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Review Article

Is prostate cancer more common and more aggressive in African men?

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ABSTRACT

The highest prostate cancer incidence and mortality rates in the world have been reported among Black African-American men (AAM) living in the United States of America. These rates are significantly higher for AAM compared to White (Caucasian) American men (CAM). However, prostate cancer is not the only malignancy which is more common in AAM compared to White American men or women. Although prostate cancer has the highest Black/White mortality ratio, it is not the only malignancy which has a higher mortality in AAM compared to CAM.

Numerous reports have shown that AAM present with higher grade and stage tumors, higher serum PSA levels, and that they are less likely to receive definitive or curative treatment and have a worse prognosis compared with CAM. It has been suggested that prostate cancer is not only more common, but also more biologically aggressive in AAM compared with CAM. Hypotheses attempting to explain this include genetic differences, dietary factors, higher testosterone levels or increased androgen receptor activity. However, the majority of reports from the USA indicate that, when controlled for major prognostic factors, the outcome for clinically localized as well as advanced prostate cancer does not depend on race. Several studies have indicated that socio-economic factors, decreased awareness of prostate cancer and limited access or decreased utilization of health care contribute to the poorer outcomes in AAM.

Earlier studies have suggested that prostate cancer is relatively rare among indigenous Black men living in Africa. However, cancer incidence data in Africa are likely to underestimate the true rates because of underdiagnosis and underreporting. The frequency distribution of cancers in African countries, as well as more recent data indicate that prostate cancer is not rare among Black men living in Africa and that the incidence is probably similar to that of White men, although not as high as that reported for Black men living outside Africa. It is well documented that African men with prostate cancer present with more advanced disease and that palliative rather than curative treatment is used in the majority of patients. There are no reliable age-adjusted prostate cancer mortality rates available for African countries. However, there is as yet no evidence that prostate cancer in Black men living inside Africa is biologically more aggressive than in other populations.

Key Words: Prostate, cancer, Africa, epidemiology

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INTRODUCTION

It may be argued that race is an ill-defined concept and a socio-political artifice rather than a biological or genetic entity, necessitating the use of self-assignment or self-identification to establish the race of study subjects. Nonetheless, the phenotypic and socio-cultural differences recognized as race remain a reality, which forms the basis

Table 1: Age-adjusted cancer incidence and mortality rates per 100,000 of the population in the USA for the period 1999-2003

Males	Incidence				Mortality		
	White	Black	Black/White ratio		White	Black	Black/White ratio
Myeloma	6.3	12.6	2.0	Prostate	26.7	65.1	2.4
Stomach	9.7	17.4	1.8	Larynx	2.2	5.1	2.3
Larynx	7.3	11.9	1.6	Stomach	5.4	12.4	2.3
Prostate	156	243	1.6	Myeloma	4.4	8.6	2.0
Esophagus	8.4	12.1	1.4	Colon	23.7	33.6	1.4
Pancreas	12.6	15.8	1.3	Esophagus	7.6	10.7	1.4
Lung	88.8	110.6	1.2	Lung	73.8	98.4	1.3
Colon	63.7	70.2	1.1	Pancreas	12	15.7	1.3

Females	Incidence				Mortality		
	White	Black	Black/White ratio		White	Black	Black/White ratio
Myeloma	4	9.3	2.3	Stomach	2.7	6	2.2
Stomach	4.4	9	2.0	Myeloma	2.9	6.4	2.2
Cervix	8.6	13	1.5	Cervix	2.4	5.1	2.1
Pancreas	9.6	13.2	1.4	Colon	16.4	23.7	1.4
Liver	2.7	3.6	1.3	Pancreas	9	12.5	1.4
Colon	45.9	53.5	1.2	Liver	2.8	3.8	1.4

of the current controversy about the incidence and biological aggressiveness of prostate cancer in different population groups [1,2].

Africa is a vast continent with immense geographic and demographic diversity. Indigenous Black Africans form the majority of the populations in sub-Saharan Africa, but do not constitute a homogeneous group, since there are numerous phenotypic, socio-cultural and language differences. Over the centuries, genetic intermingling with the Arab populations of Northern Africa and with European immigrants in various parts of Africa has led to further heterogeneity. The translocation of Black Africans as slaves to the New World, and the later migration to parts of Europe, have led to further complexity in defining Black or African race[3]. Nevertheless, numerous publications have reported racial differences in prostate cancer, and the aim of this paper is to critically analyze the available data.

INCIDENCE

The incidence of prostate cancer varies by as much as 90-fold among different populations, the highest reported rates being among Black African-American men (AAM) in the United States of America (USA), and the lowest rates in Chinese men[4]. Epidemiological studies in the USA show that, since the late 1930s, the incidence and mortality of prostate cancer has been consistently higher among AAM compared with White (Caucasian) American men (CAM). The reported rates have varied from 126.4 to 275.3/100,000

per year among AAM, compared with 74.5 to 172.9/100,000 per year in CAM[5-9].

The age-adjusted cancer incidence and mortality rates per 100,000 of the population in the USA for the period 1999-2003 are shown in Table 1[10].

Calculation of the Black/White incidence ratio shows that myeloma, stomach and larynx cancer have a Black predominance equal to or greater than that of prostate cancer, whereas esophagus, pancreas, lung and colon cancer are also more common in Black than White men. Among females, myeloma, stomach and cervix cancer have a Black predominance equal to or greater than that of prostate cancer in men, whereas pancreas, liver and colon cancer are also more common in Black than White women. Therefore, prostate cancer is by no means the only malignancy which is more common in Black compared to White American men or women in the USA. However, the fact that the incidence of prostate cancer is higher than that of any other malignancy, makes the Black/White predominance of greater importance.

Earlier studies have suggested that prostate cancer is relatively rare among indigenous Black men in Africa, with reported incidence rates of 4 to 11/100,000, compared with 33.7/100,000 for White men living in Africa[4,11-14].

However, cancer incidence data in Africa are likely to underestimate the true rates because of underdiagnosis and underreporting. In South African Black men prostate cancer is the second most common histologically diagnosed malignancy (age-standardised registration rate (ASR) 14.4/100,000), and in White men it is the third most common cancer (ASR 27.1/100,00), exceeded only by squamous and basal cell skin cancer[11]. The frequency distribution of cancers in other African countries also indicates that prostate cancer is not rare[4,12,15-28].

In Jamaica the reported prostate cancer incidence rates among men of African descent were between 15 and 24/100,000. However, a recent study from Jamaica calculated an average age-adjusted incidence rate of 304/100,000[29]. In Brazil the prevalence of prostate cancer was found to be 1.65 times higher in men of African versus European ancestry[30].

MORTALITY

In non-screened populations in the USA the age-adjusted prostate cancer mortality rate has varied in different reports from 46 to 71.1/100,000 per year among AAM compared with 22 to 33.8/100,000 among CAM. The magnitude of the higher mortality rate has been variously reported as 10% to 120%, or 2 to 3 times higher among AAM compared with CAM[5,6,9].

With regard to mortality in the USA, the Black/White ratio is highest for prostate cancer (2.4 times), but larynx and stomach cancer and myeloma also have a 2 times higher mortality in Black compared to White men, whereas colon, esophagus, lung and pancreas cancer also have a higher mortality in Black men (Table 1). Among females there are 6 malignancies which have a higher mortality in Black compared to White women. Therefore, although prostate cancer has the highest Black/White mortality ratio, it is by no means the only malignancy which has a higher mortality in Black compared to White American men and women (Table 1).

African American men and women have 40% and 20% higher death rates from all cancers combined than White men and women, respectively. Most cancers detectable by screening are diagnosed at a later stage and survival rates are lower within each stage of disease in AAM than in CAM[31,32].

AGE AT DIAGNOSIS

Epidemiological data from the USA indicate that AAM present with prostate cancer at a younger age than CAM (difference of about 3 years)[5,33,34]. However, in some reports on men with localized prostate cancer selected

for radical prostatectomy (RP) or radiotherapy (RT) or diagnosed in screening studies, there was no significant age difference, or the mean age of AAM was slightly higher (about 2 years) than for CAM[35-38].

In African countries the peak age for the occurrence of prostate cancer is about a decade earlier than that reported in most developed countries. However, because the incidence of prostate cancer increases with age, the peak age at presentation depends on the life expectancy of the population, which is considerably lower in most African countries than in developed countries[12,16,39].

STAGE AT DIAGNOSIS

Numerous reports have shown that AAM present with higher stage tumors, poorer performance status, and a worse prognosis compared with CAM[5,6,9,33]. This is generally attributed to disparities with respect to socio-economic status, education and availability or utilization of health care services[6,40].

However, some reports indicate that AAM have an increased risk of presenting with advanced prostate cancer even after adjusting for socio-economic factors[6,33]. In more recent studies of men selected for RP in equal access medical systems no significant differences were noted between AAM and CAM with regard to tumor stage[8,33,34,38,41].

Most Black men in Africa still present with locally advanced (from 41% to 96% of patients) or metastatic prostate cancer (from 16% to 59% of cases) and are usually diagnosed because of long-standing symptoms or complications due to advanced prostate cancer[8,12,13,14,16,27,39,42].

Even in countries outside Africa, such as Jamaica, the majority of Black men present with advanced prostate cancer, probably as a result of limited access to, or delayed utilization of medical services[29].

GRADE AT DIAGNOSIS

Numerous studies have reported that AAM present with higher grade prostate cancer compared with CAM.[5,36] However, in some studies of men selected for treatment with RT or RP there were no significant differences in Gleason scores between AAM and CAM[33,34,35,38,41,43].

SERUM PSA AT DIAGNOSIS

Several studies have shown a higher average or mean total PSA (tPSA) and PSA density (PSAD) in AAM compared with CAM, even after controlling for tumor stage[35,41,44].

However, in some studies multivariate analysis including tumor volume showed that race was not significantly correlated with PSA level, indicating that AAM with higher PSA levels despite similar T-stage disease may have larger tumor volumes or clinically undetected metastatic disease, rather than more aggressive tumor biology[38,44,45].

With improved awareness of prostate cancer screening, the racial disparities in serum PSA among men diagnosed with prostate cancer in the USA appear to be decreasing[33,37,44]. The absolute difference in mean tPSA values between the races, whether statistically significant or not, is in fact quite small. Because the distribution of tPSA is not normal, outliers may skew the sample means. Therefore, the median of the population may be the best statistic to compare groups. Only those studies relying on sample means consistently showed significant racial differences in tPSA levels. Most studies found higher standards of deviation from the mean in the AAM group, indicating that the higher mean tPSA levels in AAM groups may be due to a few very high outlier values.

SCREENING

In the USA, a smaller proportion of AAM compared with CAM take part in voluntary

screening studies, and a smaller proportion undergo recommended prostate biopsies, especially in lower income areas[46]. A similar problem was reported from South Africa, where a much lower proportion of Black compared with White men in an early detection study complied with the recommendation to undergo prostate biopsy[47].

In many African countries serum PSA, transrectal ultrasound (TRUS) and needle biopsy facilities are not available, therefore the diagnosis of prostate cancer is made clinically or after open or (rarely) transurethral prostatectomy[13,39,48].

TREATMENT

Some studies have suggested that AAM are less likely than CAM in the USA to receive definitive or curative treatment for localized prostate cancer, and that AAM are more likely to undergo bilateral orchidectomy (BO) than CAM regardless of income level[34,49]. AAM appear to be less likely than CAM to undergo RP, and more likely to undergo RT[36,49,50].

However, some authors found no racial disparity in the use of RP when they controlled for poverty, race and age. In equal access medical care systems there appear to be no stage-specific differences in treatment received and survival rates between AAM and CAM[44,50].

In most African countries the treatment of choice for advanced prostate cancer is BO (despite cultural aversion to the procedure) because it eliminates the problem of cost and compliance with medical treatment. For economic reasons, oral diethylstilbestrol (DES) is often used instead of luteinizing hormone releasing hormone (LHRH) agonists or anti-androgens[12,16,51].

SURVIVAL

The greater age-adjusted prostate cancer mortality rate among AAM compared with CAM in the USA may result from the higher incidence, as well as higher tumor stage and grade at presentation, or lower utilization of curative treatment modalities among AAM. However, it has also been suggested that prostate cancer is biologically more aggressive in AAM compared with CAM.

Several studies have reported a worse survival among AAM even after correcting for clinical stage at diagnosis.[5,33,35] Some authors have suggested that, stage for stage, AAM and CAM have similar survival rates, whereas others suggested that the poorer survival among AAM was only observed when they presented at a younger age (<70 years) or with local or regional disease.[5,6] In some studies of men with clinically localized prostate cancer treated with RP or RT, multivariate analysis showed a significantly worse survival among AAM compared with CAM[35,41].

However, in numerous studies of men treated with RP or RT there was no difference in survival between racial groups after multivariate analysis controlling for pretreatment cancer severity[6,34,35,36,41].

There are no reliable age-adjusted prostate cancer mortality rates available for African countries. A report from the United Kingdom reported a 70% higher prostate cancer mortality rate for Caribbean immigrants of African descent. However, as mortality is determined by both incidence and case fatality, it is not possible to directly infer whether this reflects differences in survival[52].

Meta-analysis has shown that most studies investigating racial differences in prostate cancer treatment outcomes over the past 10 years found no difference between races after controlling for tumor and patient characteristics. In one study, socio-economic status explained 50% and surgical treatment rates approximately 34% of the differences in survival between AAM and CAM[53-55].

True prostate cancer rates for Africans are most probably underestimated by the International Agency for Research on Cancer

(IARC). Unfortunately, the cancer data available from most African countries do not permit valid global comparisons of prostate cancer incidence and mortality[56].

EXPLANATION OF RACIAL DIFFERENCES

Hypotheses attempting to explain the higher incidence of prostate cancer among AAM include genetic differences (e.g. in the genes controlling the androgen receptor)[6,57,58] dietary factors (high fat and red meat intake)[4,5,59] and higher testosterone levels or increased androgen receptor activity in AAM. However, there is very little evidence to support the postulate of racial differences in serum or prostatic tissue androgen levels[57,58].

Data showing a younger age at presentation and greater risk of mortality suggest that prostate cancer in AAM is biologically more aggressive than in CAM[35]. However, the majority of reports from the USA indicate that, when controlled for major prognostic factors, the outcome for clinically localized as well as advanced prostate cancer does not depend on race[6,38].

Several studies have indicated that socio-economic factors, decreased awareness and limited access or decreased utilization of health care contribute to the poorer outcomes in AAM, even after adjusting for differences in pretreatment disease characteristics[35,38,41,60].

From 1946 to 1990 the overall 5-year mortality in the USA was generally higher among Black compared with White patients for cancers of the oropharynx, colorectum, cervix, and female breast. This has been ascribed to lower socio-economic status and more advanced disease stage at diagnosis[5,61,62].

In Africa the reported incidence rates of prostate cancer in different countries correlate directly with the per capita gross national product (GNP), i.e. countries with the highest incidence rates have the highest per capita GNP.[12] One explanation may be that the risk of prostate cancer is related to industrialization, environmental pollution or dietary factors in more affluent populations. However, a more likely explanation is that increased diagnosis and reporting of prostate cancer is responsible for the higher incidence rates. Unfortunately, true age-adjusted incidence and mortality rates for prostate cancer are not available in most African countries, because reliable cancer registries do not exist.

The calculation of reliable incidence and mortality rates depends on accurate diagnosis and reporting of all cases, as well as accurate and complete population statistics. If all cases are recorded, but the population number is underestimated, false high rates will be calculated. In a study from the USA, adjusting the data for population density and socio-economic status eliminated the racial differences for some cancers, raising the question whether relatively more unreliable population statistics among AAM could be responsible for a falsely high prostate cancer incidence in the USA[5].

CONCLUSIONS

Although the scientific evidence is deficient, the incidence of prostate cancer among Black men living inside Africa is probably similar to that of White men, but probably not as high as that reported for Black men living outside Africa. The increased prostate cancer mortality among Black men reported in the USA is probably due to higher stage at presentation or lower utilization of curative treatment, rather than greater biological tumor aggressivity. There is as yet no evidence that prostate cancer in Black men living inside Africa is biologically more aggressive than in other populations.

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