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Incidence and Survival Rates for Young Blacks With Nasopharyngeal Carcinoma in the United States

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Objectives: To compare the incidence rates of nasopharyngeal carcinoma (NPC) among US black, white, and Asian/Pacific Islander (Asian) populations, with a focus on those diagnosed before age 20 years and between ages 20 and 29 years. Our secondary objective was to determine differences in survival rates between US blacks, whites, and Asians with NPC who were younger than 30 years.

Design: Data from the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) tumor registry system were used to determine incidence and survival rates for cases of NPC diagnosed in the specified age groups between 1973 and 2002.

Patients: Blacks, whites, and Asians younger than 30 years with NPC.

Main Outcome Measures: Incidence rates and 2- and 5-year survival rates.

Results: From 1973 to 2002, incidence rates per 1 million persons, adjusted to the 2000 standard population,

for blacks, whites, and Asians younger than 20 years with NPC were 1.61 (n=43), 0.61 (n=99), and 0.95 (n=18), respectively. The incidence rate ratio of blacks to Asians younger than 20 years was 1.69 (95% confidence interval [CI], 0.96-3.12) ($P=.07$), while the rate ratio for blacks to whites was 2.66 (95% CI, 1.82-3.85) ($P<.001$). From ages 20 to 29 years, rates increased slightly in blacks (1.87) and whites (0.96), while increasing dramatically in Asians (7.18). Two- and 5-year relative survival rates in blacks younger than 30 years were 84% and 64%, respectively, with little variation between races in this age group.

Conclusions: Blacks younger than 20 years have increased incidence rates of NPC relative to whites and may be the only group having a higher NPC incidence rate than Asians. Two- and 5-year survival rates of blacks, whites, and Asians younger than 30 years with NPC are similar.

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NASOPHARYNGEAL CARCINOMA (NPC) is a rare disease in the United States, with an annual incidence rate of 7 cases diagnosed per 1 million persons based on National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) data from 1973 to 2002 (www.seer.cancer.gov). However, the incidence rates are much higher in Asia, with 150 to 500 annual cases per 1 million in southern China, and 300 to 800 per 1 million in some Cantonese regions of southern China.^{1,2} First-generation Chinese immigrants to the United States maintain this high incidence rate, while their descendants born in the United States show a decreased incidence.³ Incidence rates of NPC in Hong Kong and Singapore have decreased in recent years but remain substantially elevated relative to white populations in the

West.⁴ Environmental factors such as diet (smoked fish and nitrosamines), infection (Epstein-Barr virus [EBV]), and genetics (HLA-A2) are associated with the development of NPC.⁵

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Histologic subtypes of NPC are characterized by differences in cause and prognosis. World Health Organization (WHO)⁶ type 1 histologic subtype (keratinizing squamous carcinoma) is more common in North America (25% of all patients with NPC) than in Southern China (2%).^{7,8} In areas considered nonendemic, such as the United States and Western Europe, type 1 NPC is associated with tobacco and alcohol use and morphologically resembles other head and neck squamous

Table 1. Nasopharyngeal Carcinoma Incidence Rates per 1 Million Population by Race*

Age at Diagnosis, y	Incidence Rate (95% Confidence Interval)		
	Black	White	Asian/Other†
<20	1.61 (1.17-2.18) (n = 43)	0.61 (0.49-0.74) (n = 99)	0.95 (0.57-1.51) (n = 18)
20-29	1.87 (1.21-2.77) (n = 25)	0.96 (0.77-1.18) (n = 86)	7.18 (5.64-9.00) (n = 75)
30-44	5.30 (4.22-6.59) (n = 84)	2.26 (2.00-2.55) (n = 274)	32.65 (29.62-35.91) (n = 75)
≥45	14.16 (12.43-16.11) (n = 249)	10.81 (10.34-11.29) (n = 2018)	65.70 (61.78-69.85) (n = 1071)

*Incidence rates are age-adjusted to the 2000 US standard population.

†Prior to 1992, the Surveillance, Epidemiology, and End Results database did not stratify races beyond black, white, and other for purposes of calculating incidence rates. Asian/other is composed of 72% Asians/Pacific Islanders, 23% other, and 3% Native American/Alaska Native groups.

cell carcinomas. The WHO type 1 carcinomas are also associated with increased EBV infections, especially in regions endemic for NPC. Type 1 carcinomas tend to remain localized, without nodal spread. Type 1 is not as responsive to irradiation as WHO type 3 (undifferentiated carcinoma) and is associated with poorer 5-year survival rates, despite the tendency to remain localized.^{8,9}

World Health Organization types 3 and 2 (nonkeratinizing carcinoma) subtypes are associated with EBV. Although type 3 is undifferentiated and tends to disseminate, it carries a relatively favorable prognosis.⁹ It is the most common histologic subtype in Asia, where it makes up 95% of NPCs.⁸ Type 2 is the least common, has variable sensitivity to irradiation, and has intermediate survival rates relative to types 1 and 3.⁸

The peak incidence of NPC in Asia occurs in persons aged between 40 and 50 years. In North Africa, however, a bimodal prevalence exists, with a relatively small peak present in blacks between ages 10 and 25 years; the major prevalence peak in North Africa occurs in adults at around age 50 years, similar to that in Asia.¹⁰ Early studies reported a similar trend in the United States during the 1960s and early 1980s, with an increased incidence in blacks younger than 30 years.¹¹⁻¹³

Much of the epidemiologic focus on NPC in the United States has been directed toward Asians/Pacific Islanders (Asians). In the United States, incidence rates for all races and ages have remained stable over the last 30 years, while survival rates have gradually improved across all races.¹⁴ A recent single-institution, retrospective review was performed at our institution, the University of North Carolina Chapel Hill, and the findings suggest that NPC is more common in black populations younger than 25 years (n=10) than in groups of other races younger than 25 years (n=5).¹⁵ This review prompted a population-based epidemiologic study using the SEER tumor registry system. North Carolina is not represented in the 9 SEER registries used in the present study.

The primary objective of our study was to compare the incidence rates of NPC in US blacks, whites, and Asians over the last 30 years using data from a national population-based registry system, with a focus on those diagnosed before age 20 years and between ages 20 and 29 years. Our secondary objective was to determine dif-

ferences in survival rates between US blacks, whites, and Asians with NPC who were younger than 30 years.

METHODS

The SEER tumor registry system was used to determine incidence and survival rates for cases of NPC. Incidence rates were determined for those diagnosed before age 20 years, from ages 20 to 29 years, from ages 30 to 44 years, and at age 45 years or older in the United States during 1973 to 2002. The SEER*Stat program (version 6.1.4; National Cancer Institute, Bethesda, Md) was used to calculate incidence rates for the different age groups, age-adjusted to the 2000 US standard population. Age groups were selected so that those diagnosed before age 20 years could be compared with more than 1 group. Seven registries that date back to 1973 were used (Connecticut, Iowa, Utah, Hawaii, New Mexico, Detroit, Mich, and San Francisco-Oakland, Calif) in addition to 2 registries that were added in 1975 (Atlanta, Ga, and Seattle-Puget Sound, Wash).

The incidence rate ratio was used to assess differences in incidence rates between racial groups. A rate ratio of 1.0 indicates no difference. The SEER*Stat software was used to calculate statistical significance of differences in incidence rates between groups.

Incidence rates of WHO classifications were determined according to the following *International Statistical Classification of Diseases, 10th Revision* codes: WHO type 3 codes 8020, 8021, and 8082 (undifferentiated, lymphoepithelial, and anaplastic carcinomas), type 2 codes 8072 and 8073 (small- and large-cell nonkeratinizing epidermoid carcinomas), and type 1 codes 8070 and 8071 (keratinizing squamous cell carcinoma).

Two- and 5-year survival analyses were performed using SEER*Stat software for blacks, whites, and Asians in age groups younger than 30, 30 to 44, and 45 years or older. Relative survival was calculated with the actuarial method.

RESULTS

Incidence rates are listed in **Table 1**. Between 1973 and 2002, the incidence rates of NPC per 1 million for blacks, whites, and Asians younger than 20 years were 1.61, 0.61, and 0.95, respectively. For the age group 20 to 29 years, rates were elevated in blacks (1.87) and whites (0.96), while increasing dramatically in Asians (7.18). In cases of NPC diagnosed between the ages of 30 and 44 years, incidence rates per 1 million increased in whites (2.26),

Table 2. Nasopharyngeal Carcinoma Incidence Rate Ratios of Blacks to Other Groups*

Age at Diagnosis, y	Whites	P Value	Asians/Others	P Value
<20	2.66 (1.82-3.85)	<.001	1.69 (0.96-3.12)	.07
20-29	1.96 (1.20-3.09)	.01	0.26 (0.16-0.42)	<.001
30-44	2.34 (1.81-3.02)	<.001	0.16 (0.13-0.21)	<.001
>45	1.31 (1.14-1.50)	<.001	0.22 (0.19-0.25)	<.001

*Incidence rate ratios indicate differences in incidence rates between the 2 races being compared. A rate ratio of 1 indicates no difference.

blacks (5.30), and Asians (32.65). In cases diagnosed at age 45 years or older, the incidence rates increased in whites (10.81), blacks (14.16), and Asians (65.70).

Incidence rate ratios for blacks compared with whites and Asians are listed in **Table 2**. Incidence rate ratios in blacks younger than 20 years were 1.69 (95% confidence interval [CI], 0.96-3.12) ($P=.07$) and 2.66 (95% CI, 1.82-3.85) ($P<.001$) relative to Asians and whites, respectively. Rate ratios in blacks aged 20 to 29 years remained elevated (1.96; 95% CI, 1.20-3.09) relative to whites, while the rate ratio of blacks to Asians decreased (0.26; 95% CI, 0.16-0.42) and remained near 0.2 for all older ages. Blacks aged 30 to 44 years continued to have elevated rate ratios relative to whites (2.34; 95% CI, 1.81-3.02), while the rate ratio in blacks 45 years or older decreased (1.31; 95% CI, 1.14-1.50), indicating a convergence of incidence with whites. Blacks younger than 19 years showed a trend toward having a rate 1.7 times that of Asians.

Thirty-seven percent (37/99) of whites younger than 20 years with NPC were in metropolitan SEER registries (San Francisco Bay area, Detroit, and Atlanta), while 79% (34/43) of blacks in this age group were in these registries. Within these 3 metropolitan SEER registries, the incidence rate ratio of blacks with NPC to whites younger than age 20 and between ages 20 and 29 years were 2.48 (95% CI, 1.51-4.07) ($P<.001$) and 2.29 (95% CI, 1.20-4.27) ($P=.01$), respectively. These rate ratios are similar to ratios computed for all of the SEER registries.

Of all new cases of blacks with NPC in the 9 SEER registries used to compute the incidence rates, 17% (68/401) were diagnosed at age 30 years or younger. Eleven percent (43/401) of these were diagnosed in patients younger than 20 years, and 6% (25/401) were in patients aged 20 to 29 years. New cases occurring in whites and Asians younger than 30 years made up 7.5% (185/2477) and 5.8% (93/1599) of all new cases found in these 2 respective groups.

Incidence rates for the 29-year time period from 1973 to 2002 were divided into 2 segments, 1973 to 1988 and 1989 to 2002, to determine if changes occurred between the 2 time periods (**Table 3**). While there are slight variations in rates, the 95% CIs overlap considerably for all groups, with the exception of whites aged 45 years or older. The incidence rates in this group decreased from 11.9 (95% CI, 11.2-12.7) to 9.9 (95% CI, 9.3-10.5).

The NPC incidence rates of WHO histologic types were calculated and are listed in **Table 4**. Among all new cases of blacks with WHO type 3 NPC reported to the SEER registries between 1973 and 2002, 31% (27/87) were

younger than 30 years. Of all whites and Asians diagnosed with WHO type 3 NPC, 14.8% (54/366) and 8.2% (38/461), respectively, were younger than 30 years. Ten percent (19/187) of new cases of blacks with WHO type 1 NPC were younger than 30 years, while 3.0% and 4.8% of new type 1 NPC in whites and Asians, respectively, were in patients younger than 30 years. Type 2 NPC is the rarest histologic type, accounting for 10% to 15% of all NPCs; cases of type 2 NPC diagnosed in patients younger than 30 years were too few to yield statistically significant data.

Relative 2- and 5-year survival rates in patients with NPC diagnosed younger than 30 years were similar for blacks, whites, and Asians (**Table 5**). Relative 2-year survival was 84.3%, 82.7%, and 87.6% for blacks, whites, and Asians, respectively.

COMMENT

Studies using data acquired during the 1960s through the early 1980s have reported that a relatively small second peak in NPC may exist in young blacks in the United States.¹¹⁻¹³ The patterns seen have all been similar to the results of our study. Two reports^{12,13} used the SEER databases, and 1 of these studies¹² extracted data dating from 1969 through 1976 from 2 separate databases and combined the data sets to estimate incidence. The 1992 article¹³ used data from 1973 through 1986. Both studies reported a trend of a minor incidence peak in NPC in blacks younger than 19 years; however, the numbers of blacks younger than 19 years were limited in both ($n=4^{12}$ and $n=19^{13}$). Neither of these reports showed statistical significance of the increased NPC incidence in blacks relative to whites. The 1977 National Cancer Institute study by Greene and colleagues¹¹ examined death certificates of children in the United States younger than 20 years from 1960 to 1969. The study found that the NPC incidence rate ratio for blacks ($n=36$) relative to whites ($n=108$) younger than 20 years was 2.2 ($P<.001$). No study had enough cases of Asians to make a comparison between blacks and Asians in young age groups.

A recent retrospective review with an accompanying literature review analyzed the racial demographics of those younger than 30 years with NPC.¹⁵ In the cohorts used for these reviews, 55% to 67% of patients with NPC younger than 30 years were black. This high proportion of young blacks with NPC is consistent with our population-based epidemiologic data.

Table 3. Nasopharyngeal Carcinoma Incidence Rates and Black Incident Rate Ratios*

Age at Diagnosis, y	Study Years	Incidence Rate (95% CI)	Black Incident Rate Ratio	P Value
<30	1973-1987			
	Black (n = 33)	1.80 (1.24-2.54)	1.00	NA
	White (n = 97)	0.73 (0.59-0.90)	2.45†	<.001
	Asian/other (n = 36)	2.89 (2.02-4.02)	0.62‡	<.07
	1988-2002			
	Black (n = 35)	1.60 (1.12-1.24)	1.00	NA
	White (n = 88)	0.70 (0.56-0.87)	2.28†	<.001
	Asian/other (n = 57)	2.91 (2.20-3.78)	0.55‡	.01
	30-44	1973-1987		
Black (n = 33)	5.76 (3.92-8.21)	1.00	NA	
White (n = 126)	2.56 (2.12-3.06)	2.25†	<.001	
Asian/other (n = 152)	35.93 (30.32-42.31)	0.21‡	<.001	
1988-2002				
Black (n = 51)	5.03 (3.73-6.63)	1.00	NA	
White (n = 148)	2.07 (1.75-2.43)	2.43†	<.001	
Asian/other (n = 283)	31.15 (27.60-35.03)	0.16‡	<.001	
≥45	1973-1987			
	Black (n = 109)	14.37 (11.75-17.62)	1.00	NA
	White (n = 1018)	11.92 (11.18-12.69)	1.21†	.08
	Asian/other (n = 368)	67.82 (60.90-75.52)	0.21‡	<.001
	1988-2002			
	Black (n = 140)	13.78 (11.56-16.35)	1.00	NA
	White (n = 1000)	9.87 (9.27-10.50)	1.40†	<.001
	Asian/other (n = 703)	65.02 (60.26-70.11)	0.21‡	<.001

Abbreviations: CI, confidence interval; NA, not applicable.

*Incidence rates are expressed per 1 million population and age-adjusted to the 2000 US standard population.

†Ratio of incidence rate in blacks to incidence rate in whites.

‡Ratio of incidence rate in blacks to incidence rate in Asians/others.

Table 4. Nasopharyngeal Carcinoma Incidence Rates by WHO Type*

Age at Diagnosis, y	All Races	Blacks	Whites	Asians/Others
Undifferentiated Carcinoma (WHO Type 3)				
<30	0.36 (0.30-0.43) (n = 119)	0.69 (0.45-1.00) (n = 27)	0.21 (0.16-0.27) (n = 54)	1.20 (0.85-1.66) (n = 38)
≥30	2.18 (2.03-2.33) (n = 800)	1.81 (1.37-2.37) (n = 60)	1.01 (0.90-1.13) (n = 312)	14.54 (13.17-16.04) (n = 423)
<30, %†	13.0	31.0	14.8	8.2
Squamous Cell Carcinoma (WHO Type 1)				
<30	0.25 (0.03-0.20) (n = 85)	0.47 (0.28-0.73) (n = 19)	0.15 (0.11-0.21) (n = 41)	0.74 (0.47-1.11) (n = 24)
≥30	5.31 (5.08-5.55) (n = 1963)	5.33 (4.54-6.25) (n = 168)	4.21 (3.98-4.44) (n = 1314)	16.51 (15.04-18.12) (n = 476)
<30, %†	4.2	10.2	3.0	4.8

Abbreviations: CI, confidence interval; WHO, World Health Organization.⁶

*Unless otherwise indicated, data are reported as incidence rate per 1 million population (95% CI). Incidence rates are age-adjusted to the 2000 US standard population.

†Number of cases diagnosed in patients younger than 30 years as a percentage of cases of all ages.

A recent epidemiologic analysis of NPC in Los Angeles, Calif, and San Francisco suggests that incidence in Asians has decreased over the last 10 years in these locations, which may follow trends of decreased incidence in Hong Kong and Singapore.⁴ With a decrease in incidence, however, Asians still account for most of the cases in and outside of the United States. With an incidence rate ratio of 1.69 (95% CI, 0.96-3.12) ($P = .07$), blacks younger than 19 years may be the only age group in the United States that has a higher incidence of NPC than Asians.

Additionally, epidemiologic studies of NPC in North Africa have shown a separate small incidence peak in patients younger than 25 years.¹⁰ This young North African population is thought to represent the highest known incidence of NPC that is primarily EBV mediated.¹⁶ However, a large proportion of the North African population is of Arab descent; the sources used to obtain these data did not report the incidence rates stratified by race, so it is unknown what proportion of this population is black.

Table 5. Relative Survival Rates by Age at Diagnosis*

Survival Time, y	Age at Diagnosis, y	Blacks	Whites	Asians/Others
2	<30	84.3 (4.7) (n = 67)	82.7 (2.9) (n = 182)	87.6 (3.6) (n = 90)
	30-44	62.7 (5.7) (n = 80)	76.3 (2.7) (n = 262)	86.1 (1.8) (n = 418)
	≥45	57.3 (3.7) (n = 214)	56.5 (1.3) (n = 1176)	76.1 (1.5) (n = 999)
5	<30	64.1 (6.5) (n = 67)	67.1 (3.6) (n = 182)	69.4 (5.1) (n = 90)
	30-44	47.9 (6.0) (n = 80)	58.9 (3.2) (n = 262)	67.2 (2.5) (n = 418)
	≥45	32.3 (3.7) (n = 214)	39.7 (1.4) (n = 1176)	56.2 (1.8) (n = 999)

*Data are reported as percentage of patients achieving specified survival (standard error), based on actuarial analysis of relative survival.

The SEER registry system is the major population-based source of cancer incidence, mortality, and survival in the United States, representing approximately 14% of the US population. While the SEER is the best system available to investigate population-based cancer epidemiology in the United States, it has inherent limitations. Errors may occur with data entry such as site, histologic coding, and patient follow-up used to compute survival periods. Sampling bias may occur owing to the geographic limits of the registries. We addressed this by identifying the possible underrepresentation of young blacks with NPC outside of metropolitan areas, while young whites were well represented in these areas. For age groups younger than 20 years and 20 to 29 years, rate ratios of blacks to whites with NPC were computed only for those living in the 3 available metropolitan SEER registries (San Francisco Bay area, Detroit, and Atlanta). The ratios of blacks to whites in metropolitan areas were high, and this was similar to the ratios observed for all the SEER geographic areas.

Approximately 95% of all ethnic groups across the world are asymptomatic EBV carriers, implying that other factors must be associated with NPC pathogenesis. Genetic and/or environmental factors may lead to cellular or immune alterations, which, in the setting of EBV infection, give rise to NPC.^{17,18} Latent membrane protein 1 (LMP1) is the primary transforming protein of EBV; it is essential for EBV-induced B lymphocyte immortalization in vitro, and it functions as a classic oncogene in rodent models.¹⁷ In a Korean study, LMP1 positivity was seen more frequently in patients with NPC who were younger than 50 years than in those older than 50 years ($P = .04$).¹⁹

Epstein-Barr virus persists in B lymphocytes and in the basal epithelial layer of oropharyngeal cells, resulting in an aberrant autoimmune response.²⁰ Tumor-associated autoantibodies and autoantibodies to cell cycle regulators such as cytoskeleton and nuclear antigens are involved in the autoimmunity.¹⁶ In a study done in North Africa, antitubulin IgG autoantibodies were found in 40% of patients with NPC who were younger than 25 years and in 13% of older patients ($P = .01$).¹⁶ Similar cellular or immune defects may be prevalent in young blacks in the United States with NPC.

Previous studies concluded that survival in Asians is higher than among blacks and whites for all ages.¹⁴ This survival advantage is thought to be related to increased incidence of WHO type 3 NPC in Asians, which carries a better prognosis. When Asian and white cases of all ages were matched by age, sex, WHO type, stage, and treatment method, no differences in disease-specific survival were seen.²¹ Survival analysis of the 3 age groups in our study showed that 2- and 5-year relative survival rates among patients younger than 30 years appears relatively constant across blacks, whites, and Asians. After age 30 years, Asians had better survival rates at 2 and 5 years. Whites aged 30 to 45 years appeared to have better 2- and 5-year survival rates than blacks. The number of cases younger than 30 years limited our ability to stratify the analyses based on stage and WHO type.

Even with 30 years of data accumulated through the SEER registries, the number of cases of NPC remains limited. Compared with earlier studies that used SEER data, however, there are more available cases of NPC in patients younger than 30 years in the registries, which allows the epidemiologic factors to be further investigated. We have shown statistically significant increased NPC incidence rates in young blacks relative to whites and a trend toward increased incidence relative to Asians. Further descriptive epidemiologic and etiologic research on NPC among blacks is warranted.

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Author Contributions: Mr Richey had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Richey, Olshan, George, Shores, Zanation, Cannon, and Weissler. *Acquisition of data:* Richey, Olshan, Zanation, and Weissler. *Analysis and interpretation of data:* Richey, Olshan, Cannon, and Weissler. *Drafting of the manuscript:* Richey, Olshan, Shores, and Weissler. *Critical revision of the manuscript for important intellectual content:* Richey, Olshan, George, Zanation,

Cannon, and Weissler. *Statistical analysis*: Richey, Olshan, and George. *Obtained funding*: Richey. *Administrative, technical, and material support*: Richey, George, Shores, and Cannon. *Study supervision*: Richey, Zanation, and Weissler. **Financial Disclosure**: None reported.

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