecomastia. There was no statistically significant association or relationship between gynaecomastia and prostate cancer. There was a significant association between gynaecomastia and PSA *(p=0.008)* but none between PSA and Linea nigra. *Conclusion:* Our study shows no statistically significant association between Linea nigra and gynaecomastia with prostate cancer. There is an association between gynaecomastia and PSA that require further evaluation. More extensive studies are needed to elucidate any relationships.

Keywords: Gynaecomastia, Linea nigra, Prostate cancer, Risk factors

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1. Introduction

Linea nigra and gynaecomastia are presumably markers of estrogen function and impaired androgen receptor activity in certain disease conditions. [1,2] It appears as a linear hyperpigmented line from the umbilicus to the pubic symphysis. It is more common in pregnant women but can be seen in certain disease conditions associated with hormonal activity and is one of the earliest indicators of pregnancy. [1,2] Reduction in the sensitivity of androgen receptors and lack of estrogen has been postulated as possible causes. [3] Estrogen, augmented by progesterone, stimulates melanin production. [4,5,6] It activates intracellular oestrogen α- and β-receptors in the skin, stimulating melanocytes to increase melanin output. [6]

Gynecomastia is the enlargement of the breast in a male. It is usually due to hormonal imbalance and is typically associated with androgen deprivation therapy for prostate cancer due to increased estrogenic activity following androgen inhibition. [7] Previous studies have evaluated the relationship between benign prostatic enlargement (BPE) and prostate cancer (PCa) with gynaecomastia. [8] Prostate cancer is established to be an androgen-dependent malignancy. LN and gynaecomastia could be non-invasive modalities used in risk assessment screening and diagnosing patients with PCa. This study aims to determine the relationship between prostate cancer with Linea nigra and gynaecomastia.

2. Method

2.1. Study Type

This is a comparative descriptive cross-sectional study.

2.2. Study Area

This study was carried out at the Urology ward of the University of Port Harcourt Teaching hospital, Port Harcourt, Rivers, Nigeria, from August 2021 to November 2021.

2.3. Study Population

The study population included adult male individuals who presented at the outpatient clinic or were admitted to the urology ward of the University of Port Harcourt Teaching Hospital for BPE and prostate cancer. Their clinical notes were obtained, and demographics, clinical presentations, digital rectal examination findings, and prostate-specific antigen (PSA) were recorded.

2.4. Sample and Sampling

A purposive cross-sectional sampling of forty patients, twenty with BPE (control) and twenty with PCa, presented to the urology outpatient department or were admitted to the urology ward of the hospital.

2.5. Data Collection

A proforma data collection sheet collated demographic information, clinical presentation, PSA levels, Linea nigra and gynecomastia presence.

2.6. Data Analysis

The data collected were analyzed using the SPSS Version 25 software. Chi-square and Spearman's Rank analysis was used to test for association and relationship at a 95% confidence interval, with a $p < 0.05$ was considered significant.

3. Results

The mean age was 71.0250 ± 11.01 years, ranging from 39 to 96years. Linea nigra was seen in two (5%) and absent in thirty-eight (95%) of all the patients. The modal age range was the 70-79-year group, and none had Linea nigra. The two (18.2%) who had Linea nigra were between 60-69. One each (5%) with BPE and PCa had Linea nigra. Gynaecomastia was seen in four (10%) and absent in thirty-six (90%) of all the patients. One patient in the age range of 50 -59years, two in the 60-69years range and one in the 80-89 age range had gynaecomastia. A patient with BPE and three with PCa had gynaecomastia. There was no statistically significant association between gynaecomastia with age and prostate cancer. There was a significant relationship between gynaecomastia and PSA *(p=0.008)* but none between PSA and Linea nigra.

Table 1. Shows the demographic characteristics of the study participants

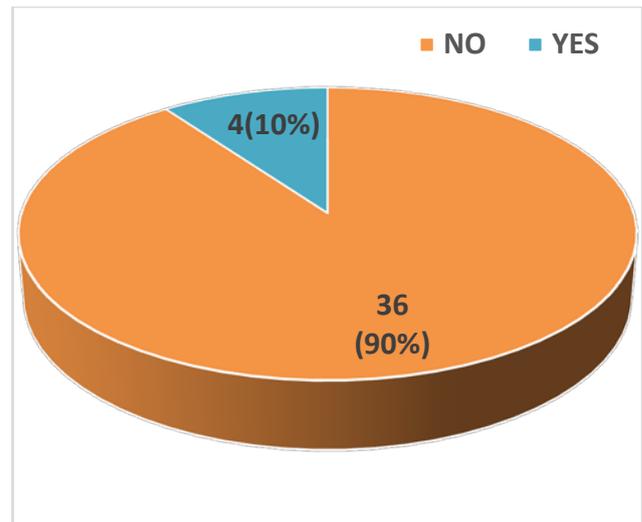|		
	Valid	40
	Missing	0
Mean		71.0250
Median		72.0000
Std. Deviation		11.01395
Range		57.00
Minimum		39.00
Maximum		96.00

Figure 1. Shows the distribution of gynaecomastia in the study population

Table 2. Association between Linea nigra with age, BPE and prostate cancer

	Linea nigra				p-value
	No		Yes		
	n	(%)	n	(%)	
Age group					
<50	2	(100.0)	0	(0.0)	
50-59	3	(100.0)	0	(0.0)	
60-69	9	(81.8)	2	(18.2)	0.352
70-79	16	(100.0)	0	(0.0)	
80-89	7	(100.0)	0	(0.0)	
>90	1	(100.0)	0	(0.0)	
Histology					
BPE	19	(95.0)	1	(5.0)	1.00
Prostate cancer	19	(95.0)	1	(5.0)	
Total	38		2		

Table 3. Shows the association of Linea nigra, PSA levels in BPE patients.

	Linea Nigra				p-value
	No		Yes		
	Mean	SD	Mean	SD	
PSA ng/ml	65.57	130.36	26.20	35.07	0.315

Table 4. Shows the association between gynaecomastia, age, benign prostatic enlargement and prostate cancer

	Gynaecomastia				p-value
	No		Yes		
	n	(%)	n	(%)	
Age group					
<50	2	(100.0)	0	(0.0)	
50-59	2	(66.7)	1	(33.3)	0.430
60-69	9	(81.8)	2	(18.2)	
70-79	16	(100.0)	0	(.0)	
80-89	6	(85.7)	1	(14.3)	
>90	1	(100.0)	0	(0.0)	
Histology					
BPH	19	(95.0)	1	(5.0)	0.292
Prostate cancer	17	(85.0)	3	(15.0)	
Total	36		4		

Table 5. Shows the association between gynaecomastia and prostate-specific antigen levels among prostate cancer patients

	Gynaecomastia				p-value
	No		Yes		
	Mean	SD	Mean	SD	
PSA ng/ml	46.19	73.00	220.36	335.28	0.008

4. Discussion

The search for a simple, noninvasive risk stratification method for prostate cancer is a subject of intense research and investigation by scientists and clinicians worldwide. Since prostate cancer is androgen-dependent, [9,10,11] analysis of physiological and biochemical processes brought about by hormonal changes, such as Linea nigra and gynaecomastia, can provide insight into the milieu interior. Our study participants had a mean age of 71.0250 ± 11.01 ranging from 39 to 96 years, as seen in Table 1. This is similar to a study on patients with benign prostatic hyperplasia in southwestern Nigeria with ages ranging from the 5th decade to >90years. [11,12] A study done to review male cancer patients in a cancer registry between 1980-1996 showed that prostate cancer was the most common cancer in Nigerian men and constitutes 11% of male cancers. The mean age was 71.4 years which is similar to this study. [12]

In our study, only 5% (2) of all the forty patients had Linea nigra (LN), one with BPE {5% (1)} and the other with PCa {5% (1)}. This is entirely different from a study in Ibadan observed Linea nigra in 48% of prostate cancer patients and 26% of BPE patients. [9] This was said to be explicable by chance. There was no significant association of LN with age group and PCa. The expression of Linea nigra is not always uniform, even in pregnancy. One study found up to 15 out of 60 pregnant women had no Linea nigra. [13] An earlier study from Ibadan found 8% of healthy pregnant women had no Linea nigra. [3] The absence of Linea nigra sometimes, despite the usually high levels of estrogen and progesterone in pregnancy, suggests that other physiological mechanisms are likely involved in stimulating melanocyte deposition of melanin in the Linea alba. These factors could modulate the degree of pigmentation responsible for the observed diversity in Linea nigra morphology and expression. [3]

It has also been noted that the Linea alba pigmentation increases in both sex to a high level by about 15 years and subsequently starts to decline, except during pregnancy; use of some medications like spironolactone, cimetidine and disease processes like liver cirrhosis. [3] In our study, none of the sixteen patients in the modal age groups of 70-79years was found to have LN, buttressing the observation that LN tends to fade with age. [3] This mitigates its use as a risk factor marker for prostate cancer.

Gynaecomastia was found in 10% (four) of the study participants, 5% (one) of the BPE and 15% (three) of PCa patients and was not statistically significant. (Table 4) Another study found gynaecomastia in 36% of PCa patients and 12% of BPE patients. [8] There was also no significant association between gynaecomastia, age and PCa. However, patients with gynaecomastia showed a significant relationship with PSA levels, as shown in Table 5. *(p=0.008).* The significance of this finding is unclear, and our small sample size precludes a meaningful deduction.

This study is a pilot study, hence the small number of participants. LN and gynaecomastia, if related to prostate cancer, could be utilized for risk stratification and identification of persons predisposed to BPE and PCa. Both tools could be used in conjunction with standard screening tools such as PSA, DRE and ultrasound to optimize the early detection of BPE and PCa.

5. Conclusion

Our study shows no significant association between Linea nigra and gynaecomastia with prostate cancer. There is an association between gynaecomastia and PSA that require further evaluation. More extensive studies are needed to elucidate any relationships.

Limitations of the Study

The sample size was small, so the study cannot categorically confirm any hypothesis.

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