We examined four clinically assessed cytogenetic subtypes (t(11;14), t(4;14), monosomy 13/del13q and monosomy 17/del17p) in 292 black patients with newly diagnosed multiple myeloma (MM) from four medical centers, who had fluorescent in situ hybridization testing results available in their medical records. We then compared the prevalence of these abnormalities with a previously characterized Mayo Clinic cohort of 471 patients with MM. We found a significant difference in the prevalence of the t(11;14) immunoglobulin heavy chain (IgH) translocation between blacks and whites, 6.5% versus 17.6%, respectively, \(P < 0.0001\). Blacks also had lower rates of the t(4;14) IgH translocation, (5.5% versus 10%); monosomy 13/del13q (29.1 versus 49.3%); and monosomy 17/del17p (7.9% versus 13%). Consequently, 63.4% of blacks versus 34.6% of whites did not have any of the four abnormalities that we studied, \(P < 0.001\). As almost all MM is associated with either an IgH translocation or trisomies, we hypothesize that MM in blacks is associated with either excess prevalence of either the trisomic (hyperdiploid) form of MM or an IgH translocation besides t(11;14) or t (4;14). We conclude that there are significant differences in the cytogenetic subtypes of MM that occur in blacks and whites.

**MATERIALS AND METHODS**

Participating institutions

Collaborations were established between Mayo Clinic (Rochester, MN, USA) and three major institutions with large African American clinical practices: University of Maryland at Baltimore, MD, USA; Cook County Hospital, Chicago, IL, USA; and Rush University Medical Center, Chicago IL, USA. Data were abstracted by AJG from the records of 292 eligible black patients across the four participating institutions. Institutional Review Board’s approval was obtained from all sites.

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RESULTS

Of the patients eligible, data were available and collected on 292 African American MM patients from the four participating institutions and the comparison group of 471 white patients from Mayo Clinic (Table 1). Median age at diagnosis was significantly younger in blacks (59 years) compared with whites (63 years; \( P < 0.0001 \)). A significant difference was found in the distribution of gender between the two patient groups (44.5% male in blacks, 60.1% male in whites; \( P < 0.0001 \)).

When examining the overall distribution across the four different cytogenetic subtypes, we found evidence of a significant difference by race (Table 1, \( P < 0.0001 \)). Further analysis of the individual cytogenetic abnormalities demonstrated lower frequencies of each of the four abnormalities in blacks compared with whites (Table 1). There was a lower prevalence of the t(11;14) translocation by race in blacks compared with whites, 6.5% in blacks versus 17.6% in whites, \( P < 0.0001 \). A difference was also observed in the prevalence of monosomy 13/del13q by race, 29.1% versus 47.3%, respectively, \( P < 0.0001 \). Blacks also had lower rates of t(4;14) and monosomy 17/del17p compared with whites (Table 1). Also, 63.4% of blacks had none of the four abnormalities studied compared with 34.6% of whites, \( P < 0.0001 \).

Patients were then stratified by age into < 60 years or \( \geq 60 \) years (Table 2). Within each age group, blacks showed lower frequencies of the four abnormalities than whites. Conversely, whites in both age groups had lower frequencies of ‘potential other’ abnormalities (Table 2, \( P < 0.0001 \)). Black patients who were aged \( \geq 60 \) years had the lowest frequency of del17p (5.7%) compared with other age groups in both races.

DISCUSSION

In the present study, we conducted a multicenter study to assess the frequency of four cytogenetic abnormalities routinely tested for with FISH probes in black patients with MM. We then compared these results with 471 white patients with MM seen at the Mayo Clinic in Rochester, MN, USA who were part of a well-defined cohort of MM that we have previously studied.2,12

Although MM is clinically considered as a unique disease, it is likely a collection of several cytogenetically unique malignancies that are considered together as one entity solely, because they arise from plasma cells and have roughly similar clinical features.15 As the racial disparity in the incidence of MM is marked (relative risk of 2.2 in blacks), it is unlikely that the increase in risk is shared by all cytogenetic subtypes of the disease. Our hypothesis is that the racial predisposition in MM is driven largely by an excess risk of one or more specific cytogenetic subtypes of MM.

In this study, we found that the frequency of the t(11;14) translocation is significantly lower in blacks compared with whites, and this difference was similar across age. We also found a lower rate of the t(4;14) translocation. Our findings are similar in this regard to that reported by Fonseca and colleagues.14 In our study, 63.4% of blacks versus 34.6% of whites did not have any of the four abnormalities that we studied, \( P < 0.001 \). As almost all MM is associated with either an IgH translocation or trisomies (or both together), we hypothesize that MM in blacks is associated with either excess prevalence of either the trisomic (hyperdiploid) form of MM or an IgH translocation besides t(11;14) or t(4;14). Based on earlier studies by Fonseca and colleagues showing lower rate of IgH translocations in blacks,14 we hypothesize that most of the disparity is due to a higher prevalence of trisomic form of MM in blacks. This form of MM has a better prognosis12 and has a better outcome with lenalidomide therapy. Thus one would expect that blacks with MM, especially those treated with lenalidomide, will have a better outcome.15 In fact, in a recent ECOG randomized trial that utilized lenalidomide in both arms, although response rates were similar, overall survival was significantly superior in non-whites (almost all blacks) compared with whites, supporting this hypothesis.17 However, additional studies with information on
trisomies and treatment will be important to confirm this hypothesis.

In addition, we found lower rates of monosomy 13/del13q and monosomy 17/del17p in blacks. Monosomy 17p/del17p has been associated with shorter survival in MM, and the disparity in prevalence of this cytogenetic abnormality may provide an additional explanation for the difference in survival seen between black and white MM patients. The effect of monosomy 13/del13q detected on FISH is of uncertain prognostic significance.

This is one of the largest studies comparing the prevalence of cytogenetic abnormalities in blacks versus whites with MM. It also draws strengths from being multi-centered and having a well-defined control group. However, as with any medical record-based investigation, there are limitations. First, as institutions and clinical laboratories use different probe-sets, we were limited in which cytogenetic abnormalities we could examine with common probe panel so as to be able to determine the exact prevalence of additional translocations and trisomies across racial groups. These will be of greater importance as the treatment options available for the disease increase, and it is likely that there will be variations in response to therapy based on the underlying cytogenetic subtype and race.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS
SVR and AJG conceived, designed the study, conducted all analyses and wrote the manuscript, with input from all authors; AJG abstracted all data; SVR, SK, RAK, RK, SP, AP, SV, AB and RC contributed data and identified patients for study from the participating institutions. All authors reviewed and approved the paper.

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