# Prevalence of Monoclonal Gammopathy of Undetermined Significance in Black South African Men

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## ABSTRACT

**Background:** Both multiple myeloma and its precursor, monoclonal gammopathy of undetermined significance (MGUS), occur twice as often within Black compared with White populations, suggesting that racial disparities lie within the development of MGUS. Nonetheless, MGUS has been studied mainly in White cohorts; the study that first described the natural history of MGUS was conducted in 97.3% White Olmsted County, Minnesota.

**Methods:** We determined the prevalence of MGUS among 386 Black South African (SA) men >30 years at Chris Hani Baragwanath Hospital in Johannesburg. We conducted serum protein electrophoresis and free light chain quantification to define MGUS by the same criteria as the Olmsted County studies. We also investigated the association between MGUS and various clinical factors, including human immunodeficiency virus (HIV) infection and smoking.

**Results:** We found the prevalence of MGUS to be 8.03% [95% confidence interval (CI), 5.32–10.74], nearly 1.6-fold higher than in the White Olmsted County male population. In a univariable logistic regression model, MGUS was associated with HIV status (OR, 2.39; 95% CI, 0.95–5.49), but in an adjusted model that included body mass index and cigarette use, the association was not statistically significant. Those who were current (vs. never) cigarette smokers were more likely to have MGUS in both univariable (OR, 5.60; 95% CI, 2.16–17.42) and multivariable models (OR, 4.49; 95% CI, 1.63–14.56).

**Conclusions:** The prevalence of MGUS in Black SA men is substantially higher than in White populations and may be associated with HIV status and cigarette use.

**Impact:** Racial disparities in MGUS exist and may be associated with potentially modifiable risk factors.

## Introduction

Racial disparities are well recognized in multiple myeloma, with the age-adjusted incidence twice as high in Black populations compared with White populations (1, 2). The precursor to multiple myeloma, monoclonal gammopathy of undetermined significance (MGUS), is characterized by plasma cells' aberrant production of a monoclonal protein. Like multiple myeloma, MGUS disproportionately affects Black individuals (2). Progression from MGUS to multiple myeloma is observed when the monoclonal protein causes end-organ damage; the cumulative risk of progression is similar between races (1), occurring at a rate of approximately 1% per year (3). Thus, the racial disparities of multiple myeloma appear to arise from the initial development of MGUS, not from its progression to malignancy.

One of the first large-scale studies of MGUS was conducted among 21,463 of the 28,000 residents ages 50 years and older in Olmsted County, Minnesota, a 97.3% White population (4). The prevalence of MGUS (both heavy- and light-chain disease) standardized for age was 4.2% (5). Other published epidemiologic studies, all of which were in largely White populations and conducted prior to the identification of light-chain disease, found heavy-chain MGUS prevalence to be less than 3.6% (6–13).

However, a subsequent analysis of ICD-9 codes assigned to all patients hospitalized at least once within the U.S. Veterans Affairs system over a 16-year period found that the prevalence of "monoclonal proteinemia" among Black patients was 3.0 times higher than that among White patients (Black veterans $n = 748{,}020$; White veterans $n = 3{,}248{,}795$; ref. 1), and another analysis of stored samples from the National Health and Nutritional Examination Survey (NHANES) III demonstrated the adjusted prevalence of MGUS to be 3.7% in Black individuals over the age of 50 ($n = 2331$) compared with 2.3% in White individuals of the same age ($n = 7{,}051$; $P < 0.001$; ref. 14). The relative risk of MGUS was even greater between Black and White populations at younger ages, with further examination of NHANES III revealing the prevalence in the Black cohort 10 to 49 years of age ($n = 4{,}073$) to be 0.88% compared with 0.22% in the White cohort of the same age group ($n = 3{,}595$; $P = 0.001$), partly explained by an earlier age of onset of MGUS within the Black cohort (15). The only published study of MGUS prevalence in a Black African population found that among 917 Ghanaian men ages 50 to 70 years, the prevalence of heavy-chain MGUS was 5.84% (16); for comparison, the prevalence among males ages 50 to 70 years in the original Olmsted County study was 2.97% (16).

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The prevalence of MGUS has also been found to vary by human immunodeficiency virus (HIV) status; estimates of MGUS within HIV-infected populations range from 3% to 26% (17–21). Several mechanisms have been postulated to explain the role of HIV in the development of MGUS, including HIV-specific oligoclonal and monoclonal proteins (21), B-cell dysregulation in the setting of T-cell impairment (21, 22), and B-cell hyperplasia in the setting of chronic stimulation (22). In a retrospective study of patients who had received an HIV test over a 10-year period in a hospital database, MGUS was found in 19.3% of the HIV-infected patients ($n = 10{,}293$) but in only 8.2% of the HIV-noninfected patients ($n = 171{,}588$; ref. 21); however, 13.4% of the HIV-infected patients were tested for MGUS compared with only 3.8% of the HIV-noninfected patients (21), suggesting that there may have been more indication to test in the HIV-infected population. This selection bias warrants further exploration of the association.

In this study, we explored the prevalence of MGUS and the association between MGUS and various clinical factors, including HIV, in a population of Black South African men.

## Materials and Methods

The Men of African Descent with Cancer of the Prostate (MADCaP) study (U01-CA184374, PI Timothy Rebbeck) has collected clinical data, demographic data, tissue, and peripheral blood for a case–control study of prostate cancer at seven sites in four countries in Africa to identify genetic markers for prostate cancer in men of African descent. All Black African men over the age of 30 years were eligible for recruitment through oncology, general medicine, or specialty clinics. Cases were excluded if they had been diagnosed with prostate cancer >6 months prior to study ascertainment. Both cases and controls who had a previous diagnosis of a cancer of any other primary were excluded. In 2017, we initiated an additional study focusing on MGUS among participants at one of the MADCaP sites, the Chris Hani Baragwanath Academic Hospital (CHBAH), University of Witwatersrand, Faculty of Health Sciences in Soweto, Johannesburg, South Africa.

Soweto, located on the southwestern edge of Johannesburg, is South Africa's largest predominantly Black urban community; although apartheid ended in 1994, Soweto's population of 1.3 million remains 98.5% Black (23). CHBAH is a public tertiary/quaternary health care facility serving the health care needs of Soweto. It is the largest hospital in Africa and the third largest in the world (24).

At CHBAH, MADCaP cases and controls provided written informed consent to additional analyses of their serum for identification of MGUS. Each consenting participant provided 20 mL of serum for analysis by the National Health Laboratory Services (NHLS) in Johannesburg, South Africa.

The study's primary outcome was diagnosis of MGUS, which was identified by serum protein electrophoresis (SPEP), free light chain (FLC) quantification (Freelite, Binding Site), and serum immunoglobulin levels. In specimens with normal SPEPs and FLC ratios <0.26 or >1.65, serum creatinine levels were obtained. Among MGUS-positive specimens, we further determined the isotype (IgG vs. IgA vs. IgM), light-chain subtype (kappa vs. lambda), and risk stratification score (described further below). Subanalysis of prevalence was calculated for those older than 50 years and then age adjusted to the 2000 U.S. Standard Population for comparison with the Olmsted County studies.

Our criteria for determining the presence of MGUS were those used in the Olmsted County studies: (i) monoclonal protein on electrophoresis, regardless of FLC ratio (heavy-chain disease), or (ii) abnormal FLC-ratio plus elevation in the involved FLC, despite normal protein electrophoresis (light-chain disease; refs. 4, 5). Notably, the original case definition did not differentiate between MGUS and multiple myeloma with end-organ damage or biomarkers of malignancy, which was maintained here for reliable comparison. Renal function dictated the delineation for normal values of the FLC ratio given the kidney's effect on kappa clearance: with adequate renal function (creatinine 64–104 μmol/L, per NHLS reference range for males), a FLC ratio <0.26 or >1.65 was considered abnormal, whereas with renal insufficiency (creatinine >104 μmol/L), a FLC ratio <0.37 or >3.1 was considered abnormal (25); to avoid overdiagnosis, if renal function was unknown, then we considered a FLC ratio <0.26 or >3.1 to be abnormal.

Because immunofixation (IFE) was not available, we classified case isotypes and light-chain subtypes based on peripheral blood immunoglobulin levels and FLC levels, respectively. If peripheral blood analysis did not favor one particular immunoglobulin or FLC over the others (i.e., all levels were within normal limits or elevated to the same extent), then the subtype was considered to be unknown. We considered the following three factors in risk stratification for progression to malignancy: M-protein >1.5 g/dL by SPEP, abnormal FLC ratio as defined above, and non-IgG heavy-chain paraprotein based on peripheral blood immunoglobulins (26); very low risk, low risk, intermediate risk, and high risk was defined by the presence of 0, 1, 2, or 3 factors, respectively (26).

We also explored the associations between MGUS and demographic, clinical, and behavioral factors based on data collected for the MADCaP study. Demographic information included age and country of origin. Clinical information included prostate cancer status, HIV status (measured by ELISA), body mass index (BMI), cardiac disease (self-reported), hypertension (measured by blood pressure), diabetes (measured by fasting glucose), and hyperlipidemia (measured by triglycerides). Behavioral information included self-reported cigarette smoking and alcohol consumption. Descriptive statistics were summarized as frequencies (percentages) for the categorial variables and median (interquartile range, IQR) for age. We investigated the associations of the aforementioned factors with MGUS by conducting both univariable and multivariable logistic regressions. All variables with a $P$ value <0.15 in the univariable analysis were included in the multivariable and/or adjusted model. Of note, few subjects had unknown HIV status due to either: patient declining testing, physician not requesting the test, or blood samples insufficient for analysis; for HIV status, models included complete data only. All statistical analyses were performed in R (v. 4.1.0) using a two-sided type I error of 0.05.

The research was approved by the Institutional Review Board at Columbia University Irving Medical Center, New York, NY and the Human Research Ethics Committee at University of the Witwatersrand, Johannesburg, Gauteng, South Africa.

### Data availability

The data generated in this study are available upon request from the corresponding author.

## Results

Between 2017 and 2019, 433 MADCaP participants were recruited at CHBAH to participate in the MGUS study; 40 (9.2%) were excluded because of incomplete data on SPEP and/or FLC, and 7 (1.6%) were excluded because we could not distinguish light-chain MGUS from kidney impairment (due to unknown renal function and FLC ratios between 1.65 and 3.1). Of the remaining 386 participants, 31 (8.03%)

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**Table 1.** Prevalence of MGUS by age among a cohort of Black South African men.

| Age | Prevalence Number of cases/total number (%) |
|---|---|
| 35–39 years | 0/10 (0) |
| 40–44 years | 2/16 (13) |
| 45–49 years | 1/26 (4) |
| 50–54 years | 1/26 (4) |
| 55–59 years | 10/65 (15) |
| 60–64 years | 4/81 (5) |
| 65–69 years | 3/71 (4) |
| 70–74 years | 8/62 (13) |
| 75–79 years | 1/19 (5) |
| 80–84 years | 0/7 (0) |
| 85+ years | 0/2 (0) |
| Unknown | 1/1 (100) |
| Total | 31/386 (8.03)[a] |

[a]Age-adjusted prevalence for the subgroup of men ages 50 years and older is 6.79% when standardized to the 2000 U.S. Population.

met criteria for MGUS. In the subgroup of men ages 50 years and older, MGUS prevalence was found to be 8.11% [95% confidence interval (CI), 5.63–11.54] (**Table 1**); age-adjusted prevalence among those ages 50 years and older was 6.79% when standardized to the 2000 U.S. Population.

A summary of the demographic, clinical, and behavioral characteristics of the study participants by MGUS status can be found in **Table 2**. The vast majority of participants were South African (95%), with the rest from other African countries. Because of the case–control design of the parent MADCaP study, 51% of participants had prostate cancer. Of those with known HIV status, 14% were HIV infected; 86.5% of those with HIV were on antiretroviral therapy (ART). The median age of those with HIV was 63.5 years (IQR: 36–84). Overall, 59.6% of participants had ever smoked cigarettes and 71.8% had ever used alcohol.

The median age of those with MGUS was 60 years (range, 40–75), while that of those without MGUS was 63 years (range, 35–87); age was not associated with MGUS status [univariable OR (95% CI): 1.00 (0.96–1.04), $P = 0.882$].

MGUS was found in 8 of 54 (14.8%) participants with HIV and 22 of 324 (6.8%) participants without HIV [univariable OR (95% CI): 2.39 (0.95–5.49), $P = 0.049$; multivariable OR (95% CI): 1.97 (0.75–4.74), $P = 0.146$]. Among participants who were HIV infected, MGUS status was not associated with receipt of ART [univariable OR (95% CI) = 0.92 (0.12–19.01), $P = 0.95$]. The median age of those with MGUS and HIV was 59.5 years (range, 55–70); the median age of those with MGUS but without HIV was 60 years (range, 40–75).

Eighteen of 115 (15.7%) active cigarette smokers but 5 of 156 (3.2%) never smokers had MGUS [univariable OR (95% CI): 5.60 (2.16–17.42), $P = 0.001$]; the association remained statistically significant with adjustment for HIV status and body mass index [multivariable OR (95% CI): 4.49 (1.63–14.56), $P = 0.006$].

Pertinent to the data source, 19 participants with MGUS (61.3%) compared with only 177 without MGUS (49.9%) had prostate cancer, but the difference was not statistically significant [univariable OR (95% CI): 1.59 (0.76–3.47), $P = 0.23$].

**Table 3** presents the distribution of MGUS subtypes in our sample. Twelve subjects (39%) had light-chain disease; of those identified with light-chain disease, 2 had unknown renal sufficiency but FLC ratios <0.26 or >3.1. Among the 19 with heavy-chain disease, 9 had IgG and 4 had IgA isotype; no one had the IgM isotype. Of all MGUS cases, kappa made up 77% of known light-chain involvement ($n = 17$). Most of those with MGUS were considered to have low risk for progression to a malignant plasma cell dyscrasia (78% of those in whom risk stratification could be determined, $n = 21$). Six of those with heavy-chain disease had an M-spike >3 mg/mL, and no MGUS case had a FLC ratio >100.

## Discussion

In our cohort of Black African men, the prevalence of MGUS, including both light- and heavy-chain disease, was 8.03% (95% CI, 5.32–10.74). MGUS prevalence among those older than 50 years was 8.11% (95% CI, 5.63–11.54); it decreased to 6.79% when standardized for age against the 2000 U.S. Population. By all such estimates, MGUS was found at higher rates in our cohort than the White Olmsted County male population ages 50 years and older, wherein age-adjusted prevalence was 5.1% (5). The age-adjusted incidence of multiple myeloma is twice as high among African Americans as among White Americans (1). This pattern suggests that the racial disparities of multiple myeloma originate in the development of MGUS. The true racial difference in MGUS prevalence between the Olmsted County population and ours may be even greater because our inclusion criteria took into account the renal reference range for patients with known kidney impairment, and we excluded those individuals in whom kidney disease could not be differentiated from light-chain MGUS; the Olmsted County study did not take renal insufficiency into account and therefore may have overdiagnosed patients with light-chain disease who did not, by our criteria, have MGUS.

Among those with MGUS, monoclonal protein presence and concentration have been shown to differ between races. Weiss and colleagues (27) found that the median M-protein concentration was 0.44 in Black patients and 1.2 in White patients ($P < 0.0005$). Landgren and colleagues (16) found M-protein concentration to be undetectable in 76% of Ghanaian men with MGUS compared with 12% of Olmsted County men with MGUS. We also found a larger proportion of our MGUS patients to have light-chain disease (39%) compared with the Olmsted County patients (20%; ref. 5).

Weiss and colleagues (27) had previously found high-risk MGUS to be less common in Black than in White patients ($P = 0.014$). In our sample, 77% of all MGUS cases had very low or low risk disease. However, Landgren and colleagues (1) found that Black and White American veterans with MGUS were similar in rate of progression to malignancy. Further exploration of the risk criteria within Black populations is needed.

Similar to the Ghanaian cohort of Black men (16), but unlike the Olmsted County cohort of White individuals (1, 5), our study found no association of MGUS with increasing age. The 917 participants in the Ghanaian study were ages 50 to 74 years; the lack of an association may have been due to the narrowness of that age range, but in the subgroup of 7,996 Olmsted County study participants in the same age range, the association was evident. Our sample differed from both prior studies because MADCaP recruited all eligible prostate cancer cases and controls over 30 years of age; however, our sample size was not powered to assess the association between prevalence and age.

Consistent with previously published literature (21, 28), we found MGUS to be associated with HIV status, but only in the univariable analysis. In multivariable logistic models controlling for BMI and cigarette use, the association was not statically significant.

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**Table 2.** ORs for MGUS in relation to demographics, clinical, and behavioral factors in a cohort of Black South African men recruited between 2017 and 2019.

| | MGUS+N (%) | MGUS-N (%) | Univariable OR (95% CI) | *P* | Overall *P* | Multivariable[a] OR (95% CI) | *P* | Overall *P* |
|---|---|---|---|---|---|---|---|---|
| Total | 31 (8.0) | 355 (92.0) | | | | | | |
| Median age (Q1, Q3) | 60.0 (57.3, 70.8) | 63.0 (57.0, 69.0) | 1.00 (0.96–1.04) | 0.88 | 0.88 | — | | |
| Country of origin | | | | | | | | |
| South Africa | 30 (96.8) | 336 (94.6) | | | | | | |
| Other[b] | 1 (3.2) | 19 (5.4) | | | | | | |
| Prostate cancer | | | | | | | | |
| Yes | 19 (61.3) | 177 (49.9) | 1.59 (0.76–3.47) | 0.23 | 0.22 | — | | |
| No | 12 (38.7) | 178 (50.1) | Ref | | | — | | |
| HIV status | | | | | | | | |
| Infected | 8 (26.6) | 46 (13.2) | 2.39 (0.95–5.49) | 0.05 | 0.04[a] | 1.97 (0.75–4.74) | 0.15 | 0.15 |
| Noninfected | 22 (73.3) | 302 (86.8) | Ref | | | Ref | | |
| Unknown | 1 | 7 | | | | | | |
| Mean BMI (SD) | 24.87 (5.15) | 27.04 (5.62) | 0.92 (0.85–0.99) | 0.04 | 0.04[a] | 0.97 (0.89–1.05) | 0.44 | 0.44 |
| Diabetes | | | | | | | | |
| Yes | 12 (38.7) | 149 (42.0) | 0.87 (0.40–1.83) | 0.72 | 0.72 | — | | |
| No | 19 (61.3) | 206 (58.0) | Ref | | | — | | |
| Hypertension | | | | | | | | |
| Yes | 19 (61.3) | 225 (63.4) | 0.91 (0.44–1.99) | 0.82 | 0.82 | — | | |
| No | 12 (38.7) | 130 (36.6) | Ref | | | — | | |
| Hypertriglyceridemia | | | | | | | | |
| Yes | 10 (32.3) | 127 (35.8) | 0.85 (0.38–1.83) | 0.70 | 0.70 | — | | |
| No | 21 (67.7) | 228 (64.2) | Ref | | | — | | |
| Cardiac disease | | | | | | | | |
| Yes | 1 (0.03) | 5 (0.01) | 2.33 (0.12–15.05) | 0.45 | 0.45 | — | | |
| No | 30 (96.8) | 349 (98.6) | Ref | | | — | | |
| Cigarette use | | | | | | | | |
| Active | 18 (58.1) | 97 (27.3) | 5.60 (2.16–17.42) | <0.01 | <0.01[a] | 4.49 (1.63–14.56) | 0.01 | 0.01 |
| Former | 8 (25.8) | 107 (30.1) | 2.26 [0.73, 7.65] | 0.16 | | 2.16 (0.69–7.37) | 0.19 | |
| Never | 5 (16.1) | 151 (42.5) | Ref | | | Ref | | |
| Alcohol use | | | | | | | | |
| Active | 15 (48.4) | 167 (47.0) | 1.31 (0.53–3.53) | 0.57 | 0.72 | — | | |
| Former | 9 (29.0) | 86 (24.2) | 1.52 (0.55–4.43) | 0.42 | | — | | |
| Never | 7 (22.6) | 102 (28.7) | Ref | | | — | | |

Abbreviations: ART, antiretroviral therapy; CI, confidence interval; OR, odds ratio; Q, quartile; SD, standard deviation.

[a]Covariates with $P < 0.15$ in univariable analysis were included in the multivariable model.

[b]The 20 non-South African countries consisted of: Mozambique ($n = 9$), Lesotho ($n = 2$), Botswana ($n = 2$), Zimbabwe ($n = 2$), Malawi ($n = 1$), Eswatini ($n = 1$), Democratic Republic of Congo ($n = 1$), and Zambia ($n = 1$); one participant did not list a country of origin.

Like others (20), we found that receipt of ART among HIV-infected subjects was not associated with MGUS, but Amara and colleagues (22) has demonstrated that initiation of ART has been found to cause a decrease in M-protein concentration. As discussed above, M-protein concentration may have prognostic value, and thus, treatment of HIV-infected patients with ART may affect progression to malignancy. Preclinical models have demonstrated HIV protease inhibitors to cause antimyeloma cell line effects (29), and HIV-noninfected patients with MGUS have been found to be 2.7 times more likely to develop a hematologic malignancy than HIV-infected patients with MGUS (21). However, the decreased progression from MGUS to malignancy in HIV-infected individuals could also be a result of current MGUS diagnostic criteria inaccurately detecting monotypic gammopathies, rather than monoclonal gammopathies, related to chronic B-cell activation in the setting of viral infection. For example, a *post hoc* analysis of FLC quantification stratified by HIV status demonstrated a statistically significant difference in FLC ratios between MGUS cases and controls, but only for the HIV-noninfected subgroup; among those that were HIV infected, MGUS cases and controls did not differ in FLC ratios (**Fig. 1**). The findings of this *post hoc* analysis should be interpreted with caution, though, as neither subgroup was powered to analyze FLC quantification, and there were far fewer subjects within the HIV-infected subgroup for statistical power. Further research into the validity of the current MGUS diagnostic criteria and the effect of ART on the natural course of MGUS is needed in patients who are HIV infected.

Prior findings regarding the association between MGUS and smoking have been mixed; some studies (30–32), but not all (33, 34), have reported a correlation. We found MGUS to be 5.6-fold more common in those who actively smoked cigarettes compared with those who had never smoked in the univariable analysis ($P = 0.001$) and 4.5-fold more common in a model that also included BMI and HIV status ($P = 0.006$).

The prospective design of our study, in which we recruited consecutive patients enrolling in the MADCaP study for reasons unrelated to plasma cell dyscrasias, minimized the risks of selection bias and recall bias. In addition, we found enough MGUS cases to characterize them by isotypes, light-chain subtypes, and risk for multiple myeloma, as well as to compare them with non-MGUS controls with respect to a number of clinical and behavioral

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**Table 3.** Distribution of MGUS characteristics in a cohort of Black South African men recruited between 2017 and 2019.

| | *n* (%) |
|---|---|
| Isotype | |
| IgG | 9 (29) |
| IgA | 6 (19) |
| IgM | 0 (0) |
| Heavy-chain, unknown subtype[a] | 4 (13) |
| Light chain | 12 (39) |
| Light-chain subtype | |
| Kappa | 17 (55) |
| Lambda | 5 (16) |
| Unknown[a] | 9 (29) |
| Risk stratification[b] | |
| Very low (0/3) | 0 (0) |
| Low (1/3) | 21 (68) |
| Intermediate (2/3) | 4 (13) |
| High (3/3) | 2 (7) |
| Unknown[a] | 4 (13) |

[a]If peripheral blood analysis did not favor one particular immunoglobulin or FLC over the others (i.e., all levels were within normal limits or elevated to the same extent), then the subtype was considered to be unknown.
[b]Risk stratification was based on counting the following risk factors in each specimen: M-protein >1.5 g/dL, abnormal FLC ratio, non-IgG heavy chain paraprotein.

variables. The associations we observed here call for examination in larger studies powered to confirm the associations and to allow us to probe them further.

Among the limitations to our study, our cohort was drawn from the MADCaP database, in which 100% were male. MGUS is more prevalent among White men than among White women (4, 5), but studies among Black African cohorts, including our study, have only included males; studies of MGUS among Black African women are needed. In addition, 100% of the database was Black, and we therefore relied on the Olmsted County data for comparisons. Notably, we defined MGUS cases by the same criteria as these studies to maximize reliability, but the case definition did not differentiate between MGUS and multiple myeloma with evidence of end-organ damage or biomarkers of malignancy; six of the heavy-chain cases identified in our cohort had M-spike >3.0 mg/mL, implying smoldering or overt multiple myeloma rather than simple MGUS. Studies involving a contemporaneous White cohort might be more informative, as differences in the sample sets or laboratory measurements may have confounded findings, and a contemporaneous design would allow for evidence of end-organ damage and biomarkers of malignancy to be attained.

Furthermore, MGUS subtypes were assumed based upon peripheral immunoglobulin and FLC levels rather than IFE. Although clearly abnormal serum levels likely represent the monoclonal protein, the International Myeloma Working Group recommends confirmatory IFE to further characterize the subtypes given IFE's high specificity. Reflex IFE should therefore be incorporated into future studies.

Importantly, our study was exploratory, and the sample sizes of the subgroups were not adequately powered to detect differences statistically significant differences.

Building on the findings we have presented above, a larger study powered to further investigate the relationships between MGUS and HIV and between MGUS and cigarette smoking in a Black African population inclusive of both genders is currently underway. Future studies designed and powered to evaluate genetics and matched environmental contributions may elucidate racial disparities and facilitate the development of targeted preventive and treatment strategies to keep MGUS from progressing to a plasma cell malignancy.

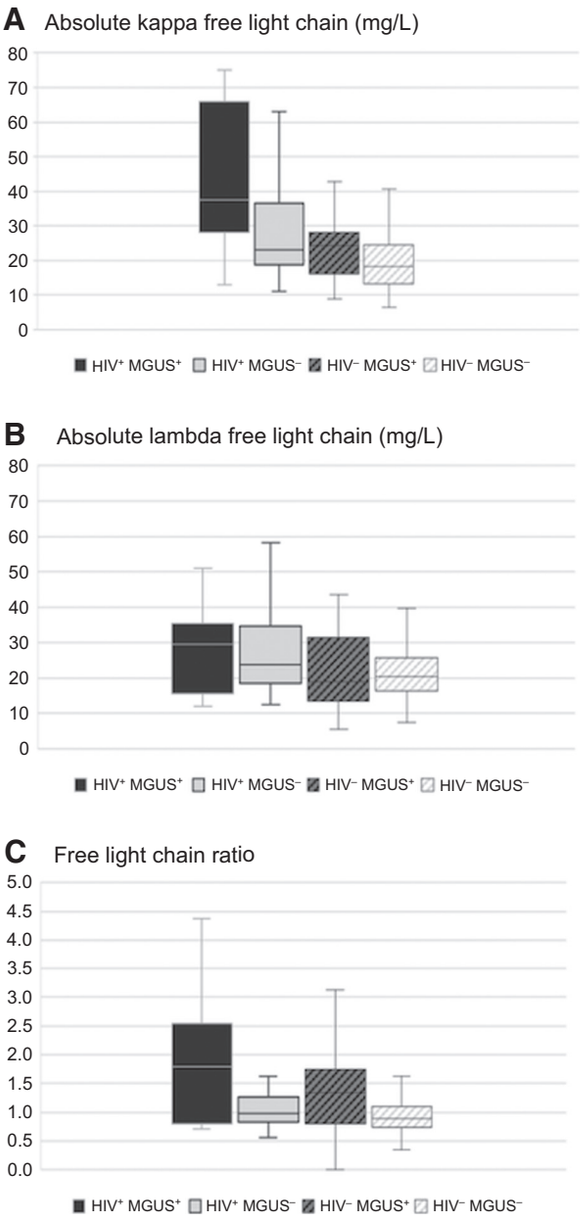


**Figure 1.**
FLC levels among MGUS cases and controls, stratified by HIV status **A**. Absolute kappa FLC levels significantly differed between MGUS cases versus controls in the HIV-noninfected subgroup (median 24.50 vs. 18.00, $P = 0.02$), but not in the HIV-infected subgroup (median 37.50 vs. 23.00, $P = 0.07$). **B,** Absolute lambda FLC levels did not significantly differ between MGUS cases versus controls in the HIV-infected subgroup (median 29.25 vs. 23.90, $P = 0.98$) or HIV-noninfected subgroup (median 19.10 vs. 20.35, $P = 0.81$). **C,** FLC ratios significantly differed between MGUS cases versus controls in the HIV-noninfected subgroup (median 1.34 vs. 0.73, $P = 0.01$), but not in the HIV-infected subgroup (median 1.78 vs. 0.98, $P = 0.15$).

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